Non-interventional PASS Study Report

Title	**Evaluation of the Effectiveness of Risk Minimisation Measures: A Survey among Health Care Professionals to Assess their Knowledge and Attitudes on Prescribing Conditions of Instanyl® in France and the Netherlands** **Study Number: Instanyl-5001**
Study report Version identifier	Version 1
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EU PAS Register number	ENCePP/SDPP/9924
Active substance	Fentanyl (ATC code: N02AB03)
Medicinal product	Fentanyl intranasal spray (Instanyl®)
Product reference	EU/1/09/531/001-021
Procedure number	EMEA/H/C/000959
Marketing authorization holder (MAH) or sponsor company	Takeda Pharma A/S Denmark
Joint PASS	No
Research question and objectives	Research question: Was the updated educational materials effective in: - Increasing the knowledge of physicians about safe use of Instanyl®, - Influencing their attitude when prescribing Instanyl®. Objective: To measure the proportion of targeted physicians who received, understood and followed the safety information about Instanyl® provided in the educational materials.
Countries of study	France and the Netherlands
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1. Abstract

Title

Evaluation of the Effectiveness of Risk Minimisation Measures: A Survey among Health Care Professionals to Assess their Knowledge and Attitudes on Prescribing Conditions of Instanyl® in France and the Netherlands

Version n°1: 30 April 2016

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Rationale and background

Instanyl® (intranasal fentanyl) is an opioid analgesic indicated for the management of breakthrough pain in adults already receiving maintenance opioid therapy for chronic cancer pain, approved throughout the European Union since July 2009. As part of a risk minimization activity, educational materials were distributed to healthcare professionals in European countries where the drug is marketed.

The educational materials were updated in late 2013 aimed at reiterating safe use and minimizing off label use of Instanyl®. This focused on Instanyl® not being used for the treatment of acute pain other than breakthrough pain, should only be used in patients regularly receiving an opioid treatment, and reiterating the risk of off-label use.

This post-authorization safety study (PASS) was designed to evaluate the process and outcome indicators to ensure that physicians received the updated educational materials, understood it and followed it when prescribing Instanyl®.

Research question and objectives

Research question:

Were the updated educational materials effective in:

- Increasing the knowledge of physicians about safe use of Instanyl®
- Influencing their attitude when prescribing Instanyl®.

Objective:
To measure the proportion of targeted physicians who received, understood and followed the safety information about Instanyl®.

Study design

An anonymous, cross sectional and non-interventional survey of a sample of physicians in France and the Netherlands who were likely to prescribe Instanyl®.

Population

Inclusion criteria:

- Physicians prescribers, or potential prescribers, of Instanyl®,
- Specialists of any of those targeted for the educational materials:
  - Oncologists,
  - Anaesthesiologists,
  - Radiologists,
  - Hospital-based General practitioners (GPs).

Exclusion criteria:

- Physicians who did not treat patients or who may have had a conflict of interest (i.e. physicians employed by regulatory bodies, pharmaceutical industries),
- Physicians who did not know Instanyl®.

Variables

The collected information included: demographics, type of practice, awareness and knowledge about safe use of Instanyl®, and the physician's consideration of the safety warnings. The proportion of appropriate answers about safe use of Instanyl® given by the physicians was assessed overall, by country and among subgroups of specialties.

Data sources

The survey was a primary data collection study conducted through a web questionnaire.

Study size

The sample size calculation was based on the survey objective, *i.e*. to evaluate the prescribers and potential prescriber awareness and knowledge about safe use of Instanyl® as per the educational materials. A conservative approach was applied and assumed a proportion of 50% of physicians knowledgeable about the safe use of Instanyl®. For a confidence interval of 95% and a precision of 6%, a total of 267 analysable web questionnaires were needed for the overall sample, 178 in France and 89 in the Netherlands.

Data analysis

Results were presented, overall, and at country level and per specialty. Continuous variables were described by the number of valid cases and missing data, mean, standard deviation, median, Q1, Q3, minimum, and maximum. No missing data was replaced. Categorical variables were described as the total number and relative percentage per category. Confidence intervals of 95% were calculated when relevant. Calculations were first performed on raw data per specialty and per country, and then weighted according to the real proportion of targeted physicians in each country to accurately reflect the population the survey seeks to measure.

Results

310 physicians agreed to participate in the study among the 6,565 that were invited (4.7%). Overall, 96.8% of participating physicians correctly identified that episodes of breakthrough cancer pain in patients already receiving an opioid medication for chronic background pain as the approved indication, and among GPs this rose to 99.2%. The daily dose (72.5%), the interval between treatments (60%), the maximum number of puffs (86.4%) reported by the physicians was equal to the recommended maximum or more conservative.

Physicians had also a high level of knowledge of the prescribing conditions of Instanyl®, and knew not to use it in patients: with recurrent epistaxis (97.2%), with severe respiratory depression or severe obstructive lung disease (91.9%), with previous facial radiotherapy (89.9%), or in patients without current maintenance opioid therapy (85.8%). Moreover, 91.0% of physicians avoided the use in patients at potential risk of substance abuse or dependence. The leading reasons when physicians did not prescribe Instanyl® for a patient where that other formulations and alternative treatments were preferred for those patients, and often that the nasal route was not accepted or understood by the patient.

15.9% of physicians reported using Instanyl® in patients without cancer pain, and there were mostly for a range of other forms of chronic pain. This was particularly prevalent among anesthesiologists, 24.7% of whom reported using in patients without cancer pain. Moreover, 14.7% of physicians also reported having used Instanyl® in patients without maintenance opioid therapy for its quick action, nasal route and ease of use.

The survey was conducted 6-12 months after the distribution of the updated educational materials in each country, and relatively few physicians (20.3%) recalled having received the materials, Physicians responded that they use a wide source of information sources to gain knowledge on medical products including presentation by the medical / pharmaceutical representatives, national health authority website, congress/symposia, and national drug dictionaries.

Limitations

The voluntary participation of physicians in a web survey is an inherent limitation and a potential source of bias. Even with actions were taken to increase the response rate and every effort was undertaken to reach the target per specialty and per country, it was particularly difficult to recruit radiologists in France, probably because they do not prescribe Instanyl® frequently and were less concerned/interested in the topic of the survey.

The overall response rate was 55.4% in France and 71.4% in the Netherlands. 6565 physicians were invited to participate by email for 310 respondents with a complete analysable questionnaire, i.e. 20 times more the target number. Web survey are restricted to physicians who had an active email address, and able and willing to answer web questionnaires, and might not have been fully representative of the whole targeted physician population. Web surveys may also promote social desirability bias, i.e. tendency to give socially desirable/expected responses instead of choosing those reflecting their current knowledge or prescribing behaviour.

Some answers to some open-ended questions were heterogeneous and sometimes irrelevant, suggesting that some physicians did not understand the question, did not know how to answer it, or answered something in order not leave to the space blank, for social desirability.

Interpretation

Given the low proportion of physicians who recalled receiving the educational materials, the physician knowledge on the indication and safe use of Instanyl® was very high. The physicians knew the approved indication, and were well aware of safety considerations when prescribing and using Instanyl.

This survey found participating physicians in France and the Netherlands were knowledgeable of the approved indication and of the safe use of Instanyl®. Some physicians reported they used Instanyl® in patients without cancer, and in patients without background opioid maintenance therapy, even though they were fully knowledgeable of the approved indication and safe use of the product. It thus seems physicians weigh up benefits versus and risks in deciding in which patients to use Instanyl®.

The low recall of receiving the educational materials could reflect physicians receiving a large amount of medical and promotional materials from pharmaceutical companies. Some physicians may have discarded before reading or may not have remembered receiving or reading the educational material, or may not have recognised the nature of the material. This highlights the importance of using multiple communications channels (SmPC, information presented by the medical/pharmaceutical representatives, national health authority website, congress/symposia, drug dictionary) to adequately spread the safety information with physicians.

Generalisability

The study design included an over-sampling of oncologists, anaesthesiologists and radiologists in the Netherlands, and an under-sampling of GPs in France. All results were weighted to reflect the sampling proportions.

The weighted results can be generalised to the population of GPs and oncologists managing or likely to manage adult cancer patients presenting with breakthrough pain in these countries. The low proportion of anesthesiologists and radiologists present in the sample, and their low frequency of prescription of Instanyl® might not reflect the general behaviour. The two countries surveyed

represent both a large and a small population of physicians with different healthcare system nuances, but the results from this survey might not be generalisable to other countries.

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Conclusion

This survey found strong knowledge about the product indication and its safe use, even though only a minority of physicians recalled having received the educational materials. This highlights the importance of including all possible communications measures (SmPC, information presented by the Medical / Pharmaceutical representatives, National Health Authority website, congress/symposia, drug dictionary) to adequately provide safety information knowing that physician have multiple channels of information and knowledge gathering.

Milestones

- Start of data collection - Fieldwork: Mid-April 2015
- End of data collection - Fieldwork: Mid-October 2015
- Submission of study report to EMA: 30 April 2016.

2. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
AE	Adverse event
AR	Adverse reaction
ASOCS	Association of Opinion and Behaviour in health field research companies
CI	Confidence interval
EMA	European Medicines Agency
EphMRA	European Pharmaceutical Marketing Research Association
GVP	Good pharmacovigilance practices
GP	General practitioner
HCP	Health care professional
PASS	Post-authorization safety study
PIL	Patient information leaflet
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic safety update report
RMM	Risk minimization measures
RMP	Risk minimization plan
SAE	Serious adverse event
SAP	Statistical analysis plan
SAR	Serious adverse reaction
SD	Standard Deviation
SOP	Standard operating procedures
SPC	Summary of product characteristics
STROBE	Strengthening the reporting of observational studies in epidemiology

3. INVESTIGATORS

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4. MILESTONES

- Start of data collection: Mid-April 2015
- End of data collection: Mid-October 2015
- Submission of study report to EMA: 30 April 2016

5. RATIONALE AND BACKGROUND

Instanyl® (intranasal fentanyl) is an opioid analgesic indicated for the management of breakthrough pain in adults already receiving maintenance opioid therapy for chronic cancer pain (1,2,3).

- Breakthrough pain is defined as a transitory exacerbation of pain that occurs on a background of otherwise controlled persistent pain.
- Patients with maintenance opioid therapy are those who are taking daily at least: 60 mg of oral morphine, 25 micrograms of transdermal fentanyl per hour, 30 mg oxycodone, at 8 mg of oral hydromorphone, or an equianalgesic dose of another opioid for a week or longer.

The European Commission granted a marketing authorisation valid throughout the European Union for Instanyl® on 20 July 2009.

Due to the opioid nature of Instanyl®, which contains fentanyl, there is a potential risk of off-label use, abuse and misuse.

In 2013 Takeda updated the product's educational materials reinforcing that Instanyl® should not be used for the treatment of acute pain other than breakthrough pain, and only be used in patients regularly receiving an opioid treatment, and reiterating the risk of off-label use. The updated educational materials were approved by the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) in July 2013 and subsequently reviewed and approved by local regulatory agencies. The MAH sent the updated educational materials to the healthcare professionals (HCPs) during 2014 in the countries where the drug is marketed. In addition, the updated revised educational materials were posted to product websites in some countries. This additional risk minimization measure (RMM) was implemented as part of the Instanyl® risk management plan (RMP).

This post-authorization safety study (PASS) was undertaken to evaluate the process and outcome indicators to ensure that physicians who received the updated safety information had understood it and followed it when prescribing Instanyl®.

5.1 RATIONALE FOR COUNTRY SELECTION

This study was conducted in France and The Netherlands, the two countries with the highest volume of Instanyl® prescribing in the EU. All other countries have minimal prescribing by comparison and therefore were not considered appropriate for the conduct of this survey.

5.2 RATIONALE FOR THE SELECTION OF THE SPECIALTIES

Takeda distributed the updated educational materials to all physicians in the study countries who were likely to prescribe Instanyl®:

- Oncologists,
- Anesthesiologists,
- Radiologists,
- General practitioners (GPs) likely to be involved in management of cancer patients.

In France and the Netherlands, market research shows minimal prescribing of Instanyl® in the primary care setting.

6. AMENDMENTS AND UPDATES

None

7. RESEARCH QUESTION AND OBJECTIVES

7.1 RESEARCH QUESTION

Were the updated educational materials effective in:

- Increasing the knowledge of physicians about safe use of Instanyl®,
- Influencing their attitude when prescribing Instanyl®.

7.2 OBJECTIVE

The objective of the survey was to measure the proportion of targeted physicians who received, understood and followed the safety information about Instanyl® provided in the updated educational materials.

8. RESEARCH METHODS

8.1 STUDY DESIGN

This survey was cross-sectional, multinational, non-interventional study of physicians and conducted anonymously.

8.2 SETTING

The survey was conducted through a web questionnaire among prescribers, or potential prescribers, of Instanyl® in settings of two European countries (France and the Netherlands).

8.2.1 Inclusion criteria

The survey was conducted among physicians meeting the following inclusion criteria:

- Prescribers, or potential prescribers, of Instanyl®, i.e. physicians who know the drug,
- Specialists of any of those targeted for the educational materials:
    - Oncologists,
    - Anesthesiologists,
    - Radiologists,
    - GPs likely to be involved in management of cancer patients.

As noted in §8.5.2 office-based GPs were also included in the sampling frame, as it was not possible to differentiate between hospital-based and community-based GPs in the physician lists used in the survey.

8.2.2 Exclusion criteria

- Inactive and retired physicians (when evidence was available to identify them).
- Physicians who did not treat patients or who may have had conflicts of interest with the survey (i.e. physicians employed by regulatory bodies, pharmaceutical industries),
- Physicians who did not know Instanyl®.

8.3 VARIABLES

The collected information from each participating physician included demographics, type of practice and potential prescription of Instanyl®. The awareness and knowledge of the safety information included in the updated educational materials, the sources of information and the intention of the physician to consider the updated safety warnings were collected.

A copy of the survey questionnaire is attached (§14.1Appendix 1)

8.4 DATA SOURCES

The survey was a primary data collection conducted through a web questionnaire. The questionnaire was developed and tested among 5-6 physicians (2-3 per country) for its comprehensibility, consistency and the appropriateness of medical terms. Physicians' comments were implemented in the final version. The local translated versions of the questionnaire from English into French and Dutch were done using the back and forth method to ensure an accurate translation.
The web questionnaire completion was estimated to take 10 to 15 minutes.

8.5 STUDY SIZE

8.5.1 **Sampling plan**

The sampling unit was the physician. For each study country, the sample survey included physicians identified and recruited from two sources:

- Takeda's list of 816 physicians, 532 in France and 284 in the Netherlands who were provided the educational material during the targeted distribution period.
- IMS Medical Radar's reference lists of specialists (oncologists, anesthesiologists and radiologists) and GPs in France and Netherlands. This list includes physicians who may have received the education materials after the targeted distribution period, and physicians who may have obtained the materials from other sources (available on the web in some countries).

The IMS Medical Radar list included community-based and hospital based GPs, and it was not possible to differentiate between these 2 groups so both were included in the sampling. While virtually 100% of the physicians on the Takeda list had been provided the educational materials, it was not known what proportion of the relevant physicians on the IMS list had received from Takeda or downloaded from the web the updated educational materials.

As per sample size defined below and the number of selected countries and specialties, physicians were stratified only by country and specialty. Other criteria such as region, age and gender of the prescriber were less relevant than country and specialty, since they might not have been available in all countries or not been a determinant as important as country or specialty. The use of more strata would have needed a larger sample size.

A random stratified sampling method was applied. As a first step, all lists were merged, and then the eligible physicians were divided into homogeneous groups, called strata, which were mutually exclusive (a physician can only belong to one stratum). This stratification was based on the following criteria:

- Country: 2 categories (France and the Netherlands),
- Specialty: 4 categories (Oncologists, Anesthesiologists, Radiologists, GPs likely to be involved in management of cancer patients).

Thus, 2 x 4 = 8 strata were formed.

The numbers of physicians were not equal in the four specialties, GPs were much more prevalent.

An independent sample was selected per stratum through a simple random sampling without replacement. In each specific stratum, physicians were contacted according to the order of draw in this stratum. When a physician did not want to participate in the survey, the next one in order of draw was contacted, and so on until reaching the required number of physicians. The target for all strata was not achieved at the end of Takeda's list. An additional randomly sampled list has been prepared using the IMS Medical Radar reference files, and the physicians contacted until the sample goal was reached.

In fact, the expected number of anesthesiologists and radiologists was high in proportion to the few physicians available on the lists. As expected the target of anesthesiologists and radiologists was not reached, and additional GPs and oncologists were recruited to compensate and preserve the overall sample size at country level.

8.5.2 **Sample size calculation**

The sample size formula, based on the normal approximation to the binomial distribution, for calculating the number of subjects required for a proportion was the following:

$$n = \frac{P \cdot (1-P) \cdot \left(Z_{1-\alpha/2}\right)^2}{e^2},$$

Where P is the expected proportion, e is one half the desired width of the confidence interval, and $Z_{1-\alpha/2}$ is the standard normal Z value corresponding to a cumulative probability of $1 - \alpha/2$. The following table provides the margin of error for 95% confidence interval based on various sample sizes and proportions of interest (Table 8.5.2-1).

Table 8.5.2-1: Sample size obtained for various precisions and various proportions

	Margin of error for 95% CI		
Proportion	**10%**	**6%**	**5%**
10%	35	97	139
30%	81	225	323
50%	97	**267**	384
70%	81	225	323
90%	35	97	139

As the proportion of physicians provided the updated educational materials was not known and there was no evidence supporting the expected proportion, a conservative approach (from a sample size perspective) was used and it was assumed that 50% of physicians received the updated educational materials. This assumption yielded the largest sample size.

To achieve a confidence interval (CI) of 95% with a half-width of 6%, a total of 267 analysable physician questionnaires were needed for the overall sample. It was estimated that about 10-15% of physicians would not complete the questionnaire or not be analysable. Taking this into account, the overall sample size of 307 participating physicians was required to reach 267 analysable questionnaires.

The overall sample size was then proportionally split between the two countries, based on the number of physicians employed in a hospital setting in each country, which was estimated at 160,314 in France and 21,541 in the Netherlands in 2009 in the last available information on Eurostat (European Commission) (16). The sample size was proportioned 88% for France and 12% for the Netherlands, i.e. 271 participating physicians in France and 36 in the Netherlands (235 analysable physicians in France and 32 in the Netherlands respectively). However, this proportioning would have led to few participants in the Netherlands. The sample size should not be lower than a threshold of 40 statistical units in each entity to ensure the robustness of statistical estimations. To comply with this constraint, an arbitrary proportioning of 2:1 was implemented resulting in a final sample size requirement of **205** participating physicians in France and **102** in the Netherlands were required (Table 8.5.2-2).

Table 8.5.2-2: Sample size per country and overall

	France	The Netherlands	Overall
*Arbitrary allocation of the sample 2:1 between France and The Netherlands **	*66.7%*	*33.3%*	*100%*
Number of participating physicians required	205	102	307
Number of participating physicians with a complete analysable questionnaire expected	178	89	267

Within each country, the sample size was then further divided into medical specialties. Takeda's detailed information on the distribution of the updated educational material was used to estimate the proportional breakdown of required sample size into targeted specialists (Table 8.5.2-3).

Table 8.5.2-3: Physicians who received the educational material by country

	France	The Netherlands	Overall
Physicians employed in a hospital setting*	160,374	21,541	181,915
Weight of each country	88.2%	11.8%	100%
Distributed educational material (# of packs)**	±3,000	±2,900	±7,900
Components by specialty**:			
GPs likely to be involved in management of cancer patients, n (vertical %)	1,500 (50.0%)	2,204 (76.0%)	
Oncologists, n (vertical %)	600 (20.0%)	464 (16.0%)	
Anesthesiologists, n (vertical %)	200 (6.7%)	116 (4.0%)	
Radiologists, n (vertical %)	700 (23.3%)	116 (4.0%)	
Components by aggregated specialties**:			
GPs likely to be involved in management of cancer patients, n (vertical %)	1,500 (50.0%)	2,204 (76.0%)	
Other specialties, n (vertical %)	1,500 (50.0%)	696 (24.0%)	

** Source: EuroStat (16)*
*** Source: Takeda*

Building a sample proportionally distributed by number of specialists yielded very small numbers for each medical specialty, mainly in the Netherlands. As a consequence, an over-sampling in the Netherlands was also applied to provide a sufficient number of analysable specialties while preserving the number of analysable GPs (Table 8.5.2-4):

- For the Netherlands: a minimal sample of 40 was assigned to the GPs category and the remaining number was equally distributed between the 3 other specialties.
- For France, since the sample was larger, a minimal sample of 50 was assigned to the GPs category and the remaining number was proportionally distributed between the 3 other specialties.

Table 8.5.2-4: Sample size per country and per specialty

n (column % per country)*	**France**	**The Netherlands**	**Overall**
Number of participating physicians required	**205**	**102**	**307**
GPs likely to be involved in management of cancer patients, n (vertical %)	70 (34.1%)	46 (45.1%)	
Oncologists, n (vertical %)	55 (26.8%)	20 (19.6%)	
Anesthesiologists, n (vertical %)	17 (8.3%)	18 (17.6%)	
Radiologists, n (vertical %)	63 (30.7%)	18 (17.6%)	
Sub-total of non-GP specialties	135 (65.9%)	56 (54.9%)	
Number of physicians with an analysable questionnaire	**178**	**89**	**267**
GPs likely to be involved in management of cancer patients, n (vertical %)	60 (33.7%)	40 (44.9%)	

n (column % per country)*	France	The Netherlands	Overall
Oncologists, n (vertical %)	48 (27.0%)	17 (19.1%)	
Anesthesiologists, n (vertical %)	15 (8.4%)	16 (18.0%)	
Radiologists, n (vertical %)	55 (30.9%)	16 (18.0%)	
Sub-total of non-GP specialties	118 (66.3%)	49 (55.1%)	

** Numbers n per specialty were rounded to the superior integer for the oncologists, otherwise to the inferior integer.*

Note that the sample has been calculated to be representative as a whole, not per country or specialty. Thus the subgroup analyses do not guarantee the same confidence intervals as the whole sample.

8.6 DATA MANAGEMENT

The survey was conducted according to the Standard Operating Procedures (SOPs) of IMS Real World Evidence Solutions and IMS Medical Radar. Collected data were entered and stored in a database specific to the survey and the country. A study database was created by merging of databases of each country.
Data were checked in terms of consistency before data analysis:

- removal of duplicates (when required),
- data labelling and data formatting,
- range and consistency checks for each variable to identify potential non admissible values,
- cross-check the consistency of data for related variables, where feasible.

The study database was locked once validated.

8.6.1 Data collection

The survey was conducted by IMS Medical Radar, a division of IMS Health specialised in the conduct of phone and web surveys for more than 20 years. IMS Medical Radar created the web-based instance survey. The lists of physicians were loaded into separate databases for the management of the survey. Physicians' answers/data were collected through the web questionnaire.

As described previously (§8.5.1: Sampling plan and §8.5.2: Study size calculation), physicians were randomly contacted, mainly by email (and some by phone when needed), according to their stratum by the IMS Medical Radar team. Their recruitment was done as follows:

- Physicians were invited to participate in the survey mainly via emails. The survey background and objectives, the contact information for questions, and the proposed compensation were explained to the physicians at this step. If they agreed to participate in the survey, they were sent a link to access the survey and the instructions for the web questionnaire completion.
- The physicians were sent a reminder by email one week after the start of the survey if the questionnaire was not completed and sent to IMS Medical Radar.
- A further reminder was done by phone 1.5 week after the start of the survey if the recruitment target was not achieved in the stratum.
- The physicians were sent a final reminder by email two weeks after the start of the survey if the recruitment target was not achieved in the stratum.

If the minimum number of required responders was not reached, the recruitment was performed by phone to achieve the target in a specific stratum. A physician was considered as contacted if he/she:

- has refused to participate,
- has been contacted at least 3 times and up to 5 times,
- was sent the survey, completed it and sent it back to IMS Medical Radar.

Moreover, a physician was considered as unreachable if he/she has been contacted between 3 and up to 5 times without any answer. For each physician, the number of contacts, and the date and time when he/she completed the web questionnaire was recorded. The recruitment in each stratum was stopped when the stratum target was reached.

8.6.2 Approaches for increasing the response rate

Physicians are increasingly contacted to participate in web or phone surveys, and overall response rate of participation is low according to international studies (5)(6)(7). Holbrook et al. showed that the response rate to surveys continues to decline over time, but a lower rate does not appear to reduce the representativeness of a demographic survey (7). VanGeest et al. conducted a systematic review of 66 published reports on efforts to perform for improving response rates (8). Two general strategies were explored: incentives-based approaches and survey design-based approaches. Financial incentives, even modest ones, were effective in improving physician response rates while non-monetary incentives were much less effective. These measures include the use of a short questionnaire, and questionnaires personalized, and approved by professional associations.

In order to maximise the response rate, three actions were applied to this survey:

1) A compensation fee was provided to physicians for their participation in the survey.
2) All physicians were sent an email or contacted by experienced operators of IMS Medical Radar with extensive experience in conducting health related surveys.
3) Each physician was emailed or called up to 3-5 times before being considered as "not reachable", and reminders were sent by email when the web questionnaire was not received.

8.7 DATA ANALYSIS

8.7.1 General statistical consideration

The statistical analysis was conducted using the SAS® software V9.4 on Windows™ (SAS Institute, North Carolina, USA). The statistical results were presented overall, by country and per physician specialty.

Continuous variables were described by their number (of valid cases, of missing values), mean, standard deviation, and median, Q1, Q3, minimum and maximum. Missing data were displayed when present (value was greater than 0). Categorical variables were described as the total number and relative percentage per category. Confidence intervals of 95% were calculated when relevant.

Calculations were performed on raw data. No projection factor was applied to generalise the results to the entire prescribers' universe. Results are presented as raw unweighted data and as weighted data. "Overall unweighted results" show the results observed on the overall sample without consideration of the sampling weights used in constructing the sampling frame. "Weighted results" at the country level are weighted for the sampling frame and reflect the population that the survey measured in this country. Additionally, "Overall weighted results" were calculated with further weighting for proportion of each country in the overall targeted population. Details of the weights are provided in the following section.

Sample adjustment:

The survey results were weighted to reflect the real proportion of the two countries and within each country to reflect the real proportion of each specialty in order to extend the survey results to the overall target population. Both unweighted (i.e. raw data) and weighted results were calculated.

A weight variable was applied to each statistical unit (i.e. the analysable physician) during the results calculation in order to correct the over-sampling of oncologists, anesthesiologists and radiologists, for the Netherlands, and the under-sampling of GPs for France. This variable indicated how many unit(s) of the population of interest an observation counted in a statistical procedure. Its

value changed per country and per specialty. The weights were normalised to obtain their sum equal to the sample size.

8.7.2 Analysis of non-participation or refusal to participate rate

The Physicians invited to participate in the survey were those who were sent an email or a fax, or tried to be contacted by phone (whatever the number of attempts).

As often required by the European and International Health Authorities, the following different cases of total non-response were distinguished and analysed:

- Targeted physicians: Physicians who had been sent an email or mail has been sent, or who had been called by telephone at least 5 times.
- Contacted physicians: The subset of targeted physicians who were successfully contacted by phone or were indicated in the email system to have opened the email.
- Physicians who agreed to participate: The subset of contacted physicians who agreed to participate in the survey (e.g. by phone or by clicking on the link provided in the recruitment email).
- Physicians with complete questionnaire: The subset of physicians who agreed to participate who actually completed the questionnaire until its end**.**

The physicians' participation in the survey was assessed through different ratios:

- Contact rate = contacted physicians / targeted physicians
- Response rate = Physicians who agreed to participate/ contacted physicians
- Cooperation rate = Physicians with complete questionnaire / Physicians who agreed to participate
- Refusal rate = (contacted physicians-physicians who agreed to participate) / Physicians targeted

The reasons for non-response were described, especially from all observed variables. This ensured that missing data were reported with enough detail to strengthen the results validity, as recommended by the STROBE guidelines (9).

8.7.3 Questionnaire analysis

The general statistical considerations described above (§8.7.1) were applied for quantitative and qualitative variables. The number of missing data has been reported (when strictly greater than 0); they were few and expected to be distributed at random. Since there was no applicable method unanimously accepted, there was no replacement or imputation of missing data (10).

Physicians' answers were analysed by subgroups of physician's specialty per country, and on the overall dataset.

8.8 QUALITY CONTROL

8.8.1 Approaches for validating the questionnaire

The questionnaire was tested among 5-6 physicians for its comprehensibility, consistency and the appropriateness of medical terms. The local translated versions of the questionnaire from English into French and Dutch was done using the back and forth method to ensure an accurate translation.

8.8.2 Approaches for validating the results

The quality control for validating the results was conducted at five levels:

1) At IMS Medical Radar management level, every efforts were done to collect complete and valid data:

   - Verification of the reliability and security of the web questionnaire interface by a qualified web-master for each country,

   - Monitoring of the quality and datasets definition by a qualified data manager. In the background of the web questionnaire, real-time checks of the answers provided by the respondents were utilized. Non admissible answers (i.e. incorrect or unusual values, outlying values) were detected and queries sent to the physician.

2) At the study database level (after merging datasets of each country), final data quality checks were applied (beyond data management process):

   - Distribution of each variable to count the number of missing values and estimate the associated relative percentage,

   - Identification and count of non-analysable questionnaires:
     - estimation of the percentage of physicians who do not know Instanyl®,
     - estimation of the percentage of physicians without complete analysable questionnaire.

Any data changes in the database were tracked and documented. The country-datasets were stored in a dedicated database. The database was locked once data was validated and quality checked.

3) At the statistical analysis level: all data management and statistical analysis programs developed and used in the analysis were documented. All versions generated were dated, kept with accompanying documentation and archived. The original database was stored and a derived database created for the new versions in order to include recoding and computing of new variables, especially stratification of continuous variables, combination of modalities for categorical variables, calculation of composite indicators, etc.

4) At the results level, a data review was done to ensure data integrity. A statistical analysis report including all data tables was provided for review and discussion with Takeda. The final statistical report took into account the reviewers' comments.

5) At the study level, all aspects of the study were conducted according the standard operating procedures (SOPs) of IMS Real World Evidence Solutions and IMS Medical Radar divisions. The study documents have been approved by people competent in medical and safety areas of IMS. According to the SOPs, an independent review of the survey results and report was done by a person who was not in charge of data management and preparation.

8.8.3 Safeguards, security and traceability of contacts

Several operators of the IMS Medical Radar call centre specialised in health surveys were assigned to the project and trained on the survey methodology prior to fieldwork. The email contact and phone calls were traced using the management software. All survey aspects from protocol development to the reporting of the results were conducted according to the SOPs of IMS Real World Evidence Solutions and IMS Medical Radar divisions. These SOPs can be consulted on site (11).

8.9 LIMITATIONS OF THE RESEARCH METHODS

8.9.1 Possible selection bias due to voluntary participation

The potential for selection bias of physicians participating in a survey is an inherent limitation to any study based on volunteer participation. In order to quantify any selection bias, the distribution of each stratification criterion of healthcare professional (country and specialty) was compared between participants and non-participants.

8.9.2 Limitations inherent to web surveys

The questionnaire included general questions followed by specific ones. As the physicians may have understood the right answer in subsequent questions, it was not possible to go back in the questionnaire and edit answers in former questions. It is possible answers recorded for a specific question may be non-specific or relate to previous questions.

In this type of survey, the generalisation and external validity of the results is restricted to physicians who have an active email address and willing (and able) to answer a questionnaire online. These physicians may not be fully representative of the whole targeted population (12).

Among non-response bias, targeted physicians may also have activated filters in their mail box in order to block spam and unsolicited emails. They may not have even seen the invitation to participate in the survey if a very strict degree of message filtering is set. Having multiple email addresses could also be a critical situation. If the one used is not the primary address or if the physicians did not check their email box frequently they would not have received the invitation during the recruitment period. This is one of the reasons why some physicians were also contacted by phone.

Moreover, web surveys may promote social desirability bias which refers to the tendency of participants to give socially desirable/expected responses instead of choosing those reflecting their current knowledge or behaviour, e.g. physicians can copy-paste information gathered online instead of giving their own opinions (12). Social desirability can affect the validity of survey research findings, but the use of pre-populated items in the questionnaire could/tends to reduce this bias (13).

The access to the web questionnaire interface was strictly limited to the invited participants, with a single possibility to participate and a traceability system. Thus stakeholder bias (multiple answers of people who have a personal interest in survey results and/or who incite peers to fulfil the survey in order to influence the results) or unverified respondents (when it is not possible to verify who responds) were not applicable.

8.9.3 Generalisation to the overall target population with adjustment

As the study design included an over-sampling of oncologists, anesthesiologists and radiologists in the Netherlands, and an under-sampling of GPs in France, the unweighted results cannot be generalised to the overall target population. Weighted results adjusted for sampling approach were used throughout when interpreting the study findings and drawing generalisations.

9. RESULTS

9.1 PARTICIPATING PHYSICIANS

9.1.1 Periods of the survey

In the Netherlands, the updated educational materials were distributed to physicians from July 21st 2014 until February 26th 2015, by the sales team during their visits. The survey's data collection and fieldwork was undertaken from April 21st to May 15th 2015, which was approximately 3-9 months after the distribution of the updated educational materials.

In France, the updated educational materials were distributed to physicians from February 2nd 2015 onwards, via sales force and via postal mail after a request from the HCP. The survey's data collection and field work was undertaken from September 19th to October 27th 2015, which was approximately 6 months after distribution of the updated educational materials.

Shown below is the distribution of questionnaire completion dates for the Netherlands (Figure 9.1.1-1) and France (Figure 9.1.1-2). The survey period was longer in France because the number of physicians to be recruited was greater than in the Netherlands.

Figure 9.1.1-1: Dates of completion of the web-questionnaire in the Netherlands

(Basis = Physicians with a complete analysable questionnaire)

First date: 21/04/2015, last date: 15/05/2015: Length: 24 days

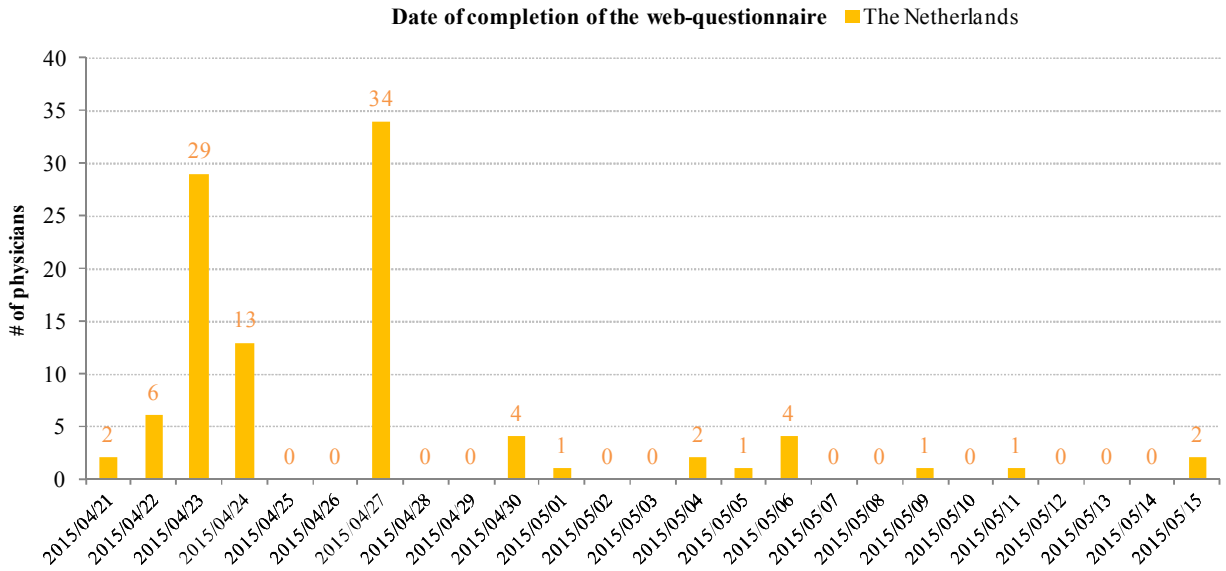
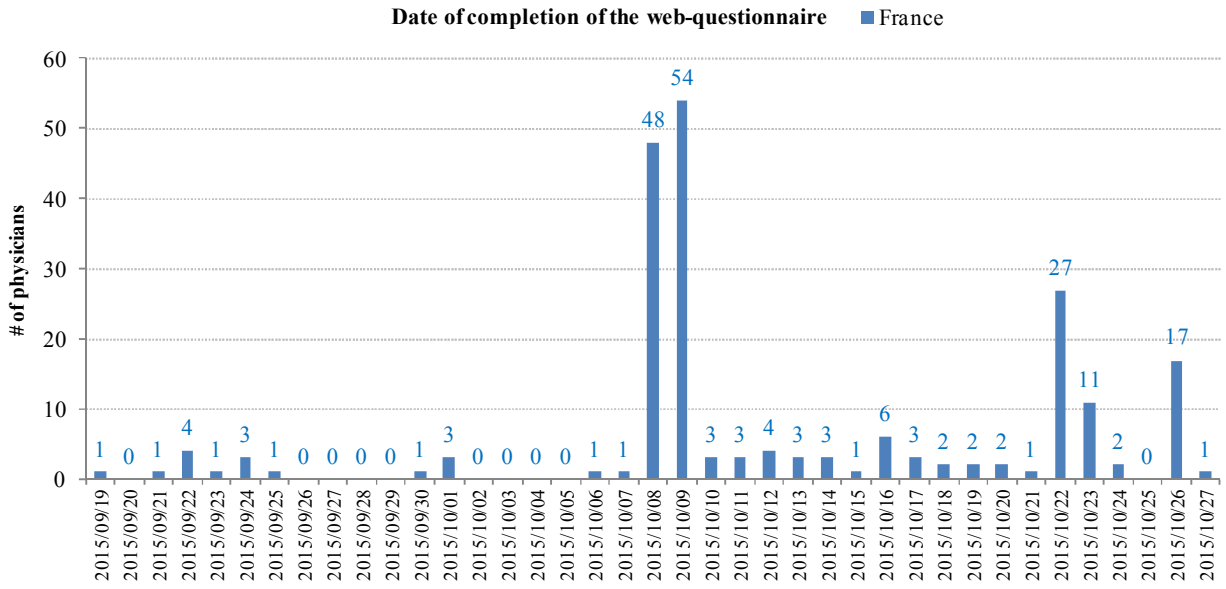


Figure 9.1.1-2: Dates of completion of the web-questionnaire in France

(Basis = Physicians with a complete analysable questionnaire)

First date: 19/09/2015, last date: 27/10/2015: Length: 38 days



9.1.2 Rate of responsiveness of the surveyed physicians

The physicians with a complete and analysable questionnaire (those who completed the questionnaire until its end and responded to all questions) were considered for the analysis.

A total of 310 physicians completed the questionnaire, 210 in France and 100 in Netherlands. The sample size targets were successfully achieved overall (N=310 respondent vs. 267 required) and in both countries (France: 210 vs. 178) and Netherlands: 100 vs. 89).

The level of participation in the survey was examined through different ratios (Definitions are provided in §8.7.2):

- Contact rate = contacted physicians / targeted physicians
- Response rate = physicians who agreed to participate / contacted physicians
- Cooperation rate = physicians with complete questionnaire / physicians who agreed to participate
- Non-response rate (complement of the response rate) = overall non-response / contacted physicians
- Refusal rate = (contacted physicians - physicians who agreed to participate) / physicians targeted

The rates of participation were presented below in Table 9.1.2-1; the main rates are as follows:

- The contact rate was 13.4% in France and 7.7% in the Netherlands.
- The response rate was 71.4% in the Netherlands and 54.5% in France.
  In the Netherlands, the response rate was the highest among oncologists (92.6%) and was similar among the other specialties. In France, the response rate was high among GPs (88.0%) and oncologists (81.8%), and very low among radiologists (12.0%).
- The cooperation rate was 83.3% in the Netherlands and 77.8% in France.
- Finally, the refusal rate among contacted physicians was low; it was of 2.2% in the Netherlands and 6.1% in France.

Table 9.1.2-1: Responsiveness of the surveyed physicians per country

	Country	GPs	Oncologists	Anesthesiologists	Radiologists	All
	France					
a	**Physicians with complete questionnaire**	**97**	**65**	**31**	**17**	**210**
b	**Physicians who agreed to participate**	**132**	**72**	**44**	**22**	**270**
c	Physicians who refused to participate	18	16	30	161	225
d=b+c	Physicians contacted	150	88	74	183	495
e	Physicians not reachable	1531	554	608	497	3190
f=c+e	**Physicians not interviewed**	**1549**	**570**	**638**	**658**	**3415**
g=d+e	Physicians targeted	1681	642	682	680	3685
h	*Non-finalised attempts*	*106*	*61*	*75*	*213*	455
z=g+h	*Physicians invited to participate*	*1787*	*703*	*757*	*893*	*4140*
i=d/g	Contact rate	8.9%	13.7%	10.9%	26.9%	13.4%
j=b/d	**Response rate**	**88.0%**	**81.8%**	**59.5%**	**12.0%**	**54.5%**
k=a/b	Cooperation rate	73.5%	90.3%	70.5%	77.3%	77.8%
l=1-j	Non-response rate	12.0%	18.2%	40.5%	88.0%	45.5%
m=(d-b)/g	Refusal rate	1.1%	2.5%	4.4%	23.7%	6.1%
	The Netherlands					
a	**Physicians with complete questionnaire**	**40**	**19**	**24**	**17**	**100**

	Country	GPs	Oncologists	Anesthesiologists	Radiologists	All
b	**Physicians who agreed to participate**	**44**	**25**	**29**	**22**	**120**
c	Physicians who refused to participate	19	2	13	14	48
d=b+c	Physicians contacted	63	27	42	36	168
e	Physicians not reachable	953	85	782	207	2027
f=c+e	**Physicians not interviewed**	**972**	**87**	**795**	**221**	**2075**
g=d+e	Physicians targeted	1016	112	824	243	2195
h	*Non-finalised attempts*	*147*	*21*	*62*	*0*	230
z=g+h	*Physicians invited to participate*	*1163*	*133*	*886*	*243*	*2425*
i=d/g	Contact rate	6.2%	24.1%	5.1%	14.8%	7.7%
j=b/d	**Response rate**	**69.8%**	**92.6%**	**69.0%**	**61.1%**	**71.4%**
k=a/b	Cooperation rate	90.9%	76.0%	82.8%	77.3%	83.3%
l=1-j	Non-response rate	30.2%	7.4%	31.0%	38.9%	28.6%
m=(d-b)/g	Refusal rate	1.9%	1.8%	1.6%	5.8%	2.2%

9.1.3 Description of the reasons of non-response

1) Description of physicians not reachable

The physicians not reachable were contacted 5 times or more without any response (e.g. no response, wrong / missing e-mail or phone number / physician temporarily unavailable or retired/ died, etc.).

The majority of the physicians not reachable did not respond to the invitation, both in France (82.5%) and in the Netherlands (99.5%).

2) Description of physicians who did not want to participate in the survey

Some physicians did not want to participate in the survey and immediately gave a response (i.e. by email or by phone). The dropout and the refusal (mainly because the physician was busy) were the main reasons for non-participation, both in France and in the Netherlands (Table 9.1.3-1).

Table 9.1.3-1: Description of the non-response - Physicians who did not want to participate

(Basis=Physicians contacted and who did not want to participate in the survey)

Reasons of non-participation	GPs		Oncologists		Anesthesiologists		Radiologists		All	
France	(N=18)		(N=16)		(N=30)		(N=161)		(N=225)	
Does not want to participate:										
Dropout	4 (22.2%)	[2]	0 (0%)	[-]	20 (66.7%)	[1]	37 (23%)	[2]	61 (27.1%)	[1]
No further contact	5 (27.8%)	[1]	5 (31.3%)	[1]	4 (13.3%)	[2]	43 (26.7%)	[1]	57 (25.3%)	[2]
Busy/no time	2 (11.1%)	[5]	3 (18.8%)	[3]	0 (0%)	[-]	27 (16.8%)	[3]	32 (14.2%)	[3]
Never responds to web surveys	3 (16.7%)	[3]	5 (31.3%)	[1]	4 (13.3%)	[2]	20 (12.4%)	[5]	32 (14.2%)	[3]
Other reason	3 (16.7%)	[3]	2 (12.5%)	[4]	0 (0%)	[-]	26 (16.1%)	[4]	31 (13.8%)	[5]
No such patients	1 (5.6%)	[6]	1 (6.3%)	[5]	2 (6.7%)	[4]	8 (5%)	[6]	12 (5.3%)	[6]
The Netherlands	(N=19)		(N=2)		(N=13)		(N=14)		(N=48)	
Does not want to participate:										
Dropout	4 (21.1%)	[2]	0 (0%)	[2]	11 (84.6%)	[1]	12 (85.7%)	[1]	27 (56.3%)	[1]
Other reason	11 (57.9%)	[1]	0 (0%)	[2]	0 (0%)	[4]	0 (0%)	[4]	11 (22.9%)	[2]

Reasons of non-participation	GPs		Oncologists		Anesthesiologists		Radiologists		All	
No such patients	0 (0%)	[5]	2 (100%)	[1]	1 (7.7%)	[2]	1 (7.1%)	[2]	4 (8.3%)	[3]
Never responds to web surveys	3 (15.8%)	[3]	0 (0%)	[2]	0 (0%)	[4]	0 (0%)	[4]	3 (6.3%)	[4]
Not interested in the study	0 (0%)	[5]	0 (0%)	[2]	1 (7.7%)	[2]	1 (7.1%)	[2]	2 (4.2%)	[5]
Busy/no time	1 (5.3%)	[4]	0 (0%)	[2]	0 (0%)	[4]	0 (0%)	[4]	1 (2.1%)	[6]

3) Description of the physicians who agreed to participate in the survey

Overall, 390 physicians agreed to participate in the survey; 120 in the Netherlands and 270 in France. Among them, 83.3% in the Netherlands and 77.8% in France sent a complete analysable questionnaire (Table 9.1.3-2).

Table 9.1.3-2: Description of the physicians who agreed to participate in the survey

(Basis = Physicians contacted and who agreed to participate)

Type of physicians who agreed to participate	GPs	Oncologists	Anesthesiologists	Radiologists	All
France	(N=132)	(N=72)	(N=44)	(N=22)	(N=270)
Complete and analysable questionnaire	97 (73.5%) [1]	65 (90.3%) [1]	31 (70.5%) [1]	17 (77.3%) [1]	210 (77.8%) [1]
Survey initiated but physician didn't complete the whole survey on his own initiative	19 (14.4%) [2]	2 (2.8%) [3]	6 (13.6%) [2]	4 (18.2%) [2]	31 (11.5%) [2]
Survey finally not started by the physician	2 (1.5%) [4]	1 (1.4%) [4]	2 (4.5%) [4]	0 (0%) [-]	5 (1.9%) [4]
Failed screening (the doctor doesn't meet the criteria as set by the specific project.)	14 (10.6%) [3]	4 (5.6%) [2]	5 (11.4%) [3]	1 (4.5%) [3]	24 (8.9%) [3]
Reason of failed screening:					
Currently employed by a pharmaceutical company or contracted by regulatory bodies (e.g. EMA)	1 (0.8%)	1 (1.4%)	0 (0%)	0 (0%)	2 (0.7%)
Doesn't know the opioid analgesic Instanyl® (intranasal fentanyl)	13 (9.8%)	2 (2.8%)	5 (11.4%)	1 (4.5%)	21 (7.8%)
Confidentiality issues associated with the reporting of AEs	0 (0%)	1 (1.4%)	0 (0%)	0 (0%)	1 (0.4%)
The Netherlands	(N=44)	(N=25)	(N=29)	(N=22)	(N=120)
Complete and analysable questionnaire	40 (90.9%) [1]	19 (76%) [1]	24 (82.8%) [1]	17 (77.3%) [1]	100 (83.3%) [1]
Survey initiated but physician didn't complete the whole survey on his own initiative	2 (4.5%) [2]	4 (16%) [2]	4 (13.8%) [2]	0 (0%) [4]	10 (8.3%) [2]
Survey finally not started by the physician	1 (2.3%) [3]	0 (0%) [-]	1 (3.4%) [3]	3 (13.6%) [2]	5 (4.2%) [3]
Failed screening (the doctor doesn't meet the criteria as set by the specific project.)	1 (2.3%) [3]	2 (8%) [3]	0 (0%) [4]	2 (9.1%) [3]	5 (4.2%) [3]
Reason of failed screening:					
Currently employed by a pharmaceutical company or contracted by regulatory bodies (e.g. EMA)	0 (0%)	1 (4%)	0 (0%)	0 (0%)	1 (0.8%)
Doesn't know the opioid analgesic Instanyl® (intranasal fentanyl)	0 (0%)	1 (4%)	0 (0%)	2 (9.1%)	3 (2.5%)
Confidentiality issues associated with the reporting of AEs	1 (2.3%)	0 (0%)	0 (0%)	0 (0%)	1 (0.8%)

9.1.4 Selection bias due to voluntary participation

Overall, the characteristics of the physicians not interviewed/not respondent were similar to those of the physicians who sent a complete analysable questionnaire (Table 9.1.4-1). The proportion of GPs is similar among respondents and non respondents (44.2% vs. 45.9%). The proportion of specialists is also comparable among the physicians who completed or not a questionnaire (55.8% vs. 54.1%).

The proportions of respondents were similar to the non-respondents, in France and the Netherlands. The proportions of specialists that participated and did not participate in the survey were similar in France (36.5% vs. 34.0%) and in the Netherlands (19.4% vs. 20.1%). Nevertheless, the radiologists in France and the anesthesiologists in the Netherlands were more reluctant to participate in the survey.

Table 9.1.4-1: Distribution of the stratification criteria of physicians between the physicians interviewed and those who refused to participate or were not reachable

(Basis: see columns)

Stratification criteria	Physicians who agreed to participate		Physicians with a complete questionnaire		Physicians not interviewed	
	Count	%	Count	%	Count	%
Country	(N=390)		(N=310)		(N=5490)	
France	270	69.2%	210	67.7%	3415	62.2%
The Netherlands	120	30.8%	100	32.3%	2075	37.8%
Specialty						
GPs	176	45.1%	137	44.2%	2521	45.9%
Oncologists	97	24.9%	84	27.1%	657	12.0%
Anesthesiologists	73	18.7%	55	17.7%	1433	26.1%
Radiologists	44	11.3%	34	11.0%	879	16.0%
Sub-total non-GP specialists	*214*	*54.9%*	*173*	*55.8%*	*2969*	*54.1%*
Stratum						
1 - France GPs	132	33.8%	97	31.3%	1549	28.2%
2 - France Oncologists	72	18.5%	65	21.0%	570	10.4%
3 - France Anesthesiologists	44	11.3%	31	10.0%	638	11.6%
4 - France Radiologists	22	5.6%	17	5.5%	658	12.0%
France Sub-total non-GP specialists	*138*	*35.4%*	*113*	*36.5%*	*1866*	*34.0%*
5 - The Netherlands GPs	44	11.3%	40	12.9%	972	17.7%
6 - The Netherlands Oncologists	25	6.4%	19	6.1%	87	1.6%
7 - The Netherlands Anesthesiologists	29	7.4%	24	7.7%	795	14.5%
8 - The Netherlands Radiologists	22	5.6%	17	5.5%	221	4.0%
The Netherlands Sub-total non-GP specialists	*76*	*19.5%*	*60*	*19.4%*	1103	*20.1%*

9.1.5 Respondent physicians

Among the physicians contacted, 310 participated in the survey and sent an analysable questionnaire. France comprised two thirds of respondents (68%, N=210), Table 9.1.5-1. The participants were: GPs (44%) followed by oncologists (27%), anaesthesiologists (18%) and radiologists (11%).

The proportion of GPs was similar in both countries (46.2% in France and 40.0% in the Netherlands). In contrast, the oncologists were proportionally more numerous in France (31.0% vs. 19.0%), and the anesthesiologists as well as radiologists were proportionally more numerous in the Netherlands.

Shown below are the sampling weights used to calculate the weighted percentages, which are presented in the reminder of the results section.

Table 9.1.5-1: Unweighted and weighted samples per country and per stratum in the survey

			Unweighted sample				Weighted sample		
Stratum ID	**Country**	**Specialty**	**Sample size - Unweighted**	**% per country - Unweighted**	**% - Unweighted**	**Weight per stratum**	**Sample size - Weighted**	**% per country - Weighted**	**% - Weighted**
1	France	GPs likely to be involved in management of cancer patients	97	46.2%	31.3%	**2.03**	197.2	70.9%	63.8%
2		Oncologists	65	31.0%	21.0%	**0.18**	11.4	4.0%	3.6%
3		Anesthesiologists	31	14.8%	10.0%	**1.69**	52.3	18.7%	16.8%
4		Radiologists	17	8.1%	5.5%	**1.09**	18.4	6.5%	5.8%
		Overall France	210	100%	68%		279.3	100%	90%
5	The Netherlands	GPs likely to be involved in management of cancer patients	40	40.0%	12.9%	**0.56**	22.4	71.0%	7.1%
6		Oncologists	19	19.0%	6.1%	**0.15**	2.9	9.7%	1.0%
7		Anesthesiologists	24	24.0%	7.7%	**0.19**	4.6	16.1%	1.6%
8		Radiologists	17	17.0%	5.5%	**0.04**	0.7	3.2%	0.3%
		Overall The Netherlands	100	100%	32%		30.6	100%	10%
	Overall	**GPs likely to be involved in management of cancer patients**	**137**	44.2%	44.2%		**219.6**	70.9%	70.9%
		Oncologists	**84**	27.1%	27.1%		**14.3**	4.5%	4.5%
		Anesthesiologists	**55**	17.7%	17.7%		**56.9**	18.4%	18.4%
		Radiologists	**34**	11.0%	11.0%		**19.1**	6.1%	6.1%
		Overall	**310**	100%	100%		**310**	100%	100%

9.1.6 Introduction and Agreement Section of the Questionnaire

Only complete and analysable questionnaires were analysed.

The screening phase confirmed that no physicians were employed by a pharmaceutical company (e.g. Takeda) or contracted by regulatory bodies (e.g. EMA) at the time of the survey, all physicians where familiar with Instanyl® (intranasal fentanyl) and all agreed with the term of adverse events/adverse reactions management and reporting.

9.2 DESCRIPTIVE DATA

Results are presented for unweighted and weighted results. The endpoint was assessed per country, per medical specialties and overall. Because of over sampling in the sample frame, the weighted results should be used when interpreting the data. Unweighted results are presented for completeness only.

9.2.1 Demographics and Practice Information

Physician specialty:
In the weighted analyses, the majority of the 310 participating physicians were GPs (70.9%), 18.4% anesthesiologists, 6.0% radiologists and 4.5% oncologists (Table 9.2.1-1). Similar proportions of GPs

(70.6% vs. 73.3%) and anesthesiologists (18.7% vs. 15.0%) were reached in France and the Netherlands, respectively.

Table 9.2.1-1: Primary medical specialty of the physicians

(Basis = Physicians with complete analysable questionnaire)

		Q3. What is your primary medical specialty?						
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Oncology	0 (0.0%)	65 (100.0%)	0 (0.0%)	0 (0.0%)	65 (57.5%)	65 (31.0%)	11.4 (4.1%)
	Anesthesiology	0 (0.0%)	0 (0.0%)	31 (100.0%)	0 (0.0%)	31 (27.4%)	31 (14.8%)	52.3 (18.7%)
	Radiology	0 (0.0%)	0 (0.0%)	0 (0.0%)	17 (100.0%)	17 (15.0%)	17 (8.1%)	18.4 (6.6%)
	General Practitioner	97 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.0 (0.0%)	97 (46.2%)	197.2 (70.6%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Oncology	0 (0.0%)	13 (68.4%)	0 (0.0%)	10 (58.8%)	23 (38.3%)	23 (23.0%)	2.4 (7.8%)
	Anesthesiology	0 (0.0%)	0 (0.0%)	24 (100.0%)	0 (0.0%)	24 (40.0%)	24 (24.0%)	4.6 (15.0%)
	Radiology	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (41.2%)	7 (11.7%)	7 (7.0%)	0.3 (0.9%)
	General Practitioner	40 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.0 (0.0%)	40 (40.0%)	22.4 (73.3%)
	Other: Urology	0 (0.0%)	6 (31.6%)	0 (0.0%)	0 (0.0%)	6 (10.0%)	6 (6.0%)	0.9 (3.0%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Oncology	0 (0.0%)	78 (92.9%)	0 (0.0%)	10 (29.4%)	88 (50.9%)	88 (28.4%)	-
	Anesthesiology	0 (0.0%)	0 (0.0%)	55 (100.0%)	0 (0.0%)	55 (31.8%)	55 (17.7%)	-
	Radiology	0 (0.0%)	0 (0.0%)	0 (0.0%)	24 (70.6%)	24 (13.9%)	24 (7.7%)	-
	General Practitioner	137 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.0 (0.0%)	137 (44.2%)	-
	Other: Urology	0 (0.0%)	6 (7.1%)	0 (0.0%)	0 (0.0%)	6 (3.5%)	6 (1.9%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Oncology	0.0 (0.0%)	13.4 (93.6%)	0.0 (0.0%)	0.4 (2.1%)	13.8 (15.3%)	-	13.8 (4.5%)
	Anesthesiology	0.0 (0.0%)	0.0 (0.0%)	56.9 (100.0%)	0.0 (0.0%)	56.9 (63.0%)	-	56.9 (18.4%)
	Radiology	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	18.7 (97.9%)	18.7 (20.7%)	-	18.7 (6.0%)
	General Practitioner	219.6 (100.0%)	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	-	219.6 (70.9%)
	Other: Urology	0.0 (0.0%)	0.9 (6.4%)	0.0 (0.0%)	0.0 (0.0%)	0.9 (1.0%)	-	0.9 (0.3%)

Note: For the Netherlands 6 physicians who declared 'Urology' as primary medical specialty were classified as Oncologists in the survey.

Gender:

The survey population comprised almost three quarters of males (72.5%), with a balanced distribution of males between General Practitioners (GPs) and specialists (71.7% vs. 74.4%), Table 9.2.1-2. Similar proportions of males were observed in France and the Netherlands.

Table 9.2.1-2: Gender of the respondents

(Basis = Physicians with complete analysable questionnaire)

		Q1. Gender?						
Country	Answer	**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Male	70 (72.2%)	41 (63.1%)	25 (80.6%)	10 (58.8%)	76 (67.3%)	146 (69.5%)	202.6 (72.5%)
	Female	27 (27.8%)	24 (36.9%)	6 (19.4%)	7 (41.2%)	37 (32.7%)	64 (30.5%)	76.8 (27.5%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Male	27 (67.5%)	17 (89.5%)	21 (87.5%)	9 (52.9%)	47 (78.3%)	74 (74.0%)	22.1 (72.3%)

Q1. Gender?								
Country	Answer	**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
	Female	13 (32.5%)	2 (10.5%)	3 (12.5%)	8 (47.1%)	13 (21.7%)	26 (26.0%)	8.5 (27.7%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Male	97 (70.8%)	58 (69.0%)	46 (83.6%)	19 (55.9%)	123 (71.1%)	220 (71.0%)	-
	Female	40 (29.2%)	26 (31.0%)	9 (16.4%)	15 (44.1%)	50 (28.9%)	90 (29.0%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Male	157.5 (71.7%)	9.8 (68.4%)	46.2 (81.2%)	11.2 (58.6%)	67.2 (74.4%)	-	224.7 (72.5%)
	Female	62.2 (28.3%)	4.5 (31.6%)	10.7 (18.8%)	7.9 (41.4%)	23.1 (25.6%)	-	85.3 (27.5%)

Notes: The sum of the observed answers may not be exactly equal to the weighted size of the country due to rounding issues linked to the application of weights with decimal. This explains potential differences of +/- 1.

Physician's age:

Overall, almost three quarters of physicians (74.4%) were aged between 40 and 59 years old: 47.5% between 50-59 years old and 26.9% between 40-49 years old (Table 9.2.1-3). The physicians were slightly younger in the Netherlands where the proportion of respondents aged between 40-49 years old was higher compared to France (45.4% vs. 24.8%). This result was mainly observed among GPs.

Table 9.2.1-3: Age category of the respondents

(Basis = Physicians with complete analysable questionnaire)

Q2. What is your age category?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	<= 30 years old	0 (0.0%)	1 (1.5%)	1 (3.2%)	0 (0.0%)	2 (1.8%)	2 (1.0%)	1.9 (0.7%)
	31-39 years old	5 (5.2%)	11 (16.9%)	1 (3.2%)	7 (41.2%)	19 (16.8%)	24 (11.4%)	21.4 (7.7%)
	40-49 years old	23 (23.7%)	28 (43.1%)	6 (19.4%)	7 (41.2%)	41 (36.3%)	64 (30.5%)	69.4 (24.8%)
	50-59 years old	50 (51.5%)	22 (33.8%)	16 (51.6%)	3 (17.6%)	41 (36.3%)	91 (43.3%)	135.8 (48.6%)
	>= 60 years old	19 (19.6%)	3 (4.6%)	7 (22.6%)	0 (0.0%)	10 (8.8%)	29 (13.8%)	51.0 (18.2%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	31-39 years old	1 (2.5%)	1 (5.3%)	2 (8.3%)	6 (35.3%)	9 (15.0%)	10 (10.0%)	1.3 (4.4%)
	40-49 years old	17 (42.5%)	7 (36.8%)	16 (66.7%)	6 (35.3%)	29 (48.3%)	46 (46.0%)	13.9 (45.4%)
	50-59 years old	16 (40.0%)	8 (42.1%)	6 (25.0%)	5 (29.4%)	19 (31.7%)	35 (35.0%)	11.5 (37.7%)
	>= 60 years old	6 (15.0%)	3 (15.8%)	0 (0.0%)	0 (0.0%)	3 (5.0%)	9 (9.0%)	3.8 (12.5%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	<= 30 years old	0 (0.0%)	1 (1.2%)	1 (1.8%)	0 (0.0%)	2 (1.2%)	2 (0.6%)	-
	31-39 years old	6 (4.4%)	12 (14.3%)	3 (5.5%)	13 (38.2%)	28 (16.2%)	34 (11.0%)	-
	40-49 years old	40 (29.2%)	35 (41.7%)	22 (40.0%)	13 (38.2%)	70 (40.5%)	110 (35.5%)	-
	50-59 years old	66 (48.2%)	30 (35.7%)	22 (40.0%)	8 (23.5%)	60 (34.7%)	126 (40.6%)	-
	>= 60 years old	25 (18.2%)	6 (7.1%)	7 (12.7%)	0 (0.0%)	13 (7.5%)	38 (12.3%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	<= 30 years old	0.0 (0.0%)	0.2 (1.2%)	1.7 (3.0%)	0.0 (0.0%)	1.9 (2.1%)	-	1.9 (0.6%)
	31-39 years old	10.7 (4.9%)	2.1 (14.6%)	2.1 (3.6%)	7.8 (41.0%)	12.0 (13.3%)	-	22.7 (7.3%)
	40-49 years old	56.3 (25.6%)	6.0 (41.8%)	13.2 (23.2%)	7.8 (41.0%)	27.0 (29.9%)	-	83.3 (26.9%)
	50-59 years old	110.6 (50.4%)	5.1 (35.5%)	28.1 (49.5%)	3.5 (18.1%)	36.7 (40.6%)	-	147.3 (47.5%)
	>= 60 years old	42.0 (19.1%)	1.0 (6.9%)	11.8 (20.8%)	0.0 (0.0%)	12.8 (14.2%)	-	54.8 (17.7%)

Physician's practice:

More than half of the survey population (57.1%) had a private practice (Table 9.2.1-4). As expected, almost all specialists (95.8%) practiced in clinics or hospitals. In France, many of the GPs worked in a clinic or hospital whereas in Netherlands virtually all GPs were in private practice.

Table 9.2.1-4: Type of setting where the physicians usually spend the majority of their time

(Basis = Physicians with complete analysable questionnaire)

Q4. In which setting do you spend the majority of your time when practicing?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Private practice	75 (77.3%)	3 (4.6%)	0 (0.0%)	2 (11.8%)	5 (4.4%)	80 (38.1%)	155.2 (55.5%)
	Clinic or Hospital practice	18 (18.6%)	56 (86.2%)	31 (100.0%)	15 (88.2%)	102 (90.3%)	120 (57.1%)	115.1 (41.2%)
	Both: Private + Clinic or Hospital practice	4 (4.1%)	6 (9.2%)	0 (0.0%)	0 (0.0%)	6 (5.3%)	10 (4.8%)	9.2 (3.3%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Private practice	39 (97.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		39 (39.0%)	21.9 (71.5%)
	Clinic or Hospital practice	0 (0.0%)	19 (100.0%)	24 (100.0%)	17 (100.0%)	60 (100.0%)	60 (60.0%)	8.2 (26.7%)
	Other: Health centre	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.0%)	0.6 (1.8%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Private practice	114 (83.2%)	3 (3.6%)	0 (0.0%)	2 (5.9%)	5 (2.9%)	119 (38.4%)	-
	Clinic or Hospital practice	18 (13.1%)	75 (89.3%)	55 (100.0%)	32 (94.1%)	162 (93.6%)	180 (58.1%)	-
	Both: Private + Clinic or Hospital practice	4 (2.9%)	6 (7.1%)	0 (0.0%)	0 (0.0%)	6 (3.5%)	10 (3.2%)	-
	Other: Health centre	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.3%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Private practice	174.3 (79.4%)	0.5 (3.7%)	0.0 (0.0%)	2.2 (11.3%)	2.7 (3.0%)	-	177.0 (57.1%)
	Clinic or Hospital practice	36.6 (16.7%)	12.7 (88.9%)	56.9 (100.0%)	17.0 (88.7%)	86.6 (95.8%)	-	123.2 (39.7%)
	Both: Private + Clinic or Hospital practice	8.1 (3.7%)	1.1 (7.4%)	0.0 (0.0%)	0.0 (0.0%)	1.1 (1.2%)	-	9.2 (3.0%)
	Other: Health centre	0.6 (0.3%)	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)		-	0.6 (0.2%)

Physician's years of Experience:

Overall, the duration of practising medicine was on average 22.5 years (SD: 8.22), median: 23 years (Table 9.2.1-5). The average duration of practice was longer for the anesthesiologists and GPs (24.8 and 23.0 years, respectively) compared to oncologists and radiologists (17.2 and 13.7 years, respectively).

Table 9.2.1-5: Length of practice of the physicians

(Basis = Physicians with complete analysable questionnaire)

Q5. For how long have you been practicing medicine? (in years)								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Mean (SD)	23.5 (7.09)	17.0 (6.07)	25.8 (8.59)	13.7 (7.65)	18.9 (8.27)	21.0 (8.06)	23.0 (9.13)
	Median	25.0	15.0	27.0	11.0	17.0	21.0	24.0
	Q1-Q3	[20.0 - 28.0]	[13.0 - 20.0]	[19.0 - 33.0]	[8.0 - 17.0]	[13.0 - 25.0]	[15.0 - 27.0]	[17.0 - 29.0]
	Range	[7.0 - 37.0]	[6.0 - 30.0]	[5.0 - 39.0]	[5.0 - 30.0]	[5.0 - 39.0]	[5.0 - 39.0]	[5.0 - 39.0]

Q5. For how long have you been practicing medicine? (in years)								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Mean (SD)	18.5 (9.95)	17.9 (7.21)	14.2 (7.25)	14.5 (9.05)	15.5 (7.84)	16.7 (8.82)	17.7 (5.19)
	Median	18.0	18.0	11.5	14.0	15.0	15.0	17.0
	Q1-Q3	[10.5 - 23.7]	[12.0 - 25.0]	[8.1 - 21.5]	[8.0 - 20.0]	[9.0 - 22.6]	[10.0 - 23.0]	[10.0 - 23.3]
	Range	[7.0 - 56.0]	[5.0 - 28.0]	[4.0 - 27.0]	[2.0 - 31.0]	[2.0 - 31.0]	[2.0 - 56.0]	[2.0 - 56.0]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Mean (SD)	22.0 (8.31)	17.2 (6.31)	20.7 (9.84)	14.1 (8.26)	17.7 (8.26)	19.6 (8.54)	-
	Median	22.0	16.0	20.0	12.5	17.0	20.0	-
	Q1-Q3	[15.0 - 27.0]	[12.5 - 22.5]	[12.0 - 29.0]	[8.0 - 20.0]	[11.0 - 24.0]	[13.0 - 25.0]	-
	Range	[7.0 - 56.0]	[5.0 - 30.0]	[4.0 - 39.0]	[2.0 - 31.0]	[2.0 - 39.0]	[2.0 - 56.0]	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Mean (SD)	23.0 (9.57)	17.2 (2.60)	24.8 (9.16)	13.7 (5.69)	21.3 (6.91)	-	22.5 (8.22)
	Median	24.0	16.0	27.0	11.0	20.0	-	23.0
	Q1-Q3	[19.0 - 28.0]	[13.0 - 22.0]	[18.0 - 32.0]	[8.0 - 17.0]	[14.1 - 30.0]	-	[17.0 - 28.0]
	Range	[7.0 - 56.0]	[5.0 - 30.0]	[4.0 - 39.0]	[2.0 - 31.0]	[2.0 - 39.0]	-	[2.0 - 56.0]

Number of patients with breakthrough cancer pain treated per Physician:
Table 9.2.1-6 shows the average number of patients with breakthrough pain treated/followed-up per month during the six months prior to the survey (Section 1, Q6).

Overall, the weighted results showed that oncologists were each treating/following-up an average of 50 patients/month with breakthrough cancer pain, followed by anesthesiologists with 23 patients/month, radiologists with 20 patients/month and GPs with 13 patients/month.

In France, the oncologists were each treating/following-up a mean of 55 patients/month with breakthrough cancer pain, followed by anesthesiologists with 24 patients/month and radiologists with 20 patients /month. French GPs, many of whom worked in a clinic or hospital setting, treated/followed-up a mean of 13 patients/month.

In Netherlands, a similar pattern was seen with the specialists with oncologists treating/following-up a mean of 31 patients/month with breakthrough cancer pain, followed by anesthesiologists with 17 patients/month and radiologists with 12 patients/month. Dutch GPs had lowest mean number of patients treated/follow-up for breakthrough cancer pain with a mean of 8 patients/month.

Interpretation:
The low number of cancer breakthrough pain patients treated by each GP in Netherlands probably reflects the GPs working in local private practices, whereas in France many of the GPs work in clinic and hospital settings and have a greater role in management of breakthrough cancer pain.

Table 9.2.1-6: Average number of patients with breakthrough cancer pain treated/followed-up per month in 6 months prior to the survey

(Basis = Physicians with complete analysable questionnaire)

Q6. How many patients with breakthrough cancer pain did you treat / follow-up per month on average in the last 6 months? (unit: patients/month)								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Mean (SD)	13.1 (26.51)	54.6 (67.84)	24.1 (37.73)	20.6 (19.62)	41.1 (57.58)	28.2 (47.91)	17.4 (37.24)
	Median	5.0	25.0	10.0	12.0	20.0	10.0	6.0
	Q1-Q3	[3.0 - 15.0]	[12.0 - 50.0]	[2.0 - 30.0]	[5.0 - 30.0]	[10.0 - 40.0]	[5.0 - 30.0]	[3.0 - 20.0]

Q6. How many patients with breakthrough cancer pain did you treat / follow-up per month on average in the last 6 months? (unit: patients/month)								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
	Range	[1.0 - 240.0]	[1.0 - 250.0]	[1.0 - 150.0]	[2.0 - 70.0]	[1.0 - 250.0]	[1.0 - 250.0]	[1.0 - 250.0]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Mean (SD)	8.3 (18.52)	30.8 (47.66)	15.0 (16.59)	12.5 (10.33)	19.3 (29.88)	14.9 (26.40)	11.5 (12.86)
	Median	5.0	15.0	10.0	10.0	10.0	7.0	5.0
	Q1-Q3	[3.0 - 9.0]	[4.0 - 30.0]	[2.0 - 27.5]	[6.0 - 15.0]	[4.0 - 25.0]	[3.0 - 15.0]	[3.0 - 10.0]
	Range	[1.0 - 120.0]	[1.0 - 200.0]	[1.0 - 50.0]	[2.0 - 40.0]	[1.0 - 200.0]	[1.0 - 200.0]	[1.0 - 200.0]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Mean (SD)	11.7 (24.48)	49.2 (64.35)	20.2 (30.48)	16.6 (15.98)	33.5 (50.72)	23.9 (42.59)	-
	Median	5.0	25.0	10.0	10.0	15.0	10.0	-
	Q1-Q3	[3.0 - 10.0]	[10.0 - 50.0]	[2.0 - 30.0]	[5.0 - 25.0]	[5.0 - 30.0]	[4.0 - 25.0]	-
	Range	[1.0 - 240.0]	[1.0 - 250.0]	[1.0 - 150.0]	[2.0 - 70.0]	[1.0 - 250.0]	[1.0 - 250.0]	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Mean (SD)	12.6 (32.67)	49.8 (26.74)	23.4 (36.93)	20.3 (14.35)	26.9 (29.41)	-	16.8 (31.52)
	Median	5.0	25.0	10.0	12.0	12.0	-	6.0
	Q1-Q3	[3.0 - 15.0]	[10.0 - 50.0]	[2.0 - 30.0]	[5.0 - 30.0]	[4.0 - 30.0]	-	[3.0 - 15.0]
	Range	[1.0 - 240.0]	[1.0 - 250.0]	[1.0 - 150.0]	[2.0 - 70.0]	[1.0 - 250.0]	-	[1.0 - 250.0]

9.3 MAIN RESULTS

9.3.1 Awareness of safety information related to Instanyl®

Recent prescribing of Instanyl®:

Table 9.3.1-1 shows the proportion of physicians who prescribed Instanyl® to patients with cancer pain in the six months prior to the survey (Section 2, Q1). Overall 72.7% of physicians had prescribed Instanyl® recently for cancer pain, the remaining 27.3% had not. Instanyl® was slightly more prescribed in the Netherlands than France (81.3% vs. 71.8%).

There was some variation between countries. In France most oncologists (92.3%) and radiologists (94.1%) had recently prescribed Instanyl® for cancer pain, while just over half of anesthesiologists (58.1%) and 72.2% of GPs had recently prescribed Instanyl® for cancer pain.

In Netherlands, the proportion of oncologists, radiologists and anesthesiologists that had recently prescribed Instanyl® for cancer pain was lower than for France, whereas the proportion of GPs who had recently prescribed Instanyl® was higher than in France (87.5% vs. 72.2%).

Interpretation:
These data suggest that in Netherlands, pain control is predominantly managed by specialists and in hospital or clinic settings. Conversely in France, the pattern is more complex. The specialist on average treats/follow-up more cancer pain patients/month than the GP but are lower prescribers of Instanyl®. This could reflect French specialists opting for other forms of fentanyl or using other approaches for pain control.

Table 9.3.1-1: Prescription of Instanyl® to patients with cancer pain within the last 6 months

(Basis = Physicians with complete analysable questionnaire)

Q1. Have you prescribed Instanyl® to patients with cancer pain in the last 6 months?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Yes	70 (72.2%)	60 (92.3%)	18 (58.1%)	16 (94.1%)	94 (83.2%)	164 (78.1%)	200.6 (71.8%)
95% Confidence Limits								[64.5% - 79.1%]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Yes	35 (87.5%)	15 (78.9%)	13 (54.2%)	12 (70.6%)	40 (66.7%)	75 (75.0%)	24.9 (81.3%)
95% Confidence Limits								[72.6% - 90.0%]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Yes	105 (76.6%)	75 (89.3%)	31 (56.4%)	28 (82.4%)	134 (77.5%)	239 (77.1%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Yes	161.9 (73.7%)	12.8 (89.6%)	32.9 (57.8%)	17.8 (93.3%)	63.5 (70.3%)	-	225.5 (72.7%)
95% Confidence Limits							-	[66.1% - 79.4%]

Proportion of patients with cancer pain recently treated with Instanyl®:

Table 9.3.1-2 shows among the physicians who prescribed Instanyl® recently for cancer pain, the proportion of their patients with cancer pain that were prescribed Instanyl® in the six months prior the survey (Section 2, Q2).

Overall, 10.2% of physicians who recently prescribed Instanyl® had prescribed to ≤5% of their patients with cancer pain, 38.2% had prescribed to ≤10% of their patients with cancer pain, and 66.0% had prescribed to ≤25% of their patients with cancer pain. Only 11.5% of physicians had prescribed Instanyl® to more than half of their patients with cancer pain, and the other 88.5% to less of half of their patients with cancer pain.

Interpretation:
These data suggest that physicians are selective in prescribing Instanyl®. Only 72% of physicians had in the prior 6 months prescribed Instanyl® for their patients with cancer pain, and of those physicians who had , 38.2% had prescribed to less than 10% of their patients with cancer pain, and 66% had prescribed Instanyl® to less than 25% of their patients with cancer pain. We assume the physicians choose to use other formulations of fentanyl or other types of pain control in the remaining patients with cancer pain, but did not collect this information in the survey.

Table 9.3.1-2: Prescription of Instanyl® to patients with cancer pain in the last 6 months

(Basis = Physicians with complete analysable questionnaire and who prescribed Instanyl® to patients with cancer pain in the last 6 months)

Q2. In the last 6 months, what proportion of patients with breakthrough cancer pain have you treated with Instanyl®?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=70)	(N=60)	(N=18)	(N=16)	(N=94)	(N=164)	(N=201)
	≤5%	7 (10.0%)	8 (13.3%)	2 (11.1%)	2 (12.5%)	12 (12.8%)	19 (11.6%)	21 (10.6%)
	6-10%	20 (28.6%)	10 (16.7%)	5 (27.8%)	4 (25.0%)	19 (20.2%)	39 (23.8%)	55 (27.5%)
	11-25%	21 (30.0%)	20 (33.3%)	4 (22.2%)	3 (18.8%)	27 (28.7%)	48 (29.3%)	56 (28.0%)
	26-50%	15 (21.4%)	11 (18.3%)	6 (33.3%)	3 (18.8%)	20 (21.3%)	35 (21.3%)	46 (22.8%)
	51-75%	2 (2.9%)	7 (11.7%)	1 (5.6%)	4 (25.0%)	12 (12.8%)	14 (8.5%)	11 (5.6%)
	76-99%	4 (5.7%)	4 (6.7%)	0 (0.0%)	0 (0.0%)	4 (4.3%)	8 (4.9%)	9 (4.4%)
	100%	1 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.6%)	2 (1.0%)
Netherlands		(N=35)	(N=15)	(N=13)	(N=12)	(N=40)	(N=75)	(N=25)

Q2. In the last 6 months, what proportion of patients with breakthrough cancer pain have you treated with Instanyl®?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
	≤5%	3 (8.6%)	1 (6.7%)	0 (0.0%)	1 (8.3%)	2 (5.0%)	5 (6.7%)	2 (7.5%)
	6-10%	10 (28.6%)	6 (40.0%)	7 (53.8%)	4 (33.3%)	17 (42.5%)	27 (36.0%)	8 (32.2%)
	11-25%	9 (25.7%)	6 (40.0%)	2 (15.4%)	2 (16.7%)	10 (25.0%)	19 (25.3%)	6 (25.8%)
	26-50%	8 (22.9%)	1 (6.7%)	1 (7.7%)	2 (16.7%)	4 (10.0%)	12 (16.0%)	5 (19.7%)
	51-75%	3 (8.6%)	1 (6.7%)	2 (15.4%)	3 (25.0%)	6 (15.0%)	9 (12.0%)	2 (9.4%)
	76-99%	2 (5.7%)	0 (0.0%)	1 (7.7%)	0 (0.0%)	1 (2.5%)	3 (4.0%)	1 (5.3%)
Overall - unweighted results		(N=105)	(N=75)	(N=31)	(N=28)	(N=134)	(N=239)	-
	≤5%	10 (9.5%)	9 (12.0%)	2 (6.5%)	3 (10.7%)	14 (10.4%)	24 (10.0%)	-
	6-10%	30 (28.6%)	16 (21.3%)	12 (38.7%)	8 (28.6%)	36 (26.9%)	66 (27.6%)	-
	11-25%	30 (28.6%)	26 (34.7%)	6 (19.4%)	5 (17.9%)	37 (27.6%)	67 (28.0%)	-
	26-50%	23 (21.9%)	12 (16.0%)	7 (22.6%)	5 (17.9%)	24 (17.9%)	47 (19.7%)	-
	51-75%	5 (4.8%)	8 (10.7%)	3 (9.7%)	7 (25.0%)	18 (13.4%)	23 (9.6%)	-
	76-99%	6 (5.7%)	4 (5.3%)	1 (3.2%)	0 (0.0%)	5 (3.7%)	11 (4.6%)	-
	100%	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	-
Overall - weighted results		(N=162)	(N=13)	(N=33)	(N=18)	(N=64)	-	(N=225)
	≤5%	16 (9.8%)	2 (12.1%)	3 (10.3%)	2 (12.4%)	7 (11.2%)	-	23 (10.2%)
	6-10%	46 (28.6%)	3 (20.8%)	10 (29.7%)	5 (25.2%)	17 (26.7%)	-	63 (28.0%)
	11-25%	48 (29.5%)	4 (34.5%)	7 (21.7%)	3 (18.7%)	15 (23.4%)	-	63 (27.8%)
	26-50%	35 (21.6%)	2 (16.3%)	10 (31.4%)	3 (18.7%)	16 (24.8%)	-	51 (22.5%)
	51-75%	6 (3.5%)	1 (10.8%)	2 (6.3%)	4 (25.0%)	8 (12.5%)	-	14 (6.1%)
	76-99%	9 (5.7%)	1 (5.5%)	0 (0.6%)	0 (0.0%)	1 (1.4%)	-	10 (4.5%)
	100%	2 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	2 (0.9%)

9.3.2 Considerations when prescribing Instanyl®

Safety Considerations

Q3 of Section 2 was an open ended question: What are the main safety considerations / measures of safety when thinking of prescribing Instanyl®? The full list of responses is provided in Table 9.3.2-1. Many of the responses were similar but not identical.

Half the physicians gave responses relating to risk of respiratory depression, and that Instanyl® should not be used without a background maintenance opioid therapy:

- 25.4%: Instanyl® should not be prescribed to patients without maintenance opioid therapy (increased risk of respiratory depression)
- 14.8%: Severe respiratory depression or severe obstructive lung conditions
- 9.2%: Risk of respiratory depression
- 1.2%: Respiratory, thoracic and mediastinal disorders (including respiratory depression).

Another set of responses pertained to dosing and frequency:

- 18.3%: Possible dose control / dose easy
- 14.2%: Patient should understand well how to use safely the drug
- 11.9%: Instructions for safe use were explained by physicians to patients, mainly about dosage and frequency
- 3.7%: Safe use
- 1.7%: Compliance.

A further set of responses pertained to nasal route

- 11.1%: Nasal conditions/discomfort: special warnings and precautions for use
- 9.5%: Nasal route administration accepted by / possible for the patient

- 8.2%: Recurrent episodes of epistaxis contraindication
- 2.5%: nasal route administration not acceptable / not understood by patient

17.7% of physicians checked that the patients presented breakthrough cancer pain, in order to not give the drug to patients who do not correspond to the indication. There was a long list of other answers, many of which listed specific adverse events or safety consideration, all are provided in the table below. Many of the responses from the Netherlands were general and not specific to the question asked, Responses included quick action (19.5%) and easy to use (17.2%) whereas the question was focused on safety considerations.

Interpretation:
A limitation of having an open-ended question is that responses may be more general and not specifically related to the question asked, as was seen here. However this limitation was outweighed by allowing investigators to list what they felt were the main consideration without having choice answers to choose from.

Table 9.3.2-1: Main safety considerations/measures of safety cited by the physicians when thinking of prescribing Instanyl®

(Basis = Physicians with complete analysable questionnaire)

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
France	.	(N=97)		(N=65)		(N=31)		(N=17)		(N=113)		(N=210)		(N=279)	
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	24 (24.7%)	[1]	13 (20.0%)	[2]	11 (35.5%)	[1]	7 (41.2%)	[1]	31 (27.4%)	[1]	55 (26.2%)	[1]	77.2 (27.6%)	[1]
	Breakthrough pain: Indication	17 (17.5%)	[2]	8 (12.3%)	[4]	7 (22.6%)	[2]	4 (23.5%)	[4]	19 (16.8%)	[4]	36 (17.1%)	[4]	52.1 (18.7%)	[2]
	Dosage: possible dose control / dosage easy	17 (17.5%)	[2]	12 (18.5%)	[3]	5 (16.1%)	[6]	5 (29.4%)	[3]	22 (19.5%)	[3]	39 (18.6%)	[3]	50.5 (18.1%)	[3]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	16 (16.5%)	[4]	6 (9.2%)	[7]	6 (19.4%)	[3]	1 (5.9%)	[9]	13 (11.5%)	[7]	29 (13.8%)	[5]	44.8 (16.0%)	[4]
	Patient should understand well how to use safely the drug	13 (13.4%)	[6]	17 (26.2%)	[1]	6 (19.4%)	[3]	4 (23.5%)	[4]	27 (23.9%)	[2]	40 (19.0%)	[2]	43.9 (15.7%)	[5]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	14 (14.4%)	[5]	4 (6.2%)	[9]	1 (3.2%)	[15]	3 (17.6%)	[6]	8 (7.1%)	[9]	22 (10.5%)	[8]	34.1 (12.2%)	[6]
	Instructions for Safe use explained by physician: mainly about dosage and frequency	10 (10.3%)	[8]	8 (12.3%)	[4]	6 (19.4%)	[3]	2 (11.8%)	[7]	16 (14.2%)	[6]	26 (12.4%)	[6]	34.0 (12.2%)	[7]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	9 (9.3%)	[9]	3 (4.6%)	[12]	5 (16.1%)	[6]	1 (5.9%)	[9]	9 (8.0%)	[8]	18 (8.6%)	[9]	28.4 (10.1%)	[8]
	Recurrent episodes of epistaxis: Contraindications	11 (11.3%)	[7]	1 (1.5%)	[24]	1 (3.2%)	[15]	1 (5.9%)	[9]	3 (2.7%)	[20]	14 (6.7%)	[10]	25.3 (9.1%)	[9]
	Nasal route admin.: accepted by / possible for the patient	6 (6.2%)	[10]	8 (12.3%)	[4]	3 (9.7%)	[9]	6 (35.3%)	[2]	17 (15.0%)	[5]	23 (11.0%)	[7]	25.2 (9.0%)	[10]

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
	Previous facial radiotherapy: Contraindications	5 (5.2%) [11]	1 (1.5%) [24]	4 (12.9%) [8]	1 (5.9%) [9]	6 (5.3%) [10]	11 (5.2%) [11]	18.2 (6.5%) [11]
	Good tolerance	5 (5.2%) [11]	2 (3.1%) [16]	2 (6.5%) [10]	0 (0.0%) -	4 (3.5%) [14]	9 (4.3%) [12]	13.9 (5.0%) [12]
	Others: Adverse reactions	5 (5.2%) [11]	2 (3.1%) [16]	2 (6.5%) [10]	0 (0.0%) -	4 (3.5%) [14]	9 (4.3%) [12]	13.9 (5.0%) [12]
	Impaired renal or hepatic function: Spe. Warnings, prec. for use	5 (5.2%) [11]	1 (1.5%) [24]	1 (3.2%) [15]	1 (5.9%) [9]	3 (2.7%) [20]	8 (3.8%) [15]	13.1 (4.7%) [14]
	Efficient	4 (4.1%) [15]	2 (3.1%) [16]	2 (6.5%) [10]	0 (0.0%) -	4 (3.5%) [14]	8 (3.8%) [15]	11.9 (4.2%) [15]
	Only for cancer pain	4 (4.1%) [15]	0 (0.0%) -	2 (6.5%) [10]	0 (0.0%) -	2 (1.8%) [26]	6 (2.9%) [19]	11.5 (4.1%) [16]
	Safe use	4 (4.1%) [15]	3 (4.6%) [12]	0 (0.0%) -	1 (5.9%) [9]	4 (3.5%) [14]	8 (3.8%) [15]	9.7 (3.5%) [17]
	Cardiac disease: Spe. Warnings, prec. for use	3 (3.1%) [19]	4 (6.2%) [9]	0 (0.0%) -	2 (11.8%) [7]	6 (5.3%) [10]	9 (4.3%) [12]	9.0 (3.2%) [18]
	Easy to use	4 (4.1%) [15]	3 (4.6%) [12]	0 (0.0%) -	0 (0.0%) -	3 (2.7%) [20]	7 (3.3%) [18]	8.7 (3.1%) [19]
	Elderly: Caution in special population	3 (3.1%) [19]	1 (1.5%) [24]	1 (3.2%) [15]	0 (0.0%) -	2 (1.8%) [26]	5 (2.4%) [24]	8.0 (2.8%) [20]
	Nasal route admin.: not accepted/not understood by the patient	2 (2.1%) [24]	2 (3.1%) [16]	2 (6.5%) [10]	0 (0.0%) -	4 (3.5%) [14]	6 (2.9%) [19]	7.8 (2.8%) [21]
	Need close monitoring	3 (3.1%) [19]	0 (0.0%) -	1 (3.2%) [15]	0 (0.0%) -	1 (0.9%) [36]	4 (1.9%) [26]	7.8 (2.8%) [22]
	Quick action: rapid/fast response	3 (3.1%) [19]	3 (4.6%) [12]	0 (0.0%) -	0 (0.0%) -	3 (2.7%) [20]	6 (2.9%) [19]	6.6 (2.4%) [23]
	No adverse events	3 (3.1%) [19]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	3 (1.4%) [29]	6.1 (2.2%) [24]
	Hypersensitivity to Morphine or exipients: Contraindications	2 (2.1%) [24]	1 (1.5%) [24]	1 (3.2%) [15]	0 (0.0%) -	2 (1.8%) [26]	4 (1.9%) [26]	5.9 (2.1%) [25]
	Pregnancy: Contraindications	2 (2.1%) [24]	1 (1.5%) [24]	1 (3.2%) [15]	0 (0.0%) -	2 (1.8%) [26]	4 (1.9%) [26]	5.9 (2.1%) [25]
	Compliance	1 (1.0%) [28]	2 (3.1%) [16]	1 (3.2%) [15]	1 (5.9%) [9]	4 (3.5%) [14]	5 (2.4%) [24]	5.2 (1.8%) [27]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	1 (1.0%) [28]	0 (0.0%) -	1 (3.2%) [15]	1 (5.9%) [9]	2 (1.8%) [26]	3 (1.4%) [29]	4.8 (1.7%) [28]
	Risk of overdose	1 (1.0%) [28]	4 (6.2%) [9]	1 (3.2%) [15]	0 (0.0%) -	5 (4.4%) [12]	6 (2.9%) [19]	4.4 (1.6%) [29]
	Other	2 (2.1%) [24]	1 (1.5%) [24]	0 (0.0%) -	0 (0.0%) -	1 (0.9%) [36]	3 (1.4%) [29]	4.2 (1.5%) [30]
	Treatment of acute pain other than breakthrough pain: Contraindications	1 (1.0%) [28]	1 (1.5%) [24]	1 (3.2%) [15]	0 (0.0%) -	2 (1.8%) [26]	3 (1.4%) [29]	3.9 (1.4%) [31]
	Do not know	1 (1.0%) [28]	0 (0.0%) -	1 (3.2%) [15]	0 (0.0%) -	1 (0.9%) [36]	2 (1.0%) [38]	3.7 (1.3%) [32]
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	1 (1.0%) [28]	0 (0.0%) -	1 (3.2%) [15]	0 (0.0%) -	1 (0.9%) [36]	2 (1.0%) [38]	3.7 (1.3%) [32]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	1 (1.0%) [28]	0 (0.0%) -	1 (3.2%) [15]	0 (0.0%) -	1 (0.9%) [36]	2 (1.0%) [38]	3.7 (1.3%) [32]

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	1 (1.0%)	[28]	1 (1.5%)	[24]	0 (0.0%)	-	1 (5.9%)	[9]	2 (1.8%)	[26]	3 (1.4%)	[29]	3.3 (1.2%)	[35]
	Serotonin Syndrome: Spe. Warnings, prec. for use	0 (0.0%)	-	1 (1.5%)	[24]	1 (3.2%)	[15]	1 (5.9%)	[9]	3 (2.7%)	[20]	3 (1.4%)	[29]	2.9 (1.1%)	[36]
	Store in dry and safe place: Safe storage	0 (0.0%)	-	1 (1.5%)	[24]	1 (3.2%)	[15]	1 (5.9%)	[9]	3 (2.7%)	[20]	3 (1.4%)	[29]	2.9 (1.1%)	[36]
	Low risk of overdose	1 (1.0%)	[28]	5 (7.7%)	[8]	0 (0.0%)	-	0 (0.0%)	-	5 (4.4%)	[12]	6 (2.9%)	[19]	2.9 (1.0%)	[38]
	Increased intracranial pressure: Spe. Warnings, prec. for use	1 (1.0%)	[28]	2 (3.1%)	[16]	0 (0.0%)	-	0 (0.0%)	-	2 (1.8%)	[26]	3 (1.4%)	[29]	2.4 (0.9%)	[39]
	Keep away from children: Safe storage	1 (1.0%)	[28]	2 (3.1%)	[16]	0 (0.0%)	-	0 (0.0%)	-	2 (1.8%)	[26]	3 (1.4%)	[29]	2.4 (0.9%)	[39]
	Chronic pulmonary disease: Spe. Warnings, prec. for use	1 (1.0%)	[28]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (0.5%)	[42]	2.0 (0.7%)	[41]
	Not applicable	0 (0.0%)	-	0 (0.0%)	-	1 (3.2%)	[15]	0 (0.0%)	-	1 (0.9%)	[36]	1 (0.5%)	[42]	1.7 (0.6%)	[42]
	Psychiatric disorders (insomnia, dependence, hallucinations): Adverse reactions	0 (0.0%)	-	0 (0.0%)	-	1 (3.2%)	[15]	0 (0.0%)	-	1 (0.9%)	[36]	1 (0.5%)	[42]	1.7 (0.6%)	[42]
	General disorders and admin. site condition (pyrexia, fatigue, malaise, peripheral oedema): Adverse reactions	0 (0.0%)	-	2 (3.1%)	[16]	0 (0.0%)	-	0 (0.0%)	-	2 (1.8%)	[26]	2 (1.0%)	[38]	0.4 (0.1%)	[44]
The Netherlands	.	(N=40)		(N=19)		(N=24)		(N=17)		(N=60)		(N=100)		(N=31)	
	Dosage: possible dose control / dosage easy	10 (25.0%)	[1]	1 (5.3%)	[7]	2 (8.3%)	[6]	2 (11.8%)	[3]	5 (8.3%)	[5]	15 (15.0%)	[3]	6.2 (20.3%)	[1]
	Quick action: rapid/fast response	8 (20.0%)	[2]	4 (21.1%)	[1]	4 (16.7%)	[2]	3 (17.6%)	[2]	11 (18.3%)	[1]	19 (19.0%)	[1]	6.0 (19.5%)	[2]
	Easy to use	7 (17.5%)	[3]	2 (10.5%)	[3]	5 (20.8%)	[1]	2 (11.8%)	[3]	9 (15.0%)	[2]	16 (16.0%)	[2]	5.3 (17.2%)	[3]
	Nasal route admin.: accepted by / possible for the patient	6 (15.0%)	[4]	2 (10.5%)	[3]	2 (8.3%)	[6]	2 (11.8%)	[3]	6 (10.0%)	[4]	12 (12.0%)	[4]	4.1 (13.5%)	[4]
	Instructions for Safe use explained by physician: mainly about dosage and frequency	4 (10.0%)	[5]	1 (5.3%)	[7]	2 (8.3%)	[6]	4 (23.5%)	[1]	7 (11.7%)	[3]	11 (11.0%)	[5]	2.9 (9.6%)	[5]
	Breakthrough pain: Indication	4 (10.0%)	[5]	0 (0.0%)	-	3 (12.5%)	[3]	2 (11.8%)	[3]	5 (8.3%)	[5]	9 (9.0%)	[6]	2.9 (9.5%)	[6]
	Efficient	4 (10.0%)	[5]	0 (0.0%)	-	3 (12.5%)	[3]	0 (0.0%)	-	3 (5.0%)	[10]	7 (7.0%)	[7]	2.8 (9.2%)	[7]
	Safe use	2 (5.0%)	[8]	2 (10.5%)	[3]	1 (4.2%)	[9]	0 (0.0%)	-	3 (5.0%)	[10]	5 (5.0%)	[8]	1.6 (5.3%)	[8]
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	2 (5.0%)	[8]	0 (0.0%)	-	1 (4.2%)	[9]	1 (5.9%)	[8]	2 (3.3%)	[12]	4 (4.0%)	[11]	1.4 (4.4%)	[9]
	Low risk of overdose	2 (5.0%)	[8]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	2 (2.0%)	[15]	1.1 (3.7%)	[10]
	No adverse events	2 (5.0%)	[8]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	2 (2.0%)	[15]	1.1 (3.7%)	[10]

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	1 (2.5%)	[12]	1 (5.3%)	[7]	1 (4.2%)	[9]	2 (11.8%)	[3]	4 (6.7%)	[8]	5 (5.0%)	[8]	1.0 (3.2%)	[12]
	Impaired renal or hepatic function: Spe. Warnings, prec. for use	1 (2.5%)	[12]	2 (10.5%)	[3]	0 (0.0%)	-	0 (0.0%)	-	2 (3.3%)	[12]	3 (3.0%)	[13]	0.9 (2.8%)	[13]
	Risk of overdose	0 (0.0%)	-	4 (21.1%)	[1]	1 (4.2%)	[9]	0 (0.0%)	-	5 (8.3%)	[5]	5 (5.0%)	[8]	0.8 (2.6%)	[14]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	1 (2.5%)	[12]	1 (5.3%)	[7]	0 (0.0%)	-	1 (5.9%)	[8]	2 (3.3%)	[12]	3 (3.0%)	[13]	0.8 (2.5%)	[15]
	Keep away from children: Safe storage	1 (2.5%)	[12]	0 (0.0%)	-	1 (4.2%)	[9]	0 (0.0%)	-	1 (1.7%)	[15]	2 (2.0%)	[15]	0.8 (2.5%)	[16]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	0 (0.0%)	-	1 (5.3%)	[7]	3 (12.5%)	[3]	0 (0.0%)	-	4 (6.7%)	[8]	4 (4.0%)	[11]	0.7 (2.4%)	[17]
	Chronic pulmonary disease: Spe. Warnings, prec. for use	1 (2.5%)	[12]	1 (5.3%)	[7]	0 (0.0%)	-	0 (0.0%)	-	1 (1.7%)	[15]	2 (2.0%)	[15]	0.7 (2.3%)	[18]
	Hypersensitivity to Morphine or exipients: Contraindications	1 (2.5%)	[12]	1 (5.3%)	[7]	0 (0.0%)	-	0 (0.0%)	-	1 (1.7%)	[15]	2 (2.0%)	[15]	0.7 (2.3%)	[18]
	Do not know	1 (2.5%)	[12]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[8]	1 (1.7%)	[15]	2 (2.0%)	[15]	0.6 (2.0%)	[20]
	Psychiatric disorders (insomnia, dependence, hallucinations): Adverse reactions	1 (2.5%)	[12]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (1.0%)	[21]	0.6 (1.8%)	[21]
	Good tolerance	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[9]	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.6%)	[22]
	Not applicable	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[9]	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.6%)	[22]
	Need close monitoring	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[9]	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.6%)	[22]
	Only for cancer pain	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[9]	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.6%)	[22]
	Others: Adverse reactions	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[9]	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.6%)	[22]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[9]	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.6%)	[22]
	Nasal conditions/discomfort: Spec. Warnings, prec. for use	0 (0.0%)	-	1 (5.3%)	[7]	0 (0.0%)	-	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.5%)	[28]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	0 (0.0%)	-	1 (5.3%)	[7]	0 (0.0%)	-	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.5%)	[28]
	Pregnancy: Contraindications	0 (0.0%)	-	1 (5.3%)	[7]	0 (0.0%)	-	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.5%)	[28]
	Recurrent episodes of epistaxis: Contraindications	0 (0.0%)	-	1 (5.3%)	[7]	0 (0.0%)	-	0 (0.0%)	-	1 (1.7%)	[15]	1 (1.0%)	[21]	0.2 (0.5%)	[28]
	Cardiac disease: Spe. Warnings, prec. for use	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[8]	1 (1.7%)	[15]	1 (1.0%)	[21]	0.0 (0.1%)	[32]

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Elderly: Caution in special population	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[8]	1 (1.7%)	[15]	1 (1.0%)	[21]	0.0 (0.1%)	[32]
	Previous facial radiotherapy: Contraindications	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[8]	1 (1.7%)	[15]	1 (1.0%)	[21]	0.0 (0.1%)	[32]
Overall - unweighted results	.	(N=137)		(N=84)		(N=55)		(N=34)		(N=173)		(N=310)		-	
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	26 (19.0%)	[2]	13 (15.5%)	[2]	12 (21.8%)	[1]	8 (23.5%)	[1]	33 (19.1%)	[1]	59 (19.0%)	[1]	-	-
	Dosage: possible dose control / dosage easy	27 (19.7%)	[1]	13 (15.5%)	[2]	7 (12.7%)	[4]	7 (20.6%)	[3]	27 (15.6%)	[2]	54 (17.4%)	[2]	-	-
	Breakthrough pain: Indication	21 (15.3%)	[3]	8 (9.5%)	[6]	10 (18.2%)	[2]	6 (17.6%)	[4]	24 (13.9%)	[4]	45 (14.5%)	[3]	-	-
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	17 (12.4%)	[4]	7 (8.3%)	[8]	7 (12.7%)	[4]	3 (8.8%)	[7]	17 (9.8%)	[7]	34 (11.0%)	[7]	-	-
	Patient should understand well how to use safely the drug	13 (9.5%)	[7]	17 (20.2%)	[1]	6 (10.9%)	[6]	4 (11.8%)	[6]	27 (15.6%)	[2]	40 (12.9%)	[4]	-	-
	Instructions for Safe use explained by physician: mainly about dosage and frequency	14 (10.2%)	[5]	9 (10.7%)	[5]	8 (14.5%)	[3]	6 (17.6%)	[4]	23 (13.3%)	[5]	37 (11.9%)	[5]	-	-
	Nasal conditions/discomfort: Spe Warnings, prec. for use	14 (10.2%)	[5]	5 (6.0%)	[10]	1 (1.8%)	[21]	3 (8.8%)	[7]	9 (5.2%)	[12]	23 (7.4%)	[9]	-	-
	Nasal route admin.: accepted by / possible for the patient	12 (8.8%)	[8]	10 (11.9%)	[4]	5 (9.1%)	[8]	8 (23.5%)	[1]	23 (13.3%)	[5]	35 (11.3%)	[6]	-	-
	Risk of Respiratory depression: Spe. Warnings, prec. for use	9 (6.6%)	[12]	3 (3.6%)	[15]	6 (10.9%)	[6]	1 (2.9%)	[14]	10 (5.8%)	[10]	19 (6.1%)	[11]	-	-
	Recurrent episodes of epistaxis: Contraindications	11 (8.0%)	[9]	2 (2.4%)	[17]	1 (1.8%)	[21]	1 (2.9%)	[14]	4 (2.3%)	[22]	15 (4.8%)	[12]	-	-
	Previous facial radiotherapy: Contraindications	5 (3.6%)	[16]	1 (1.2%)	[29]	4 (7.3%)	[11]	2 (5.9%)	[11]	7 (4.0%)	[13]	12 (3.9%)	[15]	-	-
	Efficient	8 (5.8%)	[13]	2 (2.4%)	[17]	5 (9.1%)	[8]	0 (0.0%)	-	7 (4.0%)	[13]	15 (4.8%)	[12]	-	-
	Good tolerance	5 (3.6%)	[16]	2 (2.4%)	[17]	3 (5.5%)	[14]	0 (0.0%)	-	5 (2.9%)	[17]	10 (3.2%)	[18]	-	-
	Others: Adverse reactions	5 (3.6%)	[16]	2 (2.4%)	[17]	3 (5.5%)	[14]	0 (0.0%)	-	5 (2.9%)	[17]	10 (3.2%)	[18]	-	-
	Impaired renal or hepatic function: Spe Warnings, prec. for use	6 (4.4%)	[14]	3 (3.6%)	[15]	1 (1.8%)	[21]	1 (2.9%)	[14]	5 (2.9%)	[17]	11 (3.5%)	[16]	-	-
	Easy to use	11 (8.0%)	[9]	5 (6.0%)	[10]	5 (9.1%)	[8]	2 (5.9%)	[11]	12 (6.9%)	[9]	23 (7.4%)	[9]	-	-
	Quick action: rapid/fast response	11 (8.0%)	[9]	7 (8.3%)	[8]	4 (7.3%)	[11]	3 (8.8%)	[7]	14 (8.1%)	[8]	25 (8.1%)	[8]	-	-
	Only for cancer pain	4 (2.9%)	[20]	0 (0.0%)	-	3 (5.5%)	[14]	0 (0.0%)	-	3 (1.7%)	[26]	7 (2.3%)	[22]	-	-
	Safe use	6 (4.4%)	[14]	5 (6.0%)	[10]	1 (1.8%)	[21]	1 (2.9%)	[14]	7 (4.0%)	[13]	13 (4.2%)	[14]	-	-
	Cardiac disease: Spe. Warnings, prec. for use	3 (2.2%)	[21]	4 (4.8%)	[14]	0 (0.0%)	-	3 (8.8%)	[7]	7 (4.0%)	[13]	10 (3.2%)	[18]	-	-
	Elderly: Caution in special population	3 (2.2%)	[21]	1 (1.2%)	[29]	1 (1.8%)	[21]	1 (2.9%)	[14]	3 (1.7%)	[26]	6 (1.9%)	[23]	-	-

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Need close monitoring	3 (2.2%)	[21]	0 (0.0%)	-	2 (3.6%)	[17]	0 (0.0%)	-	2 (1.2%)	[34]	5 (1.6%)	[28]	-	-
	Nasal route admin.: not accepted/not understood by the patient	2 (1.5%)	[26]	2 (2.4%)	[17]	2 (3.6%)	[17]	0 (0.0%)	-	4 (2.3%)	[22]	6 (1.9%)	[23]	-	-
	No adverse events	5 (3.6%)	[16]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	5 (1.6%)	[28]	-	-
	Hypersensitivity to Morphine or exipients: Contraindications	3 (2.2%)	[21]	2 (2.4%)	[17]	1 (1.8%)	[21]	0 (0.0%)	-	3 (1.7%)	[26]	6 (1.9%)	[23]	-	-
	Pregnancy: Contraindications	2 (1.5%)	[26]	2 (2.4%)	[17]	1 (1.8%)	[21]	0 (0.0%)	-	3 (1.7%)	[26]	5 (1.6%)	[28]	-	-
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	2 (1.5%)	[26]	1 (1.2%)	[29]	1 (1.8%)	[21]	2 (5.9%)	[11]	4 (2.3%)	[22]	6 (1.9%)	[23]	-	-
	Risk of overdose	1 (0.7%)	[33]	8 (9.5%)	[6]	2 (3.6%)	[17]	0 (0.0%)	-	10 (5.8%)	[10]	11 (3.5%)	[16]	-	-
	Compliance	1 (0.7%)	[33]	2 (2.4%)	[17]	1 (1.8%)	[21]	1 (2.9%)	[14]	4 (2.3%)	[22]	5 (1.6%)	[28]	-	-
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	1 (0.7%)	[33]	1 (1.2%)	[29]	4 (7.3%)	[11]	0 (0.0%)	-	5 (2.9%)	[17]	6 (1.9%)	[23]	-	-
	Do not know	2 (1.5%)	[26]	0 (0.0%)	-	1 (1.8%)	[21]	1 (2.9%)	[14]	2 (1.2%)	[34]	4 (1.3%)	[33]	-	-
	Other	2 (1.5%)	[26]	1 (1.2%)	[29]	0 (0.0%)	-	0 (0.0%)	-	1 (0.6%)	[40]	3 (1.0%)	[35]	-	-
	Low risk of overdose	3 (2.2%)	[21]	5 (6.0%)	[10]	0 (0.0%)	-	0 (0.0%)	-	5 (2.9%)	[17]	8 (2.6%)	[21]	-	-
	Treatment of acute pain other than breakthrough pain: Contraindications	1 (0.7%)	[33]	1 (1.2%)	[29]	1 (1.8%)	[21]	0 (0.0%)	-	2 (1.2%)	[34]	3 (1.0%)	[35]	-	-
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	1 (0.7%)	[33]	0 (0.0%)	-	1 (1.8%)	[21]	0 (0.0%)	-	1 (0.6%)	[40]	2 (0.6%)	[41]	-	-
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	1 (0.7%)	[33]	2 (2.4%)	[17]	0 (0.0%)	-	1 (2.9%)	[14]	3 (1.7%)	[26]	4 (1.3%)	[33]	-	-
	Keep away from children: Safe storage	2 (1.5%)	[26]	2 (2.4%)	[17]	1 (1.8%)	[21]	0 (0.0%)	-	3 (1.7%)	[26]	5 (1.6%)	[28]	-	-
	Serotonin Syndrome: Spe. Warnings, prec. for use	0 (0.0%)	-	1 (1.2%)	[29]	1 (1.8%)	[21]	1 (2.9%)	[14]	3 (1.7%)	[26]	3 (1.0%)	[35]	-	-
	Store in dry and safe place: Safe storage	0 (0.0%)	-	1 (1.2%)	[29]	1 (1.8%)	[21]	1 (2.9%)	[14]	3 (1.7%)	[26]	3 (1.0%)	[35]	-	-
	Chronic pulmonary disease: Spe. Warnings, prec. for use	2 (1.5%)	[26]	1 (1.2%)	[29]	0 (0.0%)	-	0 (0.0%)	-	1 (0.6%)	[40]	3 (1.0%)	[35]	-	-
	Increased intracranial pressure: Spe. Warnings, prec. for use	1 (0.7%)	[33]	2 (2.4%)	[17]	0 (0.0%)	-	0 (0.0%)	-	2 (1.2%)	[34]	3 (1.0%)	[35]	-	-

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Psychiatric disorders (insomnia, dependence, hallucinations): Adverse reactions	1 (0.7%)	[33]	0 (0.0%)	-	1 (1.8%)	[21]	0 (0.0%)	-	1 (0.6%)	[40]	2 (0.6%)	[41]	-	-
	Not applicable	0 (0.0%)	-	0 (0.0%)	-	2 (3.6%)	[17]	0 (0.0%)	-	2 (1.2%)	[34]	2 (0.6%)	[41]	-	-
	General disorders and admin. site condition (pyrexia, fatigue, malaise, peripheral oedema): Adverse reactions	0 (0.0%)	-	2 (2.4%)	[17]	0 (0.0%)	-	0 (0.0%)	-	2 (1.2%)	[34]	2 (0.6%)	[41]	-	-
Overall - weighted results	.	(N=220)		(N=14)		(N=57)		(N=19)		(N=90)		-		(N=310)	
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	49.9 (22.7%)	[1]	2.3 (16.0%)	[2]	18.8 (33.0%)	[1]	7.6 (39.9%)	[1]	28.7 (31.7%)	[1]	-	-	78.6 (25.4%)	[1]
	Dosage: possible dose control / dosage easy	40.2 (18.3%)	[2]	2.3 (15.8%)	[3]	8.8 (15.5%)	[6]	5.5 (28.8%)	[3]	16.6 (18.4%)	[4]	-	-	56.8 (18.3%)	[2]
	Breakthrough pain: Indication	36.8 (16.8%)	[3]	1.4 (9.8%)	[6]	12.4 (21.8%)	[2]	4.4 (23.1%)	[4]	18.2 (20.2%)	[2]	-	-	55.0 (17.7%)	[3]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	33.1 (15.1%)	[4]	1.2 (8.4%)	[8]	10.3 (18.1%)	[4]	1.2 (6.1%)	[9]	12.7 (14.0%)	[7]	-	-	45.8 (14.8%)	[4]
	Patient should understand well how to use safely the drug	26.4 (12.0%)	[6]	3.0 (20.9%)	[1]	10.1 (17.8%)	[5]	4.3 (22.7%)	[5]	17.5 (19.3%)	[3]	-	-	43.9 (14.2%)	[5]
	Instructions for Safe use explained by physician: mainly about dosage and frequency	22.6 (10.3%)	[7]	1.6 (10.9%)	[5]	10.5 (18.5%)	[3]	2.3 (12.2%)	[7]	14.4 (15.9%)	[5]	-	-	37.0 (11.9%)	[6]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	28.5 (13.0%)	[5]	0.9 (6.0%)	[11]	1.7 (3.0%)	[19]	3.3 (17.0%)	[6]	5.8 (6.4%)	[10]	-	-	34.3 (11.1%)	[7]
	Nasal route admin.: accepted by / possible for the patient	15.6 (7.1%)	[10]	1.7 (11.9%)	[4]	5.4 (9.6%)	[9]	6.6 (34.5%)	[2]	13.7 (15.2%)	[6]	-	-	29.3 (9.5%)	[8]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	18.3 (8.3%)	[9]	0.5 (3.7%)	[15]	8.6 (15.2%)	[7]	1.1 (5.7%)	[12]	10.2 (11.3%)	[8]	-	-	28.5 (9.2%)	[9]
	Recurrent episodes of epistaxis: Contraindications	22.4 (10.2%)	[8]	0.3 (2.3%)	[25]	1.7 (3.0%)	[19]	1.1 (5.7%)	[12]	3.1 (3.4%)	[19]	-	-	25.5 (8.2%)	[10]
	Previous facial radiotherapy: Contraindications	10.2 (4.6%)	[15]	0.2 (1.2%)	[29]	6.8 (11.9%)	[8]	1.1 (5.9%)	[10]	8.1 (8.9%)	[9]	-	-	18.2 (5.9%)	[11]
	Efficient	10.4 (4.7%)	[14]	0.4 (2.5%)	[17]	3.9 (6.9%)	[10]	0.0 (0.0%)	-	4.3 (4.8%)	[11]	-	-	14.7 (4.7%)	[12]
	Good tolerance	10.2 (4.6%)	[15]	0.4 (2.5%)	[17]	3.6 (6.3%)	[11]	0.0 (0.0%)	-	3.9 (4.3%)	[12]	-	-	14.1 (4.5%)	[13]
	Others: Adverse reactions	10.2 (4.6%)	[15]	0.4 (2.5%)	[17]	3.6 (6.3%)	[11]	0.0 (0.0%)	-	3.9 (4.3%)	[12]	-	-	14.1 (4.5%)	[13]
	Impaired renal or hepatic function: Spe. Warnings, prec. for use	10.7 (4.9%)	[12]	0.5 (3.4%)	[16]	1.7 (3.0%)	[19]	1.1 (5.7%)	[12]	3.3 (3.6%)	[16]	-	-	14.0 (4.5%)	[15]
	Easy to use	12.1 (5.5%)	[11]	0.8 (5.8%)	[12]	1.0 (1.7%)	[33]	0.1 (0.4%)	[21]	1.9 (2.1%)	[32]	-	-	13.9 (4.5%)	[16]
	Quick action: rapid/fast response	10.6 (4.8%)	[13]	1.1 (7.9%)	[9]	0.8 (1.3%)	[34]	0.1 (0.6%)	[20]	2.0 (2.2%)	[26]	-	-	12.6 (4.1%)	[17]

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Only for cancer pain	8.1 (3.7%)	[19]	0.0 (0.0%)	-	3.6 (6.3%)	[11]	0.0 (0.0%)	-	3.6 (3.9%)	[15]	-	-	11.7 (3.8%)	[18]
	Safe use	9.3 (4.2%)	[18]	0.8 (5.8%)	[12]	0.2 (0.3%)	[35]	1.1 (5.7%)	[12]	2.1 (2.3%)	[25]	-	-	11.4 (3.7%)	[19]
	Cardiac disease: Spe. Warnings, prec. for use	6.1 (2.8%)	[21]	0.7 (4.9%)	[14]	0.0 (0.0%)	-	2.2 (11.6%)	[8]	2.9 (3.2%)	[23]	-	-	9.0 (2.9%)	[20]
	Elderly: Caution in special population	6.1 (2.8%)	[21]	0.2 (1.2%)	[29]	1.7 (3.0%)	[19]	0.0 (0.2%)	[22]	1.9 (2.1%)	[29]	-	-	8.0 (2.6%)	[21]
	Need close monitoring	6.1 (2.8%)	[21]	0.0 (0.0%)	-	1.9 (3.3%)	[16]	0.0 (0.0%)	-	1.9 (2.1%)	[30]	-	-	8.0 (2.6%)	[22]
	Nasal route admin.: not accepted/not understood by the patient	4.1 (1.9%)	[25]	0.4 (2.5%)	[17]	3.4 (5.9%)	[14]	0.0 (0.0%)	-	3.7 (4.1%)	[14]	-	-	7.8 (2.5%)	[23]
	No adverse events	7.2 (3.3%)	[20]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	7.2 (2.3%)	[24]
	Hypersensitivity to Morphine or exipients: Contraindications	4.6 (2.1%)	[24]	0.3 (2.3%)	[25]	1.7 (3.0%)	[19]	0.0 (0.0%)	-	2.0 (2.2%)	[27]	-	-	6.6 (2.1%)	[25]
	Pregnancy: Contraindications	4.1 (1.9%)	[25]	0.3 (2.3%)	[25]	1.7 (3.0%)	[19]	0.0 (0.0%)	-	2.0 (2.2%)	[27]	-	-	6.1 (2.0%)	[26]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	2.6 (1.2%)	[29]	0.2 (1.1%)	[35]	1.7 (3.0%)	[19]	1.1 (5.9%)	[10]	3.0 (3.3%)	[20]	-	-	5.6 (1.8%)	[27]
	Risk of overdose	2.0 (0.9%)	[33]	1.3 (9.2%)	[7]	1.9 (3.3%)	[16]	0.0 (0.0%)	-	3.2 (3.5%)	[17]	-	-	5.2 (1.7%)	[28]
	Compliance	2.0 (0.9%)	[33]	0.4 (2.5%)	[17]	1.7 (3.0%)	[19]	1.1 (5.7%)	[12]	3.1 (3.5%)	[18]	-	-	5.2 (1.7%)	[29]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	2.0 (0.9%)	[33]	0.2 (1.1%)	[35]	2.3 (4.0%)	[15]	0.0 (0.0%)	-	2.4 (2.7%)	[24]	-	-	4.4 (1.4%)	[30]
	Do not know	2.6 (1.2%)	[29]	0.0 (0.0%)	-	1.7 (3.0%)	[19]	0.0 (0.2%)	[22]	1.7 (1.9%)	[34]	-	-	4.3 (1.4%)	[31]
	Other	4.1 (1.9%)	[25]	0.2 (1.2%)	[29]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (0.2%)	[42]	-	-	4.2 (1.4%)	[32]
	Low risk of overdose	3.2 (1.4%)	[28]	0.9 (6.1%)	[10]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.9 (1.0%)	[38]	-	-	4.0 (1.3%)	[33]
	Treatment of acute pain other than breakthrough pain: Contraindications	2.0 (0.9%)	[33]	0.2 (1.2%)	[29]	1.7 (3.0%)	[19]	0.0 (0.0%)	-	1.9 (2.1%)	[33]	-	-	3.9 (1.3%)	[34]
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	2.0 (0.9%)	[33]	0.0 (0.0%)	-	1.7 (3.0%)	[19]	0.0 (0.0%)	-	1.7 (1.9%)	[35]	-	-	3.7 (1.2%)	[35]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	2.0 (0.9%)	[33]	0.3 (2.3%)	[25]	0.0 (0.0%)	-	1.1 (5.7%)	[12]	1.4 (1.6%)	[37]	-	-	3.4 (1.1%)	[36]
	Keep away from children: Safe storage	2.6 (1.2%)	[29]	0.4 (2.5%)	[17]	0.2 (0.3%)	[35]	0.0 (0.0%)	-	0.5 (0.6%)	[39]	-	-	3.1 (1.0%)	[37]
	Serotonin Syndrome: Spe. Warnings, prec. for use	0.0 (0.0%)	-	0.2 (1.2%)	[29]	1.7 (3.0%)	[19]	1.1 (5.7%)	[12]	2.9 (3.3%)	[21]	-	-	2.9 (1.0%)	[38]
	Store in dry and safe place: Safe storage	0.0 (0.0%)	-	0.2 (1.2%)	[29]	1.7 (3.0%)	[19]	1.1 (5.7%)	[12]	2.9 (3.3%)	[21]	-	-	2.9 (1.0%)	[38]
	Chronic pulmonary disease: Spe Warnings, prec. for use	2.6 (1.2%)	[29]	0.2 (1.1%)	[35]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (0.2%)	[43]	-	-	2.7 (0.9%)	[40]

Q3. What are the main safety considerations/measures of safety when thinking of prescribing Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Increased intracranial pressure: Spe. Warnings, prec. for use	2.0 (0.9%)	[33]	0.4 (2.5%)	[17]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.4 (0.4%)	[40]	-	-	2.4 (0.8%)	[41]
	Psychiatric disorders (insomnia, dependence, hallucinations): Adverse reactions	0.6 (0.3%)	[40]	0.0 (0.0%)	-	1.7 (3.0%)	[19]	0.0 (0.0%)	-	1.7 (1.9%)	[35]	-	-	2.2 (0.7%)	[42]
	Not applicable	0.0 (0.0%)	-	0.0 (0.0%)	-	1.9 (3.3%)	[16]	0.0 (0.0%)	-	1.9 (2.1%)	[30]	-	-	1.9 (0.6%)	[43]
	General disorders and admin. site condition (pyrexia, fatigue, malaise, peripheral oedema): Adverse reactions	0.0 (0.0%)	-	0.4 (2.5%)	[17]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.4 (0.4%)	[40]	-	-	0.4 (0.1%)	[44]

Note: The main safety considerations/measures of safety are displayed in the column 'Response'. Since it is an open-ended question, multiple answers were possible. Therefore, the total exceeds 100%.

Table 9.3.2-2 summarizes the overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.2-2: Main safety considerations/measures of safety cited by the physicians when thinking of prescribing Instanyl® - 95% CI for weighted percentages

Q3. What are the main safety considerations / measures of safety when thinking of prescribing Instanyl®?

Country		Weighted percent	95% Confidence Limits, Weighted percent
France	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	27.6%	[20.5% - 34.8%]
	Breakthrough pain: Indication	18.7%	[12.4% - 24.9%]
	Dosage: possible dose control / dosage easy	18.1%	[12.0% - 24.2%]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	16.0%	[10.1% - 22.0%]
	Patient should understand well how to use safely the drug	15.7%	[10.0% - 21.4%]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	12.2%	[6.9% - 17.5%]
	Instructions for Safe use explained by physician: mainly about dosage and frequency	12.2%	[7.0% - 17.4%]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	10.1%	[5.3% - 15.0%]
	Recurrent episodes of epistaxis: Contraindications	9.1%	[4.3% - 13.8%]
	Nasal route admin.: accepted by / possible for the patient	9.0%	[4.7% - 13.3%]
	Previous facial radiotherapy: Contraindications	6.5%	[2.6% - 10.4%]
	Good tolerance	5.0%	[1.4% - 8.5%]
	Others: Adverse reactions	5.0%	[1.4% - 8.5%]
	Impaired renal or hepatic function: Spe. Warnings, prec. for use	4.7%	[1.3% - 8.1%]
	Efficient	4.2%	[1.0% - 7.5%]
	Only for cancer pain	4.1%	[0.9% - 7.4%]
	Safe use	3.5%	[0.6% - 6.4%]
	Cardiac disease: Spe. Warnings, prec. for use	3.2%	[0.5% - 5.9%]
	Easy to use	3.1%	[0.3% - 5.9%]
	Elderly: Caution in special population	2.8%	[0.1% - 5.6%]
	Nasal route admin.: not accepted/not understood by the patient	2.8%	[0.2% - 5.4%]
	Need close monitoring	2.8%	[0.1% - 5.5%]
	Quick action: rapid/fast response	2.4%	[0.0% - 4.8%]

Q3. What are the main safety considerations / measures of safety when thinking of prescribing Instanyl®?

Country		Weighted percent	95% Confidence Limits, Weighted percent
	No adverse events	2.2%	[0.0% - 4.6%]
	Hypersensitivity to Morphine or exipients: Contraindications	2.1%	[0.0% - 4.5%]
	Pregnancy: Contraindications	2.1%	[0.0% - 4.5%]
	Compliance	1.8%	[0.0% - 3.9%]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	1.7%	[0.0% - 3.7%]
	Risk of overdose	1.6%	[0.0% - 3.5%]
	Other	1.5%	[0.0% - 3.5%]
	Treatment of acute pain other than breakthrough pain: Contraindications	1.4%	[0.0% - 3.3%]
	Do not know	1.3%	[0.0% - 3.2%]
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	1.3%	[0.0% - 3.2%]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	1.3%	[0.0% - 3.2%]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	1.2%	[0.0% - 2.8%]
	Serotonin Syndrome: Spe. Warnings, prec. for use	1.1%	[0.0% - 2.5%]
	Store in dry and safe place: Safe storage	1.1%	[0.0% - 2.5%]
	Low risk of overdose	1.0%	[0.0% - 2.5%]
	Increased intracranial pressure: Spe. Warnings, prec. for use	0.9%	[0.0% - 2.3%]
	Keep away from children: Safe storage	0.9%	[0.0% - 2.3%]
	Chronic pulmonary disease: Spe. Warnings, prec. for use	0.7%	[0.0% - 2.2%]
	Not applicable	0.6%	[0.0% - 1.8%]
	Psychiatric disorders (insomnia, dependence, hallucinations): Adverse reactions	0.6%	[0.0% - 1.8%]
	General disorders and admin. site condition (pyrexia, fatigue, malaise, peripheral oedema): Adverse reactions	0.1%	[0.0% - 0.3%]
Netherlands	Dosage: possible dose control / dosage easy	20.3%	[10.0% - 30.7%]
	Quick action: rapid/fast response	19.5%	[9.8% - 29.2%]
	Easy to use	17.2%	[8.0% - 26.5%]
	Nasal route admin.: accepted by / possible for the patient	13.5%	[5.0% - 22.1%]
	Instructions for Safe use explained by physician: mainly about dosage and frequency	9.6%	[2.4% - 16.8%]
	Breakthrough pain: Indication	9.5%	[2.2% - 16.7%]
	Efficient	9.2%	[2.0% - 16.4%]
	Safe use	5.3%	[0.0% - 10.6%]
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	4.4%	[0.0% - 9.6%]
	Low risk of overdose	3.7%	[0.0% - 8.7%]
	No adverse events	3.7%	[0.0% - 8.7%]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	3.2%	[0.0% - 7.2%]
	Impaired renal or hepatic function: Spe. Warnings, prec. for use	2.8%	[0.0% - 6.7%]
	Risk of overdose	2.6%	[0.2% - 5.0%]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	2.5%	[0.0% - 6.2%]
	Keep away from children: Safe storage	2.5%	[0.0% - 6.3%]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	2.4%	[0.0% - 4.8%]
	Chronic pulmonary disease: Spe. Warnings, prec. for use	2.3%	[0.0% - 6.1%]
	Hypersensitivity to Morphine or exipients: Contraindications	2.3%	[0.0% - 6.1%]
	Do not know	2.0%	[0.0% - 5.6%]
	Psychiatric disorders (insomnia, dependence, hallucinations): Adverse reactions	1.8%	[0.0% - 5.4%]
	Good tolerance	0.6%	[0.0% - 1.9%]
	Not applicable	0.6%	[0.0% - 1.9%]
	Need close monitoring	0.6%	[0.0% - 1.9%]

Country	Q3. What are the main safety considerations / measures of safety when thinking of prescribing Instanyl®?	Weighted percent	95% Confidence Limits, Weighted percent
	Only for cancer pain	0.6%	[0.0% - 1.9%]
	Others: Adverse reactions	0.6%	[0.0% - 1.9%]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	0.6%	[0.0% - 1.9%]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	0.5%	[0.0% - 1.5%]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	0.5%	[0.0% - 1.5%]
	Pregnancy: Contraindications	0.5%	[0.0% - 1.5%]
	Recurrent episodes of epistaxis: Contraindications	0.5%	[0.0% - 1.5%]
	Cardiac disease: Spe. Warnings, prec. for use	0.1%	[0.0% - 0.4%]
	Elderly: Caution in special population	0.1%	[0.0% - 0.4%]
	Previous facial radiotherapy: Contraindications	0.1%	[0.0% - 0.4%]
Overall - weighted results	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	25.4%	[18.9% - 31.8%]
	Dosage: possible dose control / dosage easy	18.3%	[12.7% - 23.9%]
	Breakthrough pain: Indication	17.7%	[12.1% - 23.4%]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	14.8%	[9.4% - 20.1%]
	Patient should understand well how to use safely the drug	14.2%	[9.0% - 19.3%]
	Instructions for Safe use explained by physician: mainly about dosage and frequency	11.9%	[7.2% - 16.6%]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	11.1%	[6.3% - 15.8%]
	Nasal route admin.: accepted by / possible for the patient	9.5%	[5.5% - 13.4%]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	9.2%	[4.8% - 13.6%]
	Recurrent episodes of epistaxis: Contraindications	8.2%	[4.0% - 12.5%]
	Previous facial radiotherapy: Contraindications	5.9%	[2.3% - 9.4%]
	Efficient	4.7%	[1.7% - 7.8%]
	Good tolerance	4.5%	[1.4% - 7.7%]
	Others: Adverse reactions	4.5%	[1.4% - 7.7%]
	Impaired renal or hepatic function: Spe. Warnings, prec. for use	4.5%	[1.4% - 7.6%]
	Easy to use	4.5%	[1.8% - 7.2%]
	Quick action: rapid/fast response	4.1%	[1.6% - 6.5%]
	Only for cancer pain	3.8%	[0.8% - 6.7%]
	Safe use	3.7%	[1.0% - 6.4%]
	Cardiac disease: Spe. Warnings, prec. for use	2.9%	[0.5% - 5.3%]
	Elderly: Caution in special population	2.6%	[0.1% - 5.0%]
	Need close monitoring	2.6%	[0.1% - 5.0%]
	Nasal route admin.: not accepted/not understood by the patient	2.5%	[0.2% - 4.9%]
	No adverse events	2.3%	[0.1% - 4.6%]
	Hypersensitivity to Morphine or exipients: Contraindications	2.1%	[0.0% - 4.3%]
	Pregnancy: Contraindications	2.0%	[0.0% - 4.1%]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	1.8%	[0.0% - 3.6%]
	Risk of overdose	1.7%	[0.0% - 3.4%]
	Compliance	1.7%	[0.0% - 3.5%]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	1.4%	[0.0% - 3.1%]
	Do not know	1.4%	[0.0% - 3.1%]
	Other	1.4%	[0.0% - 3.2%]
	Low risk of overdose	1.3%	[0.0% - 2.7%]
	Treatment of acute pain other than breakthrough pain: Contraindications	1.3%	[0.0% - 2.9%]
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	1.2%	[0.0% - 2.9%]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	1.1%	[0.0% - 2.6%]

Q3. What are the main safety considerations / measures of safety when thinking of prescribing Instanyl®?

Country	Weighted percent	95% Confidence Limits, Weighted percent
Keep away from children: Safe storage	1.0%	[0.0% - 2.4%]
Serotonin Syndrome: Spe Warnings, prec. for use	1.0%	[0.0% - 2.2%]
Store in dry and safe place: Safe storage	1.0%	[0.0% - 2.2%]
Chronic pulmonary disease: Spe. Warnings, prec. for use	0.9%	[0.0% - 2.2%]
Increased intracranial pressure: Spe. Warnings, prec. for use	0.8%	[0.0% - 2.1%]
Psychiatric disorders (insomnia, dependence, hallucinations): Adverse reactions	0.7%	[0.0% - 1.9%]
Not applicable	0.6%	[0.0% - 1.7%]
General disorders and admin. site condition (pyrexia, fatigue, malaise, peripheral oedema): Adverse reactions	0.1%	[0.0% - 0.3%]

Reasons for not prescribing Instanyl®

Q4 of section 2 asked: When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons for non-prescription? The responses are shown in Table 9.3.2-3. The main reasons given for deciding not to prescribe Instanyl®:

- 22.2%: Other forms/other alternatives preferred
- 21.4%: Other drugs/other alternatives available/ satisfied with other agents
- 16.1%: Nasal route administration not accepted / not understood by the patient
- 10.1%: Patient's wish
- 9.5%: Physician or hospital/clinic did not use Instanyl®.

A range of other reasons were also provided (by less than 10% of physicians for each), most relating to known safety concerns such as use in the elderly, no background maintenance opioid therapy, not indicated because patient not presenting with breakthrough cancer pain, patient had epistaxis, mucositis, respiratory conditions, and risk of overdose, addiction, abuse or dependence.

Table 9.3.2-3: Reasons for non-prescription of Instanyl® within the last 6 months

(Basis = Physicians with complete analysable questionnaire)

Q4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
France	.	(N=97)		(N=65)		(N=31)		(N=17)		(N=113)		(N=210)		(N=279)	
	Other forms: other alternatives preferred	21 (21.6%)	[1]	16 (24.6%)	[1]	7 (22.6%)	[2]	6 (35.3%)	[1]	29 (25.7%)	[1]	50 (23.8%)	[1]	63.8 (22.8%)	[1]
	Other drugs: other alternatives available/ satisfied with other agents	18 (18.6%)	[2]	14 (21.5%)	[2]	11 (35.5%)	[1]	3 (17.6%)	[3]	28 (24.8%)	[2]	46 (21.9%)	[2]	60.9 (21.8%)	[2]
	Nasal route admin.: not accepted/not understood by the patient	17 (17.5%)	[3]	10 (15.4%)	[3]	5 (16.1%)	[3]	4 (23.5%)	[2]	19 (16.8%)	[3]	36 (17.1%)	[3]	49.1 (17.6%)	[3]
	Patient's wish	11 (11.3%)	[4]	2 (3.1%)	[11]	3 (9.7%)	[4]	2 (11.8%)	[4]	7 (6.2%)	[7]	18 (8.6%)	[5]	30.0 (10.7%)	[4]
	Do not use Instanyl	11 (11.3%)	[4]	5 (7.7%)	[4]	3 (9.7%)	[4]	1 (5.9%)	[10]	9 (8.0%)	[4]	20 (9.5%)	[4]	29.4 (10.5%)	[5]
	Not indicated: No breakthrough pain	8 (8.2%)	[6]	3 (4.6%)	[8]	2 (6.5%)	[6]	0 (0.0%)	-	5 (4.4%)	[9]	13 (6.2%)	[7]	20.2 (7.2%)	[6]
	Difficult to administer: nasal form	7 (7.2%)	[7]	5 (7.7%)	[4]	1 (3.2%)	[12]	2 (11.8%)	[4]	8 (7.1%)	[6]	15 (7.1%)	[6]	19.0 (6.8%)	[7]
	Patient not compliant	3 (3.1%)	[8]	5 (7.7%)	[4]	2 (6.5%)	[6]	2 (11.8%)	[4]	9 (8.0%)	[4]	12 (5.7%)	[8]	12.5 (4.5%)	[8]

Q4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Elderly: Caution in special population	3 (3.1%)	[8]	3 (4.6%)	[8]	1 (3.2%)	[12]	2 (11.8%)	[4]	6 (5.3%)	[8]	9 (4.3%)	[9]	10.5 (3.8%)	[9]
	Contraindications: other	3 (3.1%)	[8]	2 (3.1%)	[11]	1 (3.2%)	[12]	2 (11.8%)	[4]	5 (4.4%)	[9]	8 (3.8%)	[10]	10.3 (3.7%)	[10]
	Contraindicated: Patients without previous maintenance opioid therapy	3 (3.1%)	[8]	3 (4.6%)	[8]	1 (3.2%)	[12]	1 (5.9%)	[10]	5 (4.4%)	[9]	8 (3.8%)	[10]	9.4 (3.4%)	[11]
	Contraindications: e.g. mucositis	3 (3.1%)	[8]	4 (6.2%)	[7]	0 (0.0%)	-	1 (5.9%)	[10]	5 (4.4%)	[9]	8 (3.8%)	[10]	7.9 (2.8%)	[12]
	Contraindications: Respiratory affection	2 (2.1%)	[17]	2 (3.1%)	[11]	2 (6.5%)	[6]	0 (0.0%)	-	4 (3.5%)	[14]	6 (2.9%)	[13]	7.8 (2.8%)	[13]
	Needs accurate instructions	2 (2.1%)	[17]	2 (3.1%)	[11]	2 (6.5%)	[6]	0 (0.0%)	-	4 (3.5%)	[14]	6 (2.9%)	[13]	7.8 (2.8%)	[13]
	Not available in the hospital	1 (1.0%)	[22]	1 (1.5%)	[18]	2 (6.5%)	[6]	2 (11.8%)	[4]	5 (4.4%)	[9]	6 (2.9%)	[13]	7.8 (2.8%)	[15]
	Adverse reactions of Morphine	3 (3.1%)	[8]	2 (3.1%)	[11]	0 (0.0%)	-	0 (0.0%)	-	2 (1.8%)	[16]	5 (2.4%)	[16]	6.5 (2.3%)	[16]
	Contraindications: e.g. nosebleeds	3 (3.1%)	[8]	2 (3.1%)	[11]	0 (0.0%)	-	0 (0.0%)	-	2 (1.8%)	[16]	5 (2.4%)	[16]	6.5 (2.3%)	[16]
	High price/cost	3 (3.1%)	[8]	1 (1.5%)	[18]	0 (0.0%)	-	0 (0.0%)	-	1 (0.9%)	[23]	4 (1.9%)	[18]	6.3 (2.2%)	[18]
	Do not know	3 (3.1%)	[8]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	3 (1.4%)	[19]	6.1 (2.2%)	[19]
	Risk of overdose	2 (2.1%)	[17]	0 (0.0%)	-	1 (3.2%)	[12]	0 (0.0%)	-	1 (0.9%)	[23]	3 (1.4%)	[19]	5.8 (2.1%)	[20]
	Not Applicable	2 (2.1%)	[17]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[10]	1 (0.9%)	[23]	3 (1.4%)	[19]	5.2 (1.8%)	[21]
	Other	2 (2.1%)	[17]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	2 (1.0%)	[24]	4.1 (1.5%)	[22]
	Route of administration: nasal	1 (1.0%)	[22]	1 (1.5%)	[18]	1 (3.2%)	[12]	0 (0.0%)	-	2 (1.8%)	[16]	3 (1.4%)	[19]	3.9 (1.4%)	[23]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	0 (0.0%)	-	0 (0.0%)	-	2 (6.5%)	[6]	0 (0.0%)	-	2 (1.8%)	[16]	2 (1.0%)	[24]	3.4 (1.2%)	[24]
	Contraindications: Severe respiratory depression or severe obstructive lung conditions	1 (1.0%)	[22]	1 (1.5%)	[18]	0 (0.0%)	-	1 (5.9%)	[10]	2 (1.8%)	[16]	3 (1.4%)	[19]	3.3 (1.2%)	[25]
	Adverse reactions: e.g. nose irritations	0 (0.0%)	-	0 (0.0%)	-	1 (3.2%)	[12]	1 (5.9%)	[10]	2 (1.8%)	[16]	2 (1.0%)	[24]	2.8 (1.0%)	[26]
	Contraindications: Cardiac insufficiency	1 (1.0%)	[22]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (0.5%)	[28]	2.0 (0.7%)	[27]
	Contraindications: Renal insufficiency	0 (0.0%)	-	2 (3.1%)	[11]	0 (0.0%)	-	0 (0.0%)	-	2 (1.8%)	[16]	2 (1.0%)	[24]	0.4 (0.1%)	[28]
The Netherlands	.	(N=40)		(N=19)		(N=24)		(N=17)		(N=60)		(N=100)		(N=31)	
	Not Applicable	9 (22.5%)	[1]	1 (5.3%)	[4]	2 (8.3%)	[4]	0 (0.0%)	-	3 (5.0%)	[6]	12 (12.0%)	[3]	5.6 (18.2%)	[1]
	Other drugs: other alternatives available/ satisfied with other agents	6 (15.0%)	[3]	6 (31.6%)	[1]	5 (20.8%)	[1]	7 (41.2%)	[1]	18 (30.0%)	[1]	24 (24.0%)	[1]	5.5 (18.0%)	[2]
	Other forms: other alternatives preferred	7 (17.5%)	[2]	4 (21.1%)	[2]	1 (4.2%)	[6]	6 (35.3%)	[2]	11 (18.3%)	[2]	18 (18.0%)	[2]	5.0 (16.2%)	[3]
	High price/cost	6 (15.0%)	[3]	0 (0.0%)	-	3 (12.5%)	[3]	0 (0.0%)	-	3 (5.0%)	[6]	9 (9.0%)	[4]	3.9 (12.9%)	[4]
	Contraindications: e.g. nosebleeds	3 (7.5%)	[5]	0 (0.0%)	-	1 (4.2%)	[6]	0 (0.0%)	-	1 (1.7%)	[10]	4 (4.0%)	[6]	1.9 (6.1%)	[5]
	Patient's wish	2 (5.0%)	[6]	0 (0.0%)	-	1 (4.2%)	[6]	0 (0.0%)	-	1 (1.7%)	[10]	3 (3.0%)	[9]	1.3 (4.3%)	[6]
	Needs accurate instructions	2 (5.0%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	2 (2.0%)	[11]	1.1 (3.7%)	[7]
	Not indicated: No breakthrough pain	1 (2.5%)	[8]	0 (0.0%)	-	2 (8.3%)	[4]	2 (11.8%)	[3]	4 (6.7%)	[3]	5 (5.0%)	[5]	1.0 (3.3%)	[8]

Q4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Nasal route admin.: not accepted/not understood by the patient	1 (2.5%)	[8]	1 (5.3%)	[4]	1 (4.2%)	[6]	0 (0.0%)	-	2 (3.3%)	[8]	3 (3.0%)	[9]	0.9 (3.0%)	[9]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	0 (0.0%)	-	0 (0.0%)	-	4 (16.7%)	[2]	0 (0.0%)	-	4 (6.7%)	[3]	4 (4.0%)	[6]	0.8 (2.5%)	[10]
	Difficult to administer: nasal form	1 (2.5%)	[8]	1 (5.3%)	[4]	0 (0.0%)	-	0 (0.0%)	-	1 (1.7%)	[10]	2 (2.0%)	[11]	0.7 (2.3%)	[11]
	Adverse reactions: e.g. nose irritations	1 (2.5%)	[8]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[4]	1 (1.7%)	[10]	2 (2.0%)	[11]	0.6 (2.0%)	[12]
	Contraindications: other	1 (2.5%)	[8]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (1.0%)	[15]	0.6 (1.8%)	[13]
	Do not know	1 (2.5%)	[8]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (1.0%)	[15]	0.6 (1.8%)	[13]
	Elderly: Caution in special population	0 (0.0%)	-	3 (15.8%)	[3]	0 (0.0%)	-	1 (5.9%)	[4]	4 (6.7%)	[3]	4 (4.0%)	[6]	0.5 (1.6%)	[15]
	Risk of overdose	0 (0.0%)	-	1 (5.3%)	[4]	1 (4.2%)	[6]	0 (0.0%)	-	2 (3.3%)	[8]	2 (2.0%)	[11]	0.3 (1.1%)	[16]
	Contraindicated: Patients without previous maintenance opioid therapy	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[6]	0 (0.0%)	-	1 (1.7%)	[10]	1 (1.0%)	[15]	0.2 (0.6%)	[17]
	Do not use Instanyl	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[6]	0 (0.0%)	-	1 (1.7%)	[10]	1 (1.0%)	[15]	0.2 (0.6%)	[17]
	Not available in the hospital	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[6]	0 (0.0%)	-	1 (1.7%)	[10]	1 (1.0%)	[15]	0.2 (0.6%)	[17]
	Long lasting effect	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[6]	0 (0.0%)	-	1 (1.7%)	[10]	1 (1.0%)	[15]	0.2 (0.6%)	[17]
	Contraindications: e.g. mucositis	0 (0.0%)	-	1 (5.3%)	[4]	0 (0.0%)	-	0 (0.0%)	-	1 (1.7%)	[10]	1 (1.0%)	[15]	0.2 (0.5%)	[21]
	Adverse reactions of Morphine	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[4]	1 (1.7%)	[10]	1 (1.0%)	[15]	0.0 (0.1%)	[22]
	Route of administration: nasal	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[4]	1 (1.7%)	[10]	1 (1.0%)	[15]	0.0 (0.1%)	[22]
Overall - unweighted results	.	(N=137)		(N=84)		(N=55)		(N=34)		(N=173)		(N=310)		-	
	Other forms: other alternatives preferred	28 (20.4%)	[1]	20 (23.8%)	[1]	8 (14.5%)	[2]	12 (35.3%)	[1]	40 (23.1%)	[2]	68 (21.9%)	[2]	-	-
	Other drugs: other alternatives available/ satisfied with other agents	24 (17.5%)	[2]	20 (23.8%)	[1]	16 (29.1%)	[1]	10 (29.4%)	[2]	46 (26.6%)	[1]	70 (22.6%)	[1]	-	-
	Nasal route admin.: not accepted/not understood by the patient	18 (13.1%)	[3]	11 (13.1%)	[3]	6 (10.9%)	[3]	4 (11.8%)	[3]	21 (12.1%)	[3]	39 (12.6%)	[3]	-	-
	Patient's wish	13 (9.5%)	[4]	2 (2.4%)	[11]	4 (7.3%)	[5]	2 (5.9%)	[5]	8 (4.6%)	[9]	21 (6.8%)	[4]	-	-
	Do not use Instanyl	11 (8.0%)	[5]	5 (6.0%)	[6]	4 (7.3%)	[5]	1 (2.9%)	[12]	10 (5.8%)	[4]	21 (6.8%)	[4]	-	-
	Not indicated: No breakthrough pain	9 (6.6%)	[7]	3 (3.6%)	[9]	4 (7.3%)	[5]	2 (5.9%)	[5]	9 (5.2%)	[6]	18 (5.8%)	[6]	-	-
	Difficult to administer: nasal form	8 (5.8%)	[9]	6 (7.1%)	[4]	1 (1.8%)	[16]	2 (5.9%)	[5]	9 (5.2%)	[6]	17 (5.5%)	[7]	-	-
	Patient not compliant	3 (2.2%)	[14]	5 (6.0%)	[6]	2 (3.6%)	[10]	2 (5.9%)	[5]	9 (5.2%)	[6]	12 (3.9%)	[11]	-	-
	Elderly: Caution in special population	3 (2.2%)	[14]	6 (7.1%)	[4]	1 (1.8%)	[16]	3 (8.8%)	[4]	10 (5.8%)	[4]	13 (4.2%)	[9]	-	-
	Contraindications: other	4 (2.9%)	[11]	2 (2.4%)	[11]	1 (1.8%)	[16]	2 (5.9%)	[5]	5 (2.9%)	[14]	9 (2.9%)	[12]	-	-
	Not Applicable	11 (8.0%)	[5]	1 (1.2%)	[18]	2 (3.6%)	[10]	1 (2.9%)	[12]	4 (2.3%)	[15]	15 (4.8%)	[8]	-	-
	High price/cost	9 (6.6%)	[7]	1 (1.2%)	[18]	3 (5.5%)	[8]	0 (0.0%)	-	4 (2.3%)	[15]	13 (4.2%)	[9]	-	-

Q4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Contraindicated: Patients without previous maintenance opioid therapy	3 (2.2%)	[14]	3 (3.6%)	[9]	2 (3.6%)	[10]	1 (2.9%)	[12]	6 (3.5%)	[10]	9 (2.9%)	[12]	-	-
	Needs accurate instructions	4 (2.9%)	[11]	2 (2.4%)	[11]	2 (3.6%)	[10]	0 (0.0%)	-	4 (2.3%)	[15]	8 (2.6%)	[16]	-	-
	Contraindications: e.g. nosebleeds	6 (4.4%)	[10]	2 (2.4%)	[11]	1 (1.8%)	[16]	0 (0.0%)	-	3 (1.7%)	[19]	9 (2.9%)	[12]	-	-
	Contraindications: e.g. mucositis	3 (2.2%)	[14]	5 (6.0%)	[6]	0 (0.0%)	-	1 (2.9%)	[12]	6 (3.5%)	[10]	9 (2.9%)	[12]	-	-
	Not available in the hospital	1 (0.7%)	[22]	1 (1.2%)	[18]	3 (5.5%)	[8]	2 (5.9%)	[5]	6 (3.5%)	[10]	7 (2.3%)	[17]	-	-
	Contraindications: Respiratory affection	2 (1.5%)	[19]	2 (2.4%)	[11]	2 (3.6%)	[10]	0 (0.0%)	-	4 (2.3%)	[15]	6 (1.9%)	[18]	-	-
	Do not know	4 (2.9%)	[11]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	4 (1.3%)	[22]	-	-
	Adverse reactions of Morphine	3 (2.2%)	[14]	2 (2.4%)	[11]	0 (0.0%)	-	1 (2.9%)	[12]	3 (1.7%)	[19]	6 (1.9%)	[18]	-	-
	Risk of overdose	2 (1.5%)	[19]	1 (1.2%)	[18]	2 (3.6%)	[10]	0 (0.0%)	-	3 (1.7%)	[19]	5 (1.6%)	[21]	-	-
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	0 (0.0%)	-	0 (0.0%)	-	6 (10.9%)	[3]	0 (0.0%)	-	6 (3.5%)	[10]	6 (1.9%)	[18]	-	-
	Other	2 (1.5%)	[19]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	2 (0.6%)	[26]	-	-
	Route of administration: nasal	1 (0.7%)	[22]	1 (1.2%)	[18]	1 (1.8%)	[16]	1 (2.9%)	[12]	3 (1.7%)	[19]	4 (1.3%)	[22]	-	-
	Adverse reactions: e.g. nose irritations	1 (0.7%)	[22]	0 (0.0%)	-	1 (1.8%)	[16]	2 (5.9%)	[5]	3 (1.7%)	[19]	4 (1.3%)	[22]	-	-
	Contraindications: Severe respiratory depression or severe obstructive lung conditions	1 (0.7%)	[22]	1 (1.2%)	[18]	0 (0.0%)	-	1 (2.9%)	[12]	2 (1.2%)	[24]	3 (1.0%)	[25]	-	-
	Contraindications: Cardiac insufficiency	1 (0.7%)	[22]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (0.3%)	[28]	-	-
	Contraindications: Renal insufficiency	0 (0.0%)	-	2 (2.4%)	[11]	0 (0.0%)	-	0 (0.0%)	-	2 (1.2%)	[24]	2 (0.6%)	[26]	-	-
	Long lasting effect	0 (0.0%)	-	0 (0.0%)	-	1 (1.8%)	[16]	0 (0.0%)	-	1 (0.6%)	[26]	1 (0.3%)	[28]	-	-
Overall - weighted results	.	(N=220)		(N=14)		(N=57)		(N=19)		(N=90)		-		(N=310)	
	Other forms: other alternatives preferred	46.6 (21.2%)	[1]	3.4 (23.9%)	[1]	12.0 (21.1%)	[2]	6.8 (35.3%)	[1]	22.2 (24.5%)	[2]	-	-	68.8 (22.2%)	[1]
	Other drugs: other alternatives available/ satisfied with other agents	40.0 (18.2%)	[2]	3.4 (23.6%)	[2]	19.5 (34.3%)	[1]	3.5 (18.5%)	[3]	26.4 (29.3%)	[1]	-	-	66.4 (21.4%)	[2]
	Nasal route admin.: not accepted/not understood by the patient	35.1 (16.0%)	[3]	1.9 (13.3%)	[3]	8.6 (15.2%)	[3]	4.3 (22.7%)	[2]	14.9 (16.5%)	[3]	-	-	50.0 (16.1%)	[3]
	Patient's wish	23.5 (10.7%)	[4]	0.4 (2.5%)	[11]	5.3 (9.2%)	[4]	2.2 (11.3%)	[5]	7.8 (8.6%)	[4]	-	-	31.3 (10.1%)	[4]
	Do not use Instanyl	22.4 (10.2%)	[5]	0.9 (6.1%)	[6]	5.3 (9.2%)	[4]	1.1 (5.7%)	[11]	7.2 (8.0%)	[5]	-	-	29.6 (9.5%)	[5]
	Not indicated: No breakthrough pain	16.8 (7.7%)	[6]	0.5 (3.7%)	[9]	3.8 (6.6%)	[7]	0.1 (0.4%)	[16]	4.4 (4.8%)	[10]	-	-	21.2 (6.8%)	[6]
	Difficult to administer: nasal form	14.8 (6.7%)	[7]	1.0 (7.2%)	[4]	1.7 (3.0%)	[14]	2.2 (11.3%)	[5]	4.9 (5.4%)	[8]	-	-	19.7 (6.3%)	[7]
	Patient not compliant	6.1 (2.8%)	[13]	0.9 (6.1%)	[6]	3.4 (5.9%)	[9]	2.2 (11.3%)	[5]	6.4 (7.1%)	[6]	-	-	12.5 (4.0%)	[8]
	Elderly: Caution in special population	6.1 (2.8%)	[13]	1.0 (6.9%)	[5]	1.7 (3.0%)	[14]	2.2 (11.6%)	[4]	4.9 (5.4%)	[9]	-	-	11.0 (3.5%)	[9]

Q4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Contraindications: other	6.7 (3.0%)	[11]	0.4 (2.5%)	[11]	1.7 (3.0%)	[14]	2.2 (11.3%)	[5]	4.2 (4.7%)	[11]	-	-	10.9 (3.5%)	[10]
	Not Applicable	9.1 (4.1%)	[9]	0.2 (1.1%)	[22]	0.4 (0.7%)	[20]	1.1 (5.7%)	[11]	1.6 (1.8%)	[20]	-	-	10.7 (3.5%)	[11]
	High price/cost	9.5 (4.3%)	[8]	0.2 (1.2%)	[18]	0.6 (1.0%)	[19]	0.0 (0.0%)	-	0.7 (0.8%)	[22]	-	-	10.2 (3.3%)	[12]
	Contraindicated: Patients without previous maintenance opioid therapy	6.1 (2.8%)	[13]	0.5 (3.7%)	[9]	1.9 (3.3%)	[12]	1.1 (5.7%)	[11]	3.5 (3.9%)	[15]	-	-	9.6 (3.1%)	[13]
	Needs accurate instructions	5.2 (2.4%)	[18]	0.4 (2.5%)	[11]	3.4 (5.9%)	[9]	0.0 (0.0%)	-	3.7 (4.1%)	[13]	-	-	8.9 (2.9%)	[14]
	Contraindications: e.g. nosebleeds	7.8 (3.5%)	[10]	0.4 (2.5%)	[11]	0.2 (0.3%)	[21]	0.0 (0.0%)	-	0.5 (0.6%)	[23]	-	-	8.3 (2.7%)	[15]
	Contraindications: e.g. mucositis	6.1 (2.8%)	[13]	0.9 (6.0%)	[8]	0.0 (0.0%)	-	1.1 (5.7%)	[11]	1.9 (2.1%)	[18]	-	-	8.0 (2.6%)	[16]
	Not available in the hospital	2.0 (0.9%)	[22]	0.2 (1.2%)	[18]	3.6 (6.3%)	[8]	2.2 (11.3%)	[5]	5.9 (6.5%)	[7]	-	-	7.9 (2.6%)	[17]
	Contraindications: Respiratory affection	4.1 (1.9%)	[19]	0.4 (2.5%)	[11]	3.4 (5.9%)	[9]	0.0 (0.0%)	-	3.7 (4.1%)	[13]	-	-	7.8 (2.5%)	[18]
	Do not know	6.7 (3.0%)	[11]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	6.7 (2.1%)	[19]
	Adverse reactions of Morphine	6.1 (2.8%)	[13]	0.4 (2.5%)	[11]	0.0 (0.0%)	-	0.0 (0.2%)	[17]	0.4 (0.4%)	[24]	-	-	6.5 (2.1%)	[20]
	Risk of overdose	4.1 (1.9%)	[19]	0.2 (1.1%)	[22]	1.9 (3.3%)	[12]	0.0 (0.0%)	-	2.0 (2.2%)	[17]	-	-	6.1 (2.0%)	[21]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	0.0 (0.0%)	-	0.0 (0.0%)	-	4.1 (7.3%)	[6]	0.0 (0.0%)	-	4.1 (4.6%)	[12]	-	-	4.1 (1.3%)	[22]
	Other	4.1 (1.9%)	[19]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	4.1 (1.3%)	[23]
	Route of administration: nasal	2.0 (0.9%)	[22]	0.2 (1.2%)	[18]	1.7 (3.0%)	[14]	0.0 (0.2%)	[17]	1.9 (2.1%)	[19]	-	-	3.9 (1.3%)	[24]
	Adverse reactions: e.g. nose irritations	0.6 (0.3%)	[26]	0.0 (0.0%)	-	1.7 (3.0%)	[14]	1.1 (5.9%)	[10]	2.8 (3.1%)	[16]	-	-	3.4 (1.1%)	[25]
	Contraindications: Severe respiratory depression or severe obstructive lung conditions	2.0 (0.9%)	[22]	0.2 (1.2%)	[18]	0.0 (0.0%)	-	1.1 (5.7%)	[11]	1.3 (1.4%)	[21]	-	-	3.3 (1.1%)	[26]
	Contraindications: Cardiac insufficiency	2.0 (0.9%)	[22]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	2.0 (0.7%)	[27]
	Contraindications: Renal insufficiency	0.0 (0.0%)	-	0.4 (2.5%)	[11]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.4 (0.4%)	[25]	-	-	0.4 (0.1%)	[28]
	Long lasting effect	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (0.3%)	[21]	0.0 (0.0%)	-	0.2 (0.2%)	[26]	-	-	0.2 (0.1%)	[29]

Note: The reasons of non prescription of Instanyl® are displayed in the column 'Response'. Since it is an open-ended question, multiple answers were possible. Therefore, the total exceeds 100%.

Table 9.3.2-4 summarizes the overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.2-4: Reasons for non-prescription of Instanyl® within the last 6 months: 95% CI for weighted percentages

Q4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?

Country		Weighted percent	95% Confidence Limits, Weighted percent
France	Other forms: other alternatives preferred	22.8%	[16.2% - 29.5%]
	Other drugs: other alternatives available/ satisfied with other agents	21.8%	[15.2% - 28.4%]

Q4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?

Country		Weighted percent	95% Confidence Limits, Weighted percent
	Nasal route admin.: not accepted/not understood by the patient	17.6%	[11.5% - 23.7%]
	Patient's wish	10.7%	[5.7% - 15.7%]
	Do not use Instanyl	10.5%	[5.6% - 15.5%]
	Not indicated: No breakthrough pain	7.2%	[3.0% - 11.5%]
	Difficult to administer: nasal form	6.8%	[2.8% - 10.8%]
	Patient not compliant	4.5%	[1.3% - 7.6%]
	Elderly: Caution in special population	3.8%	[0.8% - 6.7%]
	Contraindications: other	3.7%	[0.8% - 6.6%]
	Contraindicated: Patients without previous maintenance opioid therapy	3.4%	[0.5% - 6.2%]
	Contraindications: e.g. mucositis	2.8%	[0.2% - 5.4%]
	Contraindications: Respiratory affection	2.8%	[0.2% - 5.4%]
	Needs accurate instructions	2.8%	[0.2% - 5.4%]
	Not available in the hospital	2.8%	[0.3% - 5.2%]
	Adverse reactions of Morphine	2.3%	[0.0% - 4.8%]
	Contraindications: e.g. nosebleeds	2.3%	[0.0% - 4.8%]
	High price/cost	2.2%	[0.0% - 4.7%]
	Do not know	2.2%	[0.0% - 4.6%]
	Risk of overdose	2.1%	[0.0% - 4.4%]
	Not Applicable	1.8%	[0.0% - 4.0%]
	Other	1.5%	[0.0% - 3.5%]
	Route of administration: nasal	1.4%	[0.0% - 3.3%]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	1.2%	[0.0% - 2.9%]
	Contraindications: Severe respiratory depression or severe obstructive lung conditions	1.2%	[0.0% - 2.8%]
	Adverse reactions: e.g. nose irritations	1.0%	[0.0% - 2.4%]
	Contraindications: Cardiac insufficiency	0.7%	[0.0% - 2.2%]
	Contraindications: Renal insufficiency	0.1%	[0.0% - 0.3%]
Netherlands	Not Applicable	18.2%	[8.3% - 28.2%]
	Other drugs: other alternatives available/ satisfied with other agents	18.0%	[9.1% - 26.9%]
	Other forms: other alternatives preferred	16.2%	[7.1% - 25.3%]
	High price/cost	12.9%	[4.3% - 21.4%]
	Contraindications: e.g. nosebleeds	6.1%	[0.0% - 12.4%]
	Patient's wish	4.3%	[0.0% - 9.5%]
	Needs accurate instructions	3.7%	[0.0% - 8.7%]
	Not indicated: No breakthrough pain	3.3%	[0.0% - 7.4%]
	Nasal route admin.: not accepted/not understood by the patient	3.0%	[0.0% - 6.9%]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	2.5%	[0.0% - 5.0%]
	Difficult to administer: nasal form	2.3%	[0.0% - 6.1%]
	Adverse reactions: e.g. nose irritations	2.0%	[0.0% - 5.6%]
	Contraindications: other	1.8%	[0.0% - 5.4%]
	Do not know	1.8%	[0.0% - 5.4%]
	Elderly: Caution in special population	1.6%	[0.0% - 3.4%]
	Risk of overdose	1.1%	[0.0% - 2.7%]
	Contraindicated: Patients without previous maintenance opioid therapy	0.6%	[0.0% - 1.9%]
	Do not use Instanyl	0.6%	[0.0% - 1.9%]
	Not available in the hospital	0.6%	[0.0% - 1.9%]
	Long lasting effect	0.6%	[0.0% - 1.9%]
	Contraindications: e.g. mucositis	0.5%	[0.0% - 1.5%]
	Adverse reactions of Morphine	0.1%	[0.0% - 0.4%]
	Route of administration: nasal	0.1%	[0.0% - 0.4%]
Overall - weighted results	Other forms: other alternatives preferred	22.2%	[16.1% - 28.3%]
	Other drugs: other alternatives available/ satisfied with other agents	21.4%	[15.5% - 27.4%]

Q4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?

Country	Weighted percent	95% Confidence Limits, Weighted percent
Nasal route admin.: not accepted/not understood by the patient	16.1%	[10.6% - 21.6%]
Patient's wish	10.1%	[5.5% - 14.6%]
Do not use Instanyl	9.5%	[5.1% - 14.0%]
Not indicated: No breakthrough pain	6.8%	[3.0% - 10.7%]
Difficult to administer: nasal form	6.3%	[2.7% - 10.0%]
Patient not compliant	4.0%	[1.2% - 6.9%]
Elderly: Caution in special population	3.5%	[0.9% - 6.2%]
Contraindications: other	3.5%	[0.9% - 6.2%]
Not Applicable	3.5%	[1.2% - 5.7%]
High price/cost	3.3%	[0.9% - 5.7%]
Contraindicated: Patients without previous maintenance opioid therapy	3.1%	[0.5% - 5.6%]
Needs accurate instructions	2.9%	[0.5% - 5.3%]
Contraindications: e.g. nosebleeds	2.7%	[0.4% - 5.0%]
Contraindications: e.g. mucositis	2.6%	[0.3% - 4.9%]
Not available in the hospital	2.6%	[0.4% - 4.8%]
Contraindications: Respiratory affection	2.5%	[0.2% - 4.9%]
Do not know	2.1%	[0.0% - 4.4%]
Adverse reactions of Morphine	2.1%	[0.0% - 4.3%]
Risk of overdose	2.0%	[0.0% - 4.1%]
Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	1.3%	[0.0% - 2.9%]
Other	1.3%	[0.0% - 3.1%]
Route of administration: nasal	1.3%	[0.0% - 2.9%]
Adverse reactions: e.g. nose irritations	1.1%	[0.0% - 2.4%]
Contraindications: Severe respiratory depression or severe obstructive lung conditions	1.1%	[0.0% - 2.5%]
Contraindications: Cardiac insufficiency	0.7%	[0.0% - 1.9%]
Contraindications: Renal insufficiency	0.1%	[0.0% - 0.3%]
Long lasting effect	0.1%	[0.0% - 0.2%]

Use of Instanyl® in patients without cancer

Q5 of Section 2 asked: In the last 6 months, have you prescribed Instanyl® in patients without cancer pain? The responses are in Table 9.3.2-5.

Overall, 15.9% of physicians responded that they had prescribed Instanyl® in patients without cancer pain. The vast majority of physicians (84.5%) did not prescribe it to non-cancer patients.

There was marked variation by physician specialty. As expected, oncologists (9.7%, n=14) and radiologists (0%, n=19) had the lowest level of off-label use, as they specialise in treatment of cancer patients. Nevertheless, the samples are very low (n<40); the results and interpretations should be done with caution. Anesthesiologists (24.7%) had the highest level of off-label use. GP's off label use was intermediate between the specialist physicians.

Interpretation:
This observation reflects the broader group of patients managed by the anesthesiologists.

Table 9.3.2-5: Prescription of Instanyl® in patients without cancer within the last 6 months

(Basis = Physicians with complete analysable questionnaire)

Q5. In the last 6 months, have you prescribed Instanyl® in patients without cancer pain?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Yes	15 (15.5%)	7 (10.8%)	8 (25.8%)	0 (0.0%)	15 (13.3%)	30 (14.3%)	45.2 (16.2%)
95% Confidence Limits								[10.2% - 22.1%]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Yes	6 (15.0%)	1 (5.3%)	3 (12.5%)	0 (0.0%)	4 (6.7%)	10 (10.0%)	4.1 (13.4%)
95% Confidence Limits								[4.8% - 21.9%]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Yes	21 (15.3%)	8 (9.5%)	11 (20.0%)	0 (0.0%)	19 (11.0%)	40 (12.9%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Yes	33.9 (15.4%)	1.4 (9.7%)	14.1 (24.7%)	0.0 (0.0%)	15.5 (17.1%)	-	49.3 (15.9%)
95% Confidence Limits								[10.5% - 21.3%]

Q5a of Section 2 asked the 40 physicians who prescribed Instanyl® in patients without cancer pain: Why did they choose Instanyl® instead of another drug? Their reasons are listed below in Table 9.3.2-6 and Table 9.3.2-7.

The dominant answer (54.9%) was because Instanyl® was easy to use. Other answers included because of Instanyl's quick action, its efficacy, and because of the nasal administration route.

Table 9.3.2-6: Reasons of choosing Instanyl® instead of another drug

(Basis = Physicians with complete analysable questionnaire, who prescribed Instanyl® in patients without cancer pain and who answered 'Yes' to Q5)

Q5a. If yes, why did you choose Instanyl® instead of another drug?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
France	.	(N=15)		(N=7)		(N=8)		(N=0)		(N=15)		(N=30)		(N=45)	
	Easy to use	10 (66.7%)	[1]	2 (28.6%)	[3]	3 (37.5%)	[1]	-		5 (33.3%)	[2]	15 (50.0%)	[1]	25.7 (56.9%)	[1]
	Quick action: rapid/fast response	2 (13.3%)	[2]	3 (42.9%)	[2]	2 (25.0%)	[2]	-		5 (33.3%)	[2]	7 (23.3%)	[2]	8.0 (17.6%)	[2]
	Efficient	2 (13.3%)	[2]	1 (14.3%)	[4]	2 (25.0%)	[2]	-		3 (20.0%)	[4]	5 (16.7%)	[4]	7.6 (16.8%)	[3]
	Route of administration: nasal	1 (6.7%)	[5]	4 (57.1%)	[1]	2 (25.0%)	[2]	-		6 (40.0%)	[1]	7 (23.3%)	[2]	6.1 (13.5%)	[4]
	For severe pain (other than cancer pain)	2 (13.3%)	[2]	0 (0.0%)	-	1 (12.5%)	[6]	-		1 (6.7%)	[6]	3 (10.0%)	[5]	5.8 (12.7%)	[5]
	For breakthrough pain: indication	1 (6.7%)	[5]	0 (0.0%)	-	2 (25.0%)	[2]	-		2 (13.3%)	[5]	3 (10.0%)	[5]	5.4 (12.0%)	[6]
	Selective action	1 (6.7%)	[5]	0 (0.0%)	-	1 (12.5%)	[6]	-		1 (6.7%)	[6]	2 (6.7%)	[7]	3.7 (8.2%)	[7]
	Other	0 (0.0%)	-	0 (0.0%)	-	1 (12.5%)	[6]	-		1 (6.7%)	[6]	1 (3.3%)	[8]	1.7 (3.7%)	[8]
	Good tolerance	0 (0.0%)	-	1 (14.3%)	[4]	0 (0.0%)	-	-		1 (6.7%)	[6]	1 (3.3%)	[8]	0.2 (0.4%)	[9]
The Netherlands	.	(N=6)		(N=1)		(N=3)		(N=0)		(N=4)		(N=10)		(N=4)	
	Easy to use	2 (33.3%)	[1]	0 (0.0%)	-	1 (33.3%)	[1]	-		1 (25.0%)	[1]	3 (30.0%)	[1]	1.3 (32.1%)	[1]
	Route of administration: nasal	2 (33.3%)	[1]	1 (100.0%)	[1]	0 (0.0%)	-	-		1 (25.0%)	[1]	3 (30.0%)	[1]	1.3 (31.1%)	[2]

Q5a. If yes, why did you choose Instanyl® instead of another drug?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists	Specialists		All - Unweighted sample		All - Weighted sample	
	Quick action: rapid/fast response	1 (16.7%)	[3]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (10.0%)	[3]	0.6 (13.7%)	[3]
	For high speed operation	1 (16.7%)	[3]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (10.0%)	[3]	0.6 (13.7%)	[3]
	Nasal route admin.: not accepted/not understood by the patient	1 (16.7%)	[3]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (10.0%)	[3]	0.6 (13.7%)	[3]
	For severe pain (other than cancer pain)	0 (0.0%)	-	0 (0.0%)	-	1 (33.3%)	[1]	-	1 (25.0%)	[1]	1 (10.0%)	[3]	0.2 (4.7%)	[6]
	Safe use	0 (0.0%)	-	0 (0.0%)	-	1 (33.3%)	[1]	-	1 (25.0%)	[1]	1 (10.0%)	[3]	0.2 (4.7%)	[6]
Overall - unweighted results	.	(N=21)		(N=8)		(N=11)		(N=0)	(N=19)		(N=40)		-	
	Easy to use	12 (57.1%)	[1]	2 (25.0%)	[3]	4 (36.4%)	[1]	-	6 (31.6%)	[2]	18 (45.0%)	[1]	-	-
	Quick action: rapid/fast response	3 (14.3%)	[2]	3 (37.5%)	[2]	2 (18.2%)	[2]	-	5 (26.3%)	[3]	8 (20.0%)	[3]	-	-
	Efficient	2 (9.5%)	[4]	1 (12.5%)	[4]	2 (18.2%)	[2]	-	3 (15.8%)	[4]	5 (12.5%)	[4]	-	-
	Route of administration: nasal	3 (14.3%)	[2]	5 (62.5%)	[1]	2 (18.2%)	[2]	-	7 (36.8%)	[1]	10 (25.0%)	[2]	-	-
	For severe pain (other than cancer pain)	2 (9.5%)	[4]	0 (0.0%)	-	2 (18.2%)	[2]	-	2 (10.5%)	[5]	4 (10.0%)	[5]	-	-
	For breakthrough pain: indication	1 (4.8%)	[6]	0 (0.0%)	-	2 (18.2%)	[2]	-	2 (10.5%)	[5]	3 (7.5%)	[6]	-	-
	Selective action	1 (4.8%)	[6]	0 (0.0%)	-	1 (9.1%)	[7]	-	1 (5.3%)	[7]	2 (5.0%)	[7]	-	-
	Other	0 (0.0%)	-	0 (0.0%)	-	1 (9.1%)	[7]	-	1 (5.3%)	[7]	1 (2.5%)	[8]	-	-
	For high speed operation	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[8]	-	-
	Nasal route admin.: not accepted/not understood by the patient	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[8]	-	-
	Safe use	0 (0.0%)	-	0 (0.0%)	-	1 (9.1%)	[7]	-	1 (5.3%)	[7]	1 (2.5%)	[8]	-	-
	Good tolerance	0 (0.0%)	-	1 (12.5%)	[4]	0 (0.0%)	-	-	1 (5.3%)	[7]	1 (2.5%)	[8]	-	-
Overall - weighted results	.	(N=34)		(N=1)		(N=14)		(N=0)	(N=15)		-		(N=49)	
	Easy to use	21.5 (63.4%)	[1]	0.4 (25.4%)	[3]	5.3 (37.3%)	[1]	-	5.6 (36.3%)	[1]	-	-	27.1 (54.9%)	[1]
	Quick action: rapid/fast response	4.6 (13.7%)	[2]	0.5 (38.1%)	[2]	3.4 (24.0%)	[2]	-	3.9 (25.3%)	[3]	-	-	8.5 (17.3%)	[2]
	Efficient	4.1 (12.0%)	[3]	0.2 (12.7%)	[4]	3.4 (24.0%)	[2]	-	3.6 (23.0%)	[4]	-	-	7.6 (15.4%)	[3]
	Route of administration: nasal	3.2 (9.3%)	[5]	0.9 (61.9%)	[1]	3.4 (24.0%)	[2]	-	4.2 (27.4%)	[2]	-	-	7.4 (15.0%)	[4]
	For severe pain (other than cancer pain)	4.1 (12.0%)	[3]	0.0 (0.0%)	-	1.9 (13.3%)	[6]	-	1.9 (12.2%)	[6]	-	-	5.9 (12.1%)	[5]

Q5a. If yes, why did you choose Instanyl® instead of another drug? (Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)														
Country	n (%) [rank]	**GPs**		**Oncologists**		**Anesthesiologists**		**Radiologists**	**Specialists**		**All - Unweighted sample**		**All - Weighted sample**	
	For breakthrough pain: indication	2.0 (6.0%)	[6]	0.0 (0.0%)	-	3.4 (24.0%)	[2]	-	3.4 (21.8%)	[5]	-	-	5.4 (11.0%)	[6]
	Selective action	2.0 (6.0%)	[6]	0.0 (0.0%)	-	1.7 (12.0%)	[7]	-	1.7 (10.9%)	[7]	-	-	3.7 (7.5%)	[7]
	Other	0.0 (0.0%)	-	0.0 (0.0%)	-	1.7 (12.0%)	[7]	-	1.7 (10.9%)	[7]	-	-	1.7 (3.4%)	[8]
	For high speed operation	0.6 (1.7%)	[8]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-	-	-	0.6 (1.1%)	[9]
	Nasal route admin.: not accepted/not understood by the patient	0.6 (1.7%)	[8]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-	-	-	0.6 (1.1%)	[9]
	Safe use	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.4%)	[9]	-	0.2 (1.2%)	[9]	-	-	0.2 (0.4%)	[11]
	Good tolerance	0.0 (0.0%)	-	0.2 (12.7%)	[4]	0.0 (0.0%)	-	-	0.2 (1.1%)	[10]	-	-	0.2 (0.4%)	[12]

Notes: The reasons of choosing Instanyl® instead of another drug are displayed in the column 'Response'. Since it is an open-ended question, multiple answers were possible. Therefore, the total exceeds 100%.

Table 9.3.2-7 summarizes the overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.2-7: Reasons of choosing Instanyl® instead of another drug (Q5a) - 95% CI for weighted percentages

(Basis = Physicians with complete analysable questionnaire, who prescribed Instanyl® in patients without cancer pain and who answered 'Yes' to Q5)

Q5a. If yes, why did you choose Instanyl® instead of another drug?			
Country		**Weighted percent**	**95% Confidence Limits, Weighted percent**
France	Easy to use	56.9%	[36.0% - 77.8%]
	Quick action: rapid/fast response	17.6%	[1.9% - 33.4%]
	Efficient	16.8%	[1.1% - 32.6%]
	Route of administration: nasal	13.5%	[0.0% - 27.2%]
	For severe pain (other than cancer pain)	12.7%	[0.0% - 27.0%]
	For breakthrough pain: indication	12.0%	[0.0% - 25.5%]
	Selective action	8.2%	[0.0% - 19.9%]
	Other	3.7%	[0.0% - 11.4%]
	Good tolerance	0.4%	[0.0% - 1.2%]
The Netherlands	Easy to use	32.1%	[0.0% - 71.0%]
	Route of administration: nasal	31.1%	[0.0% - 69.9%]
	Quick action: rapid/fast response	13.7%	[0.0% - 43.8%]
	For high speed operation	13.7%	[0.0% - 43.8%]
	Nasal route admin.: not accepted/not understood by the patient	13.7%	[0.0% - 43.8%]
	For severe pain (other than cancer pain)	4.7%	[0.0% - 16.0%]
	Safe use	4.7%	[0.0% - 16.0%]
Overall - weighted results	Easy to use	54.9%	[35.7% - 74.0%]
	Quick action: rapid/fast response	17.3%	[2.9% - 31.7%]
	Efficient	15.4%	[1.2% - 29.7%]

Q5a. If yes, why did you choose Instanyl® instead of another drug?		
Country	**Weighted percent**	**95% Confidence Limits, Weighted percent**
Route of administration: nasal	15.0%	[2.3% - 27.7%]
For severe pain (other than cancer pain)	12.1%	[0.0% - 25.0%]
For breakthrough pain: indication	11.0%	[0.0% - 23.2%]
Selective action	7.5%	[0.0% - 18.1%]
Other	3.4%	[0.0% - 10.3%]
For high speed operation	1.1%	[0.0% - 3.5%]
Nasal route admin.: not accepted/not understood by the patient	1.1%	[0.0% - 3.5%]
Safe use	0.4%	[0.0% - 1.2%]
Good tolerance	0.4%	[0.0% - 1.1%]

Q5b of Section 2 asked the same 40 physicians who prescribed Instanyl® in patients without cancer pain: What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label? The responses are shown in Table 9.3.2-8 and Table 9.3.2-9.

The predominant answer was non cancer pain or pain not further specified:
- 27.5%: Pain other than cancer pain
- 13.5%: Pain, e.g. in rheumatoid arthritis patients
- 13.5%: Breakthrough pain
- 11.0%: Breakthrough pain other than cancer pain

7.2% responded they used off label in cancer patients without providing further details.

Several of the responses gave reasons for prescribing off label, and were similar to the reasons described in the previous question.

Table 9.3.2-8: Underlying conditions of the patients in whom the physician used Instanyl® off label

(Basis = Physicians with complete analysable questionnaire, who prescribed Instanyl® in patients without cancer pain and who answered 'Yes' to Q5)

Q5b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label? (Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)																	
Country	n (%) [rank]	**GPs**		**Oncologists**		**Anesthesiologists**		**Radiologists**		**Specialists**		**All - Unweighted sample**		**All - Weighted sample**	
France	.	(N=15)		(N=7)		(N=8)		(N=0)		(N=15)		(N=30)		(N=45)	
	Pain (other than cancer pain)	5 (33.3%)	[1]	0 (0.0%)	-	2 (25.0%)	[1]	-		2 (13.3%)	[2]	7 (23.3%)	[1]	13.5 (29.9%)	[1]
	Pain	3 (20.0%)	[2]	0 (0.0%)	-	0 (0.0%)	-	-			-	3 (10.0%)	[3]	6.1 (13.5%)	[2]
	Breakthrough Pain	2 (13.3%)	[3]	1 (14.3%)	[2]	1 (12.5%)	[4]	-		2 (13.3%)	[2]	4 (13.3%)	[2]	5.9 (13.1%)	[3]
	Breakthrough Pain (other than cancer pain)	1 (6.7%)	[5]	0 (0.0%)	-	2 (25.0%)	[1]	-		2 (13.3%)	[2]	3 (10.0%)	[3]	5.4 (12.0%)	[4]
	Elderly	2 (13.3%)	[3]	0 (0.0%)	-	0 (0.0%)	-	-			-	2 (6.7%)	[6]	4.1 (9.0%)	[5]
	Cancer	0 (0.0%)	-	1 (14.3%)	[2]	2 (25.0%)	[1]	-		3 (20.0%)	[1]	3 (10.0%)	[3]	3.6 (7.9%)	[6]
	Easy to use	1 (6.7%)	[5]	0 (0.0%)	-	0 (0.0%)	-	-			-	1 (3.3%)	[8]	2.0 (4.5%)	[7]
	Efficient	1 (6.7%)	[5]	0 (0.0%)	-	0 (0.0%)	-	-			-	1 (3.3%)	[8]	2.0 (4.5%)	[7]
	Not applicable	1 (6.7%)	[5]	0 (0.0%)	-	0 (0.0%)	-	-			-	1 (3.3%)	[8]	2.0 (4.5%)	[7]
	Quick action: rapid/fast response	1 (6.7%)	[5]	0 (0.0%)	-	0 (0.0%)	-	-			-	1 (3.3%)	[8]	2.0 (4.5%)	[7]
	Patient understood the treatment/compliant	0 (0.0%)	-	0 (0.0%)	-	1 (12.5%)	[4]	-		1 (6.7%)	[6]	1 (3.3%)	[8]	1.7 (3.7%)	[11]

Q5b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists	Specialists		All - Unweighted sample		All - Weighted sample	
	Form of administration/Oral route not possible	0 (0.0%)	-	2 (28.6%)	[1]	0 (0.0%)	-	-	2 (13.3%)	[2]	2 (6.7%)	[6]	0.4 (0.8%)	[12]
	Do not know/ recall	0 (0.0%)	-	1 (14.3%)	[2]	0 (0.0%)	-	-	1 (6.7%)	[6]	1 (3.3%)	[8]	0.2 (0.4%)	[13]
	Other	0 (0.0%)	-	1 (14.3%)	[2]	0 (0.0%)	-	-	1 (6.7%)	[6]	1 (3.3%)	[8]	0.2 (0.4%)	[13]
The Netherlands	.	(N=6)		(N=1)		(N=3)		(N=0)	(N=4)		(N=10)		(N=4)	
	Chronic pain syndrome	2 (33.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	-		-	2 (20.0%)	[1]	1.1 (27.4%)	[1]
	Pain	1 (16.7%)	[2]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (10.0%)	[2]	0.6 (13.7%)	[2]
	Decubitus	1 (16.7%)	[2]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (10.0%)	[2]	0.6 (13.7%)	[2]
	Tetraparesis	1 (16.7%)	[2]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (10.0%)	[2]	0.6 (13.7%)	[2]
	Compression fracture	1 (16.7%)	[2]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (10.0%)	[2]	0.6 (13.7%)	[2]
	Do not know/ recall	0 (0.0%)	-	0 (0.0%)	-	1 (33.3%)	[1]	-	1 (25.0%)	[1]	1 (10.0%)	[2]	0.2 (4.7%)	[6]
	Laparotomy	0 (0.0%)	-	0 (0.0%)	-	1 (33.3%)	[1]	-	1 (25.0%)	[1]	1 (10.0%)	[2]	0.2 (4.7%)	[6]
	Post-herpetic pain	0 (0.0%)	-	0 (0.0%)	-	1 (33.3%)	[1]	-	1 (25.0%)	[1]	1 (10.0%)	[2]	0.2 (4.7%)	[6]
	Trauma	0 (0.0%)	-	1 (100.0%)	[1]	0 (0.0%)	-	-	1 (25.0%)	[1]	1 (10.0%)	[2]	0.2 (3.7%)	[9]
Overall - unweighted results	.	(N=21)		(N=8)		(N=11)		(N=0)	(N=19)		(N=40)		-	
	Pain (other than cancer pain)	5 (23.8%)	[1]	0 (0.0%)	-	2 (18.2%)	[1]	-	2 (10.5%)	[2]	7 (17.5%)	[1]	-	-
	Pain	4 (19.0%)	[2]	0 (0.0%)	-	0 (0.0%)	-	-		-	4 (10.0%)	[2]	-	-
	Breakthrough Pain	2 (9.5%)	[3]	1 (12.5%)	[2]	1 (9.1%)	[4]	-	2 (10.5%)	[2]	4 (10.0%)	[2]	-	-
	Breakthrough Pain (other than cancer pain)	1 (4.8%)	[6]	0 (0.0%)	-	2 (18.2%)	[1]	-	2 (10.5%)	[2]	3 (7.5%)	[4]	-	-
	Elderly	2 (9.5%)	[3]	0 (0.0%)	-	0 (0.0%)	-	-		-	2 (5.0%)	[6]	-	-
	Cancer	0 (0.0%)	-	1 (12.5%)	[2]	2 (18.2%)	[1]	-	3 (15.8%)	[1]	3 (7.5%)	[4]	-	-
	Easy to use	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[10]	-	-
	Efficient	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[10]	-	-
	Not applicable	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[10]	-	-
	Quick action: rapid/fast response	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[10]	-	-
	Patient understood the treatment/compliant	0 (0.0%)	-	0 (0.0%)	-	1 (9.1%)	[4]	-	1 (5.3%)	[7]	1 (2.5%)	[10]	-	-
	Chronic pain syndrome	2 (9.5%)	[3]	0 (0.0%)	-	0 (0.0%)	-	-		-	2 (5.0%)	[6]	-	-
	Decubitus	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[10]	-	-
	Tetraparesis	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[10]	-	-
	Compression fracture	1 (4.8%)	[6]	0 (0.0%)	-	0 (0.0%)	-	-		-	1 (2.5%)	[10]	-	-
	Do not know/ recall	0 (0.0%)	-	1 (12.5%)	[2]	1 (9.1%)	[4]	-	2 (10.5%)	[2]	2 (5.0%)	[6]	-	-
	Form of administration/Oral route not possible	0 (0.0%)	-	2 (25.0%)	[1]	0 (0.0%)	-	-	2 (10.5%)	[2]	2 (5.0%)	[6]	-	-
	Laparotomy	0 (0.0%)	-	0 (0.0%)	-	1 (9.1%)	[4]	-	1 (5.3%)	[7]	1 (2.5%)	[10]	-	-
	Post-herpetic pain	0 (0.0%)	-	0 (0.0%)	-	1 (9.1%)	[4]	-	1 (5.3%)	[7]	1 (2.5%)	[10]	-	-
	Other	0 (0.0%)	-	1 (12.5%)	[2]	0 (0.0%)	-	-	1 (5.3%)	[7]	1 (2.5%)	[10]	-	-
	Trauma	0 (0.0%)	-	1 (12.5%)	[2]	0 (0.0%)	-	-	1 (5.3%)	[7]	1 (2.5%)	[10]	-	-
Overall - weighted results	.	(N=34)		(N=1)		(N=14)		(N=0)	(N=15)		-		(N=49)	
	Pain (other than cancer pain)	10.2 (30.0%)	[1]	0.0 (0.0%)	-	3.4 (24.0%)	[1]	-	3.4 (21.8%)	[2]	-	-	13.5 (27.5%)	[1]

Q5b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Pain	6.7 (19.7%)	[2]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	6.7 (13.5%)	[2]
	Breakthrough Pain	4.1 (12.0%)	[3]	0.2 (12.7%)	[2]	1.7 (12.0%)	[4]	-		1.9 (12.1%)	[4]	-	-	5.9 (12.0%)	[3]
	Breakthrough Pain (other than cancer pain)	2.0 (6.0%)	[5]	0.0 (0.0%)	-	3.4 (24.0%)	[1]	-		3.4 (21.8%)	[2]	-	-	5.4 (11.0%)	[4]
	Elderly	4.1 (12.0%)	[3]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	4.1 (8.2%)	[5]
	Cancer	0.0 (0.0%)	-	0.2 (12.7%)	[2]	3.4 (24.0%)	[1]	-		3.6 (23.0%)	[1]	-	-	3.6 (7.2%)	[6]
	Easy to use	2.0 (6.0%)	[5]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	2.0 (4.1%)	[7]
	Efficient	2.0 (6.0%)	[5]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	2.0 (4.1%)	[7]
	Not applicable	2.0 (6.0%)	[5]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	2.0 (4.1%)	[7]
	Quick action: rapid/fast response	2.0 (6.0%)	[5]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	2.0 (4.1%)	[7]
	Patient understood the treatment/compliant	0.0 (0.0%)	-	0.0 (0.0%)	-	1.7 (12.0%)	[4]	-		1.7 (10.9%)	[5]	-	-	1.7 (3.4%)	[11]
	Chronic pain syndrome	1.1 (3.3%)	[10]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	1.1 (2.3%)	[12]
	Decubitus	0.6 (1.7%)	[11]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	0.6 (1.1%)	[13]
	Tetraparesis	0.6 (1.7%)	[11]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	0.6 (1.1%)	[13]
	Compression fracture	0.6 (1.7%)	[11]	0.0 (0.0%)	-	0.0 (0.0%)	-	-		-		-	-	0.6 (1.1%)	[13]
	Do not know/ recall	0.0 (0.0%)	-	0.2 (12.7%)	[2]	0.2 (1.4%)	[6]	-		0.4 (2.4%)	[6]	-	-	0.4 (0.7%)	[16]
	Form of administration/Oral route not possible	0.0 (0.0%)	-	0.4 (25.4%)	[1]	0.0 (0.0%)	-	-		0.4 (2.3%)	[7]	-	-	0.4 (0.7%)	[17]
	Laparotomy	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.4%)	[6]	-		0.2 (1.2%)	[8]	-	-	0.2 (0.4%)	[18]
	Post-herpetic pain	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.4%)	[6]	-		0.2 (1.2%)	[8]	-	-	0.2 (0.4%)	[18]
	Other	0.0 (0.0%)	-	0.2 (12.7%)	[2]	0.0 (0.0%)	-	-		0.2 (1.1%)	[10]	-	-	0.2 (0.4%)	[20]
	Trauma	0.0 (0.0%)	-	0.2 (11.0%)	[6]	0.0 (0.0%)	-	-		0.2 (1.0%)	[11]	-	-	0.2 (0.3%)	[21]

Note: The underlying condition(s) of using Instanyl® off label are displayed in the column 'Response'. Since it is an open-ended question, multiple answers were possible. Therefore, the total exceeds 100%.

Table 9.3.2-9 summarizes the above overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.2-9: Underlying conditions of the patients in whom the physician used Instanyl® off label - 95% CI for weighted percentages

(Basis = Physicians with complete analysable questionnaire and who prescribed Instanyl® in patients without cancer pain)

Q5b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?

Country		Weighted percent	95% Confidence Limits, Weighted percent
France	Pain (other than cancer pain)	29.9%	[10.3% - 49.6%]
	Pain	13.5%	[0.0% - 28.5%]
	Breakthrough Pain	13.1%	[0.0% - 27.4%]
	Breakthrough Pain (other than cancer pain)	12.0%	[0.0% - 25.5%]
	Elderly	9.0%	[0.0% - 21.6%]
	Cancer	7.9%	[0.0% - 18.5%]

Q5b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?			
Country		**Weighted percent**	**95% Confidence Limits, Weighted percent**
	Easy to use	4.5%	[0.0% - 13.6%]
	Efficient	4.5%	[0.0% - 13.6%]
	Not applicable	4.5%	[0.0% - 13.6%]
	Quick action: rapid/fast response	4.5%	[0.0% - 13.6%]
	Patient understood the treatment/compliant	3.7%	[0.0% - 11.4%]
	Form of administration/Oral route not possible	0.8%	[0.0% - 2.0%]
	Do not know/ recall	0.4%	[0.0% - 1.2%]
	Other	0.4%	[0.0% - 1.2%]
The Netherlands	Chronic pain syndrome	27.4%	[0.0% - 65.9%]
	Pain	13.7%	[0.0% - 43.8%]
	Decubitus	13.7%	[0.0% - 43.8%]
	Tetraparesis	13.7%	[0.0% - 43.8%]
	Compression fracture	13.7%	[0.0% - 43.8%]
	Do not know/ recall	4.7%	[0.0% - 16.0%]
	Laparotomy	4.7%	[0.0% - 16.0%]
	Post-herpetic pain	4.7%	[0.0% - 16.0%]
	Trauma	3.7%	[0.0% - 12.8%]
Overall - weighted results	Pain (other than cancer pain)	27.5%	[9.6% - 45.3%]
	Pain	13.5%	[0.0% - 27.2%]
	Breakthrough Pain	12.0%	[0.0% - 25.0%]
	Breakthrough Pain (other than cancer pain)	11.0%	[0.0% - 23.2%]
	Elderly	8.2%	[0.0% - 19.6%]
	Cancer	7.2%	[0.0% - 16.8%]
	Easy to use	4.1%	[0.0% - 12.4%]
	Efficient	4.1%	[0.0% - 12.4%]
	Not applicable	4.1%	[0.0% - 12.4%]
	Quick action: rapid/fast response	4.1%	[0.0% - 12.4%]
	Patient understood the treatment/compliant	3.4%	[0.0% - 10.3%]
	Chronic pain syndrome	2.3%	[0.0% - 5.6%]
	Decubitus	1.1%	[0.0% - 3.5%]
	Tetraparesis	1.1%	[0.0% - 3.5%]
	Compression fracture	1.1%	[0.0% - 3.5%]
	Do not know/ recall	0.7%	[0.0% - 1.9%]
	Form of administration/Oral route not possible	0.7%	[0.0% - 1.8%]
	Laparotomy	0.4%	[0.0% - 1.2%]
	Post-herpetic pain	0.4%	[0.0% - 1.2%]
	Other	0.4%	[0.0% - 1.1%]
	Trauma	0.3%	[0.0% - 1.0%]

Use of Instanyl® in cancer patients without background maintenance opioid therapy:

All survey participants were asked in Q6 of Section 2: In last 6 months, have you prescribed Instanyl® to patients without maintenance therapy for chronic cancer pain? The responses are shown in Table 9.3.2-10.

Overall 85.3% reported they had not prescribed Instanyl® without a background of maintenance opioid therapy, only 14.7% responded that they had. Within GPs there was a slightly higher proportion who had prescribed Instanyl® without maintenance opioid therapy (16.6%) than among the specialists (10.0%).

Table 9.3.2-10: Prescription of Instanyl® in patients without maintenance opioid therapy for chronic cancer pain

(Basis = Physicians with complete analysable questionnaire)

Q6. In the last 6 months, have you prescribed Instanyl® in patients without maintenance opioid therapy for chronic cancer pain?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Yes	16 (16.5%)	8 (12.3%)	3 (9.7%)	2 (11.8%)	13 (11.5%)	29 (13.8%)	41 (14.7%)
95% Confidence Limits								[9.0% - 20.5%]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Yes	7 (17.5%)	1 (5.3%)	1 (4.2%)	2 (11.8%)	4 (6.7%)	11 (11.0%)	4 (14.2%)
95% Confidence Limits								[5.2% - 23.2%]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Yes	23 (16.8%)	9 (10.7%)	4 (7.3%)	4 (11.8%)	17 (9.8%)	40 (12.9%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Yes	36.5 (16.6%)	1.6 (10.9%)	5.3 (9.2%)	2.3 (11.8%)	9.1 (10.0%)	-	45.5 (14.7%)
95% Confidence Limits								[9.5% - 19.9%]

Of the 40 physicians who responded 'Yes' to prescribing Instanyl® without a background of maintenance opioid therapy, Q6a of Section 2 asked: why they chose Instanyl® instead of another drug? The responses are shown in Table 9.3.2-11 and Table 9.3.2-12

The range of responses was similar to those in the earlier Q5a which asked the reasons for using Instanyl® in non-cancer patients.
The predominant reasons were:

- 26.6%: Quick action; the response is rapid/fast
- 25.2%: The nasal form/route of administration is used in specific cases , e.g. when other routes are not possible
- 21.6%: It is easy to use
- 13.4%: It is efficient
- 10.9%: Used to relieve breakthrough pain, e.g. other than cancer pain.

One notable difference was in the Netherlands where 29.3% responded that the reason was 'the patient wish', this was the most frequently reported reason in the Netherlands.

Table 9.3.2-11: Reasons for choosing Instanyl® instead of another drug in patients without maintenance opioid therapy for chronic cancer pain

(Basis = Physicians with complete analysable questionnaire and who prescribed Instanyl® in patients without maintenance opioid therapy for chronic cancer pain)

Q6a. If yes, why did you choose Instanyl® instead of another drug?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
France	.	(N=16)		(N=8)		(N=3)		(N=2)		(N=13)		(N=29)		(N=41)	
	Quick action: rapid/fast response	4 (25.0%)	[1]	0 (0.0%)	-	1 (33.3%)	[1]	1 (50.0%)	[1]	2 (15.4%)	[4]	6 (20.7%)	[3]	10.9 (26.5%)	[1]
	Route of administration: nasal	4 (25.0%)	[1]	3 (37.5%)	[1]	1 (33.3%)	[1]	0 (0.0%)	-	4 (30.8%)	[1]	8 (27.6%)	[1]	10.3 (25.1%)	[2]

Q6a. If yes, why did you choose Instanyl® instead of another drug?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Easy to use	3 (18.8%)	[3]	2 (25.0%)	[2]	1 (33.3%)	[1]	1 (50.0%)	[1]	4 (30.8%)	[1]	7 (24.1%)	[2]	9.2 (22.4%)	[3]
	Other	3 (18.8%)	[3]	1 (12.5%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (7.7%)	[5]	4 (13.8%)	[4]	6.3 (15.2%)	[4]
	Efficient	3 (18.8%)	[3]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	3 (10.3%)	[6]	6.1 (14.8%)	[5]
	For breakthrough pain	1 (6.3%)	[6]	1 (12.5%)	[3]	1 (33.3%)	[1]	1 (50.0%)	[1]	3 (23.1%)	[3]	4 (13.8%)	[4]	5.0 (12.1%)	[6]
	For severe pain (other than cancer pain)	1 (6.3%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (3.4%)	[7]	2.0 (4.9%)	[7]
The Netherlands	.	(N=7)		(N=1)		(N=1)		(N=2)		(N=4)		(N=11)		(N=4)	
	Patient's wish	2 (28.6%)	[1]	1 (100.0%)	[1]	0 (0.0%)	-	0 (0.0%)	-	1 (25.0%)	[2]	3 (27.3%)	[2]	1.3 (29.3%)	[1]
	Quick action: rapid/fast response	2 (28.6%)	[1]	0 (0.0%)	-	0 (0.0%)	-	2 (100.0%)	[1]	2 (50.0%)	[1]	4 (36.4%)	[1]	1.2 (27.6%)	[2]
	Route of administration: nasal	2 (28.6%)	[1]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	2 (18.2%)	[3]	1.1 (25.8%)	[3]
	Dosage: possible dose control / dosage easy	1 (14.3%)	[4]	1 (100.0%)	[1]	0 (0.0%)	-	0 (0.0%)	-	1 (25.0%)	[2]	2 (18.2%)	[3]	0.7 (16.4%)	[4]
	Easy to use	1 (14.3%)	[4]	0 (0.0%)	-	0 (0.0%)	-	1 (50.0%)	[2]	1 (25.0%)	[2]	2 (18.2%)	[3]	0.6 (13.8%)	[5]
	No/few adverse events	1 (14.3%)	[4]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (9.1%)	[6]	0.6 (12.9%)	[6]
	Safe use	0 (0.0%)	-	0 (0.0%)	-	1 (100.0%)	[1]	0 (0.0%)	-	1 (25.0%)	[2]	1 (9.1%)	[6]	0.2 (4.4%)	[7]
Overall - unweighted results	.	(N=23)		(N=9)		(N=4)		(N=4)		(N=17)		(N=40)		-	
	Quick action: rapid/fast response	6 (26.1%)	[1]	0 (0.0%)	-	1 (25.0%)	[1]	3 (75.0%)	[1]	4 (23.5%)	[2]	10 (25.0%)	[1]	-	-
	Route of administration: nasal	6 (26.1%)	[1]	3 (33.3%)	[1]	1 (25.0%)	[1]	0 (0.0%)	-	4 (23.5%)	[2]	10 (25.0%)	[1]	-	-
	Easy to use	4 (17.4%)	[3]	2 (22.2%)	[2]	1 (25.0%)	[1]	2 (50.0%)	[2]	5 (29.4%)	[1]	9 (22.5%)	[3]	-	-
	Other	3 (13.0%)	[4]	1 (11.1%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[5]	4 (10.0%)	[4]	-	-
	Efficient	3 (13.0%)	[4]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	3 (7.5%)	[6]	-	-
	For breakthrough pain	1 (4.3%)	[7]	1 (11.1%)	[3]	1 (25.0%)	[1]	1 (25.0%)	[3]	3 (17.6%)	[4]	4 (10.0%)	[4]	-	-
	For severe pain (other than cancer pain)	1 (4.3%)	[7]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[9]	-	-
	Patient's wish	2 (8.7%)	[6]	1 (11.1%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[5]	3 (7.5%)	[6]	-	-
	Dosage: possible dose control / dosage easy	1 (4.3%)	[7]	1 (11.1%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[5]	2 (5.0%)	[8]	-	-
	No/few adverse events	1 (4.3%)	[7]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[9]	-	-
	Safe use	0 (0.0%)	-	0 (0.0%)	-	1 (25.0%)	[1]	0 (0.0%)	-	1 (5.9%)	[5]	1 (2.5%)	[9]	-	-
Overall - weighted results	.	(N=36)		(N=2)		(N=5)		(N=2)		(N=9)		-		(N=46)	
	Quick action: rapid/fast response	9.3 (25.4%)	[1]	0.0 (0.0%)	-	1.7 (32.1%)	[1]	1.2 (51.8%)	[1]	2.9 (31.5%)	[3]	-	-	12.1 (26.6%)	[1]
	Route of administration: nasal	9.3 (25.4%)	[1]	0.5 (33.8%)	[1]	1.7 (32.1%)	[1]	0.0 (0.0%)	-	2.2 (24.4%)	[4]	-	-	11.5 (25.2%)	[2]
	Easy to use	6.7 (18.3%)	[3]	0.4 (22.6%)	[2]	1.7 (32.1%)	[1]	1.1 (50.0%)	[2]	3.2 (34.9%)	[1]	-	-	9.8 (21.6%)	[3]
	Other	6.1 (16.7%)	[4]	0.2 (11.3%)	[3]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.9%)	[6]	-	-	6.3 (13.8%)	[4]
	Efficient	6.1 (16.7%)	[4]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	6.1 (13.4%)	[5]
	For breakthrough pain	2.0 (5.6%)	[6]	0.2 (11.3%)	[3]	1.7 (32.1%)	[1]	1.1 (48.2%)	[3]	2.9 (32.5%)	[2]	-	-	5.0 (10.9%)	[6]

Q6a. If yes, why did you choose Instanyl® instead of another drug? (Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)																
Country	n (%) [rank]	**GPs**		**Oncologists**		**Anesthesiologists**		**Radiologists**		**Specialists**		**All - Unweighted sample**			**All - Weighted sample**	
	For severe pain (other than cancer pain)	2.0 (5.6%)	[6]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-		2.0 (4.5%)	[7]
	Patient's wish	1.1 (3.1%)	[8]	0.2 (9.8%)	[5]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.7%)	[7]	-	-		1.3 (2.8%)	[8]
	Dosage: possible dose control / dosage easy	0.6 (1.5%)	[9]	0.2 (9.8%)	[5]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.7%)	[7]	-	-		0.7 (1.6%)	[9]
	No/few adverse events	0.6 (1.5%)	[9]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-		0.6 (1.2%)	[10]
	Safe use	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (3.6%)	[5]	0.0 (0.0%)	-	0.2 (2.1%)	[5]	-	-		0.2 (0.4%)	[11]

Notes: The reasons of choosing Instanyl® instead of another drug are displayed in the column 'Response'. Since it is an open-ended question, multiple answers were possible. Therefore, the total exceeds 100%.

Table 9.3.2-12 summarizes the above overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.2-12: Reasons of choosing Instanyl® instead of another drug - 95% CI for weighted percentages

Q6a. If yes, why did you choose Instanyl® instead of another drug?			
Country		**Weighted percent**	**95% Confidence Limits, Weighted percent**
France	Quick action: rapid/fast response	26.5%	[6.8% - 46.2%]
	Route of administration: nasal	25.1%	[5.8% - 44.5%]
	Easy to use	22.4%	[4.2% - 40.6%]
	Other	15.2%	[0.0% - 31.6%]
	Efficient	14.8%	[0.0% - 31.2%]
	For breakthrough pain	12.1%	[0.0% - 25.8%]
	For severe pain (other than cancer pain)	4.9%	[0.0% - 15.0%]
The Netherlands	Patient's wish	29.3%	[0.0% - 65.9%]
	Quick action: rapid/fast response	27.6%	[0.0% - 63.9%]
	Route of administration: nasal	25.8%	[0.0% - 62.0%]
	Dosage: possible dose control / dosage easy	16.4%	[0.0% - 45.2%]
	Easy to use	13.8%	[0.0% - 41.8%]
	No/few adverse events	12.9%	[0.0% - 40.9%]
	Safe use	4.4%	[0.0% - 14.8%]
Overall - weighted results	Quick action: rapid/fast response	26.6%	[8.9% - 44.3%]
	Route of administration: nasal	25.2%	[7.8% - 42.6%]
	Easy to use	21.6%	[5.2% - 38.0%]
	Other	13.8%	[0.0% - 28.4%]
	Efficient	13.4%	[0.0% - 28.0%]
	For breakthrough pain	10.9%	[0.0% - 23.1%]
	For severe pain (other than cancer pain)	4.5%	[0.0% - 13.4%]
	Patient's wish	2.8%	[0.0% - 6.5%]
	Dosage: possible dose control / dosage easy	1.6%	[0.0% - 4.2%]
	No/few adverse events	1.2%	[0.0% - 3.8%]
	Safe use	0.4%	[0.0% - 1.3%]

The same 40 physicians who prescribed Instanyl® without a background of maintenance opioid therapy were asked in Q6b of Section 2: what condition did these patients have? The responses are shown in Table 9.3.2-13 and Table 9.3.2-14.

The main conditions being treated were:
- 23.6%: General pain (23.6%)
- 20.3%: Pain other than cancer pain (20.3%)
- 13.4%: Breakthrough pain (13.4%)
- 10.2%: Cancer pain (10.2%).

Table 9.3.2-13: Underlying conditions of the patients in whom the physician used Instanyl® without maintenance opioid therapy for cancer pain

(Basis = Physicians with complete analysable questionnaire and who prescribed Instanyl® in patients without maintenance opioid therapy for chronic cancer pain)

Q6b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
France	.	(N=16)		(N=8)		(N=3)		(N=2)		(N=13)		(N=29)		(N=41)	
	Pain	3 (18.8%)	[2]	1 (12.5%)	[3]	2 (66.7%)	[1]	1 (50.0%)	[1]	4 (30.8%)	[1]	7 (24.1%)	[1]	10.7 (26.1%)	[1]
	Pain (other than cancer pain)	4 (25.0%)	[1]	0 (0.0%)	-	0 (0.0%)	-	1 (50.0%)	[1]	1 (7.7%)	[4]	5 (17.2%)	[2]	9.2 (22.4%)	[2]
	Breakthrough Pain	3 (18.8%)	[2]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	3 (10.3%)	[3]	6.1 (14.8%)	[3]
	Cancer	2 (12.5%)	[4]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	2 (6.9%)	[5]	4.1 (9.9%)	[4]
	Do not know/ recall	1 (6.3%)	[5]	2 (25.0%)	[1]	0 (0.0%)	-	0 (0.0%)	-	2 (15.4%)	[2]	3 (10.3%)	[3]	2.4 (5.8%)	[5]
	Drug efficient in this patient	1 (6.3%)	[5]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (3.4%)	[7]	2.0 (4.9%)	[6]
	Elderly	1 (6.3%)	[5]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (3.4%)	[7]	2.0 (4.9%)	[6]
	Other	0 (0.0%)	-	0 (0.0%)	-	1 (33.3%)	[2]	0 (0.0%)	-	1 (7.7%)	[4]	1 (3.4%)	[7]	1.7 (4.1%)	[8]
	Not applicable	0 (0.0%)	-	2 (25.0%)	[1]	0 (0.0%)	-	0 (0.0%)	-	2 (15.4%)	[2]	2 (6.9%)	[5]	0.4 (0.9%)	[9]
	Form of administration/Oral route not possible	0 (0.0%)	-	1 (12.5%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (7.7%)	[4]	1 (3.4%)	[7]	0.2 (0.4%)	[10]
	Patient understood the treatment/compliant	0 (0.0%)	-	1 (12.5%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (7.7%)	[4]	1 (3.4%)	[7]	0.2 (0.4%)	[10]
The Netherlands	.	(N=7)		(N=1)		(N=1)		(N=2)		(N=4)		(N=11)		(N=4)	
	Do not know/ recall	1 (14.3%)	[1]	1 (100.0%)	[1]	0 (0.0%)	-	0 (0.0%)	-	1 (25.0%)	[2]	2 (18.2%)	[1]	0.7 (16.4%)	[1]
	Cancer	1 (14.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (9.1%)	[3]	0.6 (12.9%)	[2]
	End-stage renal failure	1 (14.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (9.1%)	[3]	0.6 (12.9%)	[2]
	Metastatic liver cancer	1 (14.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (9.1%)	[3]	0.6 (12.9%)	[2]
	Oesophageal cancer	1 (14.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (9.1%)	[3]	0.6 (12.9%)	[2]
	Osteoarthritis	1 (14.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (9.1%)	[3]	0.6 (12.9%)	[2]
	Spondyloarthritis	1 (14.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (9.1%)	[3]	0.6 (12.9%)	[2]
	Laparotomy	0 (0.0%)	-	0 (0.0%)	-	1 (100.0%)	[1]	0 (0.0%)	-	1 (25.0%)	[2]	1 (9.1%)	[3]	0.2 (4.4%)	[8]
	Bone metastasis	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-	2 (100.0%)	[1]	2 (50.0%)	[1]	2 (18.2%)	[1]	0.1 (1.8%)	[9]
Overall - unweighted	.	(N=23)		(N=9)		(N=4)		(N=4)		(N=17)		(N=40)		-	
	Pain	3 (13.0%)	[2]	1 (11.1%)	[3]	2 (50.0%)	[1]	1 (25.0%)	[2]	4 (23.5%)	[1]	7 (17.5%)	[1]	-	-
	Pain (other than cancer pain)	4 (17.4%)	[1]	0 (0.0%)	-	0 (0.0%)	-	1 (25.0%)	[2]	1 (5.9%)	[5]	5 (12.5%)	[2]	-	-

Q6b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
results	Breakthrough Pain	3 (13.0%)	[2]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	3 (7.5%)	[4]	-	-
	Cancer	3 (13.0%)	[2]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	3 (7.5%)	[4]	-	-
	Do not know/ recall	2 (8.7%)	[5]	3 (33.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	3 (17.6%)	[2]	5 (12.5%)	[2]	-	-
	Drug efficient in this patient	1 (4.3%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[8]	-	-
	Elderly	1 (4.3%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[8]	-	-
	Other	0 (0.0%)	-	0 (0.0%)	-	1 (25.0%)	[2]	0 (0.0%)	-	1 (5.9%)	[5]	1 (2.5%)	[8]	-	-
	End-stage renal failure	1 (4.3%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[8]	-	-
	Metastatic liver cancer	1 (4.3%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[8]	-	-
	Oesophageal cancer	1 (4.3%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[8]	-	-
	Osteoarthritis	1 (4.3%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[8]	-	-
	Spondyloarthritis	1 (4.3%)	[6]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (2.5%)	[8]	-	-
	Not applicable	0 (0.0%)	-	2 (22.2%)	[2]	0 (0.0%)	-	0 (0.0%)	-	2 (11.8%)	[3]	2 (5.0%)	[6]	-	-
	Laparotomy	0 (0.0%)	-	0 (0.0%)	-	1 (25.0%)	[2]	0 (0.0%)	-	1 (5.9%)	[5]	1 (2.5%)	[8]	-	-
	Form of administration/Oral route not possible	0 (0.0%)	-	1 (11.1%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[5]	1 (2.5%)	[8]	-	-
	Patient understood the treatment/compliant	0 (0.0%)	-	1 (11.1%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[5]	1 (2.5%)	[8]	-	-
	Bone metastasis	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-	2 (50.0%)	[1]	2 (11.8%)	[3]	2 (5.0%)	[6]	-	-
Overall - weighted results	.	(N=36)		(N=2)		(N=5)		(N=2)		(N=9)		-		(N=46)	
	Pain	6.1 (16.7%)	[2]	0.2 (11.3%)	[3]	3.4 (64.2%)	[1]	1.1 (48.2%)	[1]	4.6 (51.2%)	[1]	-	-	10.7 (23.6%)	[1]
	Pain (other than cancer pain)	8.1 (22.3%)	[1]	0.0 (0.0%)	-	0.0 (0.0%)	-	1.1 (48.2%)	[1]	1.1 (12.0%)	[3]	-	-	9.2 (20.3%)	[2]
	Breakthrough Pain	6.1 (16.7%)	[2]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	6.1 (13.4%)	[3]
	Cancer	4.6 (12.7%)	[4]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	4.6 (10.2%)	[4]
	Do not know/ recall	2.6 (7.1%)	[5]	0.5 (32.3%)	[1]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.5 (5.6%)	[4]	-	-	3.1 (6.8%)	[5]
	Drug efficient in this patient	2.0 (5.6%)	[6]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	2.0 (4.5%)	[6]
	Elderly	2.0 (5.6%)	[6]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	2.0 (4.5%)	[6]
	Other	0.0 (0.0%)	-	0.0 (0.0%)	-	1.7 (32.1%)	[2]	0.0 (0.0%)	-	1.7 (18.6%)	[2]	-	-	1.7 (3.7%)	[8]
	End-stage renal failure	0.6 (1.5%)	[8]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	0.6 (1.2%)	[9]
	Metastatic liver cancer	0.6 (1.5%)	[8]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	0.6 (1.2%)	[9]
	Oesophageal cancer	0.6 (1.5%)	[8]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	0.6 (1.2%)	[9]
	Osteoarthritis	0.6 (1.5%)	[8]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	0.6 (1.2%)	[9]
	Spondyloarthritis	0.6 (1.5%)	[8]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	0.6 (1.2%)	[9]
	Not applicable	0.0 (0.0%)	-	0.4 (22.6%)	[2]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.4 (3.9%)	[5]	-	-	0.4 (0.8%)	[14]
	Laparotomy	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (3.6%)	[3]	0.0 (0.0%)	-	0.2 (2.1%)	[6]	-	-	0.2 (0.4%)	[15]
	Form of administration/Oral route not possible	0.0 (0.0%)	-	0.2 (11.3%)	[3]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.9%)	[7]	-	-	0.2 (0.4%)	[16]
	Patient understood the treatment/compliant	0.0 (0.0%)	-	0.2 (11.3%)	[3]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.9%)	[7]	-	-	0.2 (0.4%)	[16]

Q6b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label? (Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)																	
Country	n (%) [rank]	**GPs**		**Oncologists**		**Anesthesiologists**		**Radiologists**		**Specialists**		**All - Unweighted sample**		**All - Weighted sample**	
	Bone metastasis	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-	0.1 (3.6%)	[3]	0.1 (0.9%)	[9]	-	-	0.1 (0.2%)	[18]

Note: The underlying condition(s) of using Instanyl® off label are displayed in the column 'Response'. Since it is an open-ended question, multiple answers were possible. Therefore, the total exceeds 100%.

Table 9.3.2-14 summarizes the above overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.2-14: Underlying conditions of the patients in whom the physician used Instanyl® without maintenance opioid therapy - 95% CI for weighted percentages

Q6b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?			
Country		**Weighted percent**	**95% Confidence Limits, Weighted percent**
France	Pain	26.1%	[6.8% - 45.4%]
	Pain (other than cancer pain)	22.4%	[3.7% - 41.1%]
	Breakthrough Pain	14.8%	[0.0% - 31.2%]
	Cancer	9.9%	[0.0% - 23.6%]
	Do not know/ recall	5.8%	[0.0% - 15.9%]
	Drug efficient in this patient	4.9%	[0.0% - 15.0%]
	Elderly	4.9%	[0.0% - 15.0%]
	Other	4.1%	[0.0% - 12.5%]
	Not applicable	0.9%	[0.0% - 2.2%]
	Form of administration/Oral route not possible	0.4%	[0.0% - 1.3%]
	Patient understood the treatment/compliant	0.4%	[0.0% - 1.3%]
The Netherlands	Do not know/ recall	16.4%	[0.0% - 45.2%]
	Cancer	12.9%	[0.0% - 40.9%]
	End-stage renal failure	12.9%	[0.0% - 40.9%]
	Metastatic liver cancer	12.9%	[0.0% - 40.9%]
	Oesophageal cancer	12.9%	[0.0% - 40.9%]
	Osteoarthritis	12.9%	[0.0% - 40.9%]
	Spondyloarthritis	12.9%	[0.0% - 40.9%]
	Laparotomy	4.4%	[0.0% - 14.8%]
	Bone metastasis	1.8%	[0.0% - 5.2%]
Overall - weighted results	Pain	23.6%	[6.4% - 40.8%]
	Pain (other than cancer pain)	20.3%	[3.5% - 37.0%]
	Breakthrough Pain	13.4%	[0.0% - 28.0%]
	Cancer	10.2%	[0.0% - 22.6%]
	Do not know/ recall	6.8%	[0.0% - 16.1%]
	Drug efficient in this patient	4.5%	[0.0% - 13.4%]
	Elderly	4.5%	[0.0% - 13.4%]
	Other	3.7%	[0.0% - 11.2%]
	End-stage renal failure	1.2%	[0.0% - 3.8%]
	Metastatic liver cancer	1.2%	[0.0% - 3.8%]
	Oesophageal cancer	1.2%	[0.0% - 3.8%]
	Osteoarthritis	1.2%	[0.0% - 3.8%]
	Spondyloarthritis	1.2%	[0.0% - 3.8%]
	Not applicable	0.8%	[0.0% - 1.9%]

Q6b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?			
Country		**Weighted percent**	**95% Confidence Limits, Weighted percent**
	Laparotomy	0.4%	[0.0% - 1.3%]
	Form of administration/Oral route not possible	0.4%	[0.0% - 1.2%]
	Patient understood the treatment/compliant	0.4%	[0.0% - 1.2%]
	Bone metastasis	0.2%	[0.0% - 0.4%]

9.3.3 Understanding of the appropriate use of Instanyl®

Q7 of Section 2 assessed knowledge of the approved indication for Instanyl®. The physicians were asked: Which of the following condition(s) represent the approved indication(s) for Instanyl®:

a. Acute pain other than breakdown pain
b. Any short-term pain or any pain status
c. As a maintenance treatment for cancer pain
d. All episodes of breakthrough cancer pain
e. Episodes of breakthrough cancer pain and already receiving an opioid medication for chronic breakthrough pain.

Table 9.3.3-1: Percent of physicians that responded 'Yes' to each possible indication

(Basis = Physicians with complete analysable questionnaire)

Country	**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All- Unweighted sample**	**All - Weighted sample**
Q7a. Acute pain other than breakthrough pain?							
Yes	53.8 (24.5%)	3.3 (23.2%)	8.3 (14.5%)	2.4 (12.6%)	14.0 (15.5%)	-	67.8 (21.9%)
95% Confidence Limits							[15.8% - 27.9%]
Q7b. Any short-term pain or any pain status?							
Yes	42.6 (19.4%)	1.7 (12.1%)	4.1 (7.3%)	1.2 (6.5%)	7.1 (7.9%)	-	49.7 (16.0%)
95% Confidence Limits							[10.6% - 21.5%]
Q7c. As a maintenance treatment for cancer pain?							
Yes	16.5 (7.5%)	0.7 (4.9%)	2.1 (3.6%)	0.1 (0.4%)	2.9 (3.2%)	-	19.3 (6.2%)
95% Confidence Limits							[2.7% - 9.8%]
Q7d. All episodes of breakthrough cancer pain?							
Yes	148.1 (67.4%)	8.7 (60.8%)	28.4 (49.9%)	13.2 (68.9%)	50.3 (55.6%)	-	198.3 (64.0%)
95% Confidence Limits							[57.0% - 71.0%]
Q7e. **Episodes of breakthrough cancer pain and already receiving an opioid medication for chronic background pain**?							
Yes	218.0 (99.2%)	13.4 (93.5%)	50.9 (89.4%)	17.7 (92.7%)	82.0 (90.7%)	-	300.0 (96.8%)
95% Confidence Limits							[94.7% - 98.9%]

Overall 96.8% of physicians correctly identified (e) as the approved indication. There was some variation between physician specialties, with 99.2% of GPs correctly selecting (e) compared with only 89.4% of anaesthiologists.

In addition many also selected more than one indication. 64.0% had selected (d) which is close to the approved indication. The least scored answers were (c) as a maintenance treatment for cancer pain and (b) for any short-term pain or any pain status.

Interpretation:

These findings show a high level of physician awareness of the patient population in which Instanyl® should be used. Why 64% also indicated (d) is unclear. It most likely reflects the web design of the questionnaire with (d) being highly scored as it was the first option that mentioned breakthrough cancer pain and hence close to the approved indication.

It was encouraging that 99.0% of GPs correctly identified (e), as the GPs in this survey were mostly in private practice, which could result in isolation, whereas the specialist physicians were in hospitals and thus more able to share prescribing knowledge with colleagues.

The slightly lower response rate to (e) in anesthesiologists was interesting, as this group of physicians are probably the most highly trained and skilled in pain control.

Table 9.3.3-2 to Table 9.3.3-6 show the full set of responses per country and overall. It is to be noted that in France 100% of GPs ticked the correct answer.

Table 9.3.3-2: Condition(s) which represent the approved indications of Instanyl® - Acute pain other than breakthrough pain

(Basis = Physicians with complete analysable questionnaire)

Q7a. Which of the following condition(s) represent the approved indication(s) of Instanyl®: Acute pain other than breakthrough pain?

	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France							
	(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
No	64 (66.0%)	44 (67.7%)	27 (87.1%)	12 (70.6%)	83 (73.5%)	147 (70.0%)	196.5 (70.3%)
Yes	24 (24.7%)	18 (27.7%)	4 (12.9%)	2 (11.8%)	24 (21.2%)	48 (22.9%)	60.9 (21.8%)
95% Confidence Limits							[15.1% - 28.4%]
Do not know/recall	9 (9.3%)	3 (4.6%)	0 (0.0%)	3 (17.6%)	6 (5.3%)	15 (7.1%)	22.1 (7.9%)
Netherlands							
	(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
No	29 (72.5%)	13 (68.4%)	14 (58.3%)	7 (41.2%)	34 (56.7%)	63 (63.0%)	21.2 (69.3%)
Yes	9 (22.5%)	1 (5.3%)	8 (33.3%)	6 (35.3%)	15 (25.0%)	24 (24.0%)	7.0 (22.8%)
95% Confidence Limits							[12.6% - 33.0%]
Do not know/recall	2 (5.0%)	5 (26.3%)	2 (8.3%)	4 (23.5%)	11 (18.3%)	13 (13.0%)	2.4 (7.9%)
Overall - unweighted results							
	(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
No	93 (67.9%)	57 (67.9%)	41 (74.5%)	19 (55.9%)	117 (67.6%)	210 (67.7%)	-
Yes	33 (24.1%)	19 (22.6%)	12 (21.8%)	8 (23.5%)	39 (22.5%)	72 (23.2%)	-
Do not know/recall	11 (8.0%)	8 (9.5%)	2 (3.6%)	7 (20.6%)	17 (9.8%)	28 (9.0%)	-
Overall - weighted results							
	(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
No	146.4 (66.6%)	9.7 (67.8%)	48.2 (84.8%)	13.3 (69.5%)	71.3 (78.9%)	-	217.6 (70.2%)
Yes	53.8 (24.5%)	3.3 (23.2%)	8.3 (14.5%)	2.4 (12.6%)	14.0 (15.5%)	-	67.8 (21.9%)
95% Confidence Limits							[15.8% - 27.9%]
Do not know/recall	19.4 (8.8%)	1.3 (9.0%)	0.4 (0.7%)	3.4 (17.9%)	5.1 (5.6%)	-	24.5 (7.9%)

Table 9.3.3-3: Condition(s) which represent the approved indications of Instanyl® - Any short-term pain or any pain status

(Basis = Physicians with complete analysable questionnaire)

Q7b. Which of the following condition(s) represent the approved indication(s) of Instanyl®: Any short-term pain or any pain status?

	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France							
	(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
No	71 (73.2%)	54 (83.1%)	29 (93.5%)	16 (94.1%)	99 (87.6%)	170 (81.0%)	220.2 (78.8%)
Yes	19 (19.6%)	9 (13.8%)	2 (6.5%)	1 (5.9%)	12 (10.6%)	31 (14.8%)	44.7 (16.0%)
95% Confidence Limits							[10.0% - 22.0%]
Do not know/recall	7 (7.2%)	2 (3.1%)	0 (0.0%)	0 (0.0%)	2 (1.8%)	9 (4.3%)	14.6 (5.2%)
Netherlands							
	(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
No	29 (72.5%)	13 (68.4%)	19 (79.2%)	7 (41.2%)	39 (65.0%)	68 (68.0%)	22.1 (72.4%)
Yes	7 (17.5%)	1 (5.3%)	4 (16.7%)	4 (23.5%)	9 (15.0%)	16 (16.0%)	5.0 (16.4%)
95% Confidence Limits							[7.2% - 25.5%]
Do not know/recall	4 (10.0%)	5 (26.3%)	1 (4.2%)	6 (35.3%)	12 (20.0%)	16 (16.0%)	3.4 (11.2%)
Overall - unweighted results							
	(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
No	100 (73.0%)	67 (79.8%)	48 (87.3%)	23 (67.6%)	138 (79.8%)	238 (76.8%)	-
Yes	26 (19.0%)	10 (11.9%)	6 (10.9%)	5 (14.7%)	21 (12.1%)	47 (15.2%)	-
Do not know/recall	11 (8.0%)	7 (8.3%)	1 (1.8%)	6 (17.6%)	14 (8.1%)	25 (8.1%)	-
Overall - weighted results							
	(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
No	160.6 (73.1%)	11.5 (80.1%)	52.6 (92.4%)	17.6 (92.2%)	81.7 (90.4%)	-	242.3 (78.2%)
Yes	42.6 (19.4%)	1.7 (12.1%)	4.1 (7.3%)	1.2 (6.5%)	7.1 (7.9%)	-	49.7 (16.0%)
95% Confidence Limits							[10.6% - 21.5%]
Do not know/recall	16.5 (7.5%)	1.1 (7.8%)	0.2 (0.3%)	0.2 (1.3%)	1.5 (1.7%)	-	18.0 (5.8%)

Table 9.3.3-4: Condition(s) which represent the approved indications of Instanyl® - As a maintenance treatment for cancer pain

(Basis = Physicians with complete analysable questionnaire)

Q7c. Which of the following condition(s) represent the approved indication(s) of Instanyl®: As a maintenance treatment for cancer pain?

	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France							
	(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
No	90 (92.8%)	61 (93.8%)	29 (93.5%)	17 (100.0%)	107 (94.7%)	197 (93.8%)	261.1 (93.4%)
Yes	7 (7.2%)	4 (6.2%)	1 (3.2%)	0 (0.0%)	5 (4.4%)	12 (5.7%)	16.6 (5.9%)
95% Confidence Limits							[2.1% - 9.8%]
Do not know/recall	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	1 (0.9%)	1 (0.5%)	1.7 (0.6%)
Netherlands							
	(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
No	33 (82.5%)	16 (84.2%)	21 (87.5%)	12 (70.6%)	49 (81.7%)	82 (82.0%)	25.4 (83.1%)
Yes	4 (10.0%)	0 (0.0%)	2 (8.3%)	2 (11.8%)	4 (6.7%)	8 (8.0%)	2.7 (8.8%)
95% Confidence Limits							[1.7% - 16.0%]
Do not know/recall	3 (7.5%)	3 (15.8%)	1 (4.2%)	3 (17.6%)	7 (11.7%)	10 (10.0%)	2.4 (8.0%)
Overall - unweighted results							
	(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
No	123 (89.8%)	77 (91.7%)	50 (90.9%)	29 (85.3%)	156 (90.2%)	279 (90.0%)	-
Yes	11 (8.0%)	4 (4.8%)	3 (5.5%)	2 (5.9%)	9 (5.2%)	20 (6.5%)	-
Do not know/recall	3 (2.2%)	3 (3.6%)	2 (3.6%)	3 (8.8%)	8 (4.6%)	11 (3.5%)	-
Overall - weighted results							
	(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)

Q7c. Which of the following condition(s) represent the approved indication(s) of Instanyl®:
As a maintenance treatment for cancer pain?

	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
No	201.5 (91.7%)	13.2 (91.9%)	53.0 (93.1%)	18.9 (99.0%)	85.1 (94.1%)	-	286.5 (92.4%)
Yes	16.5 (7.5%)	0.7 (4.9%)	2.1 (3.6%)	0.1 (0.4%)	2.9 (3.2%)	-	19.3 (6.2%)
95% Confidence Limits							[2.7% - 9.8%]
Do not know/recall	1.7 (0.8%)	0.5 (3.2%)	1.9 (3.3%)	0.1 (0.6%)	2.5 (2.7%)	-	4.1 (1.3%)

Table 9.3.3-5: Condition(s) which represent the approved indications of Instanyl® - All episodes of breakthrough cancer pain

(Basis = Physicians with complete analysable questionnaire)

Q7d. Which of the following condition(s) represent the approved indication(s) of Instanyl®:
All episodes of breakthrough cancer pain?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	No	28 (28.9%)	23 (35.4%)	16 (51.6%)	4 (23.5%)	43 (38.1%)	71 (33.8%)	92.3 (33.0%)
	Yes	64 (66.0%)	40 (61.5%)	15 (48.4%)	12 (70.6%)	67 (59.3%)	131 (62.4%)	175.5 (62.8%)
	95% Confidence Limits							[55.1% - 70.5%]
	Do not know/recall	5 (5.2%)	2 (3.1%)	0 (0.0%)	1 (5.9%)	3 (2.7%)	8 (3.8%)	11.6 (4.2%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	No	4 (10.0%)	4 (21.1%)	7 (29.2%)	9 (52.9%)	20 (33.3%)	24 (24.0%)	4.5 (14.9%)
	Yes	32 (80.0%)	11 (57.9%)	16 (66.7%)	4 (23.5%)	31 (51.7%)	63 (63.0%)	22.8 (74.7%)
	95% Confidence Limits							[64.6% - 84.7%]
	Do not know/recall	4 (10.0%)	4 (21.1%)	1 (4.2%)	4 (23.5%)	9 (15.0%)	13 (13.0%)	3.2 (10.5%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	No	32 (23.4%)	27 (32.1%)	23 (41.8%)	13 (38.2%)	63 (36.4%)	95 (30.6%)	-
	Yes	96 (70.1%)	51 (60.7%)	31 (56.4%)	16 (47.1%)	98 (56.6%)	194 (62.6%)	-
	Do not know/recall	9 (6.6%)	6 (7.1%)	1 (1.8%)	5 (14.7%)	12 (6.9%)	21 (6.8%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	No	59.2 (26.9%)	4.7 (32.5%)	28.3 (49.8%)	4.7 (24.6%)	37.7 (41.7%)	-	96.9 (31.2%)
	Yes	148.1 (67.4%)	8.7 (60.8%)	28.4 (49.9%)	13.2 (68.9%)	50.3 (55.6%)	-	198.3 (64.0%)
	95% Confidence Limits							[57.0% - 71.0%]
	Do not know/recall	12.4 (5.6%)	1.0 (6.7%)	0.2 (0.3%)	1.2 (6.5%)	2.4 (2.7%)	-	14.8 (4.8%)

Table 9.3.3-6: Condition(s) which represent the approved indications of Instanyl® - Episodes of breakthrough cancer pain and already receiving an opioid medication for chronic background pain -Approved indication

(Basis = Physicians with complete analysable questionnaire)

Q7e. Which of the following condition(s) represent the approved indication(s) of Instanyl®: **Episodes of breakthrough cancer pain and already receiving an opioid medication for chronic background pain**?

Country	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France	(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)

Q7e. Which of the following condition(s) represent the approved indication(s) of Instanyl®: **Episodes of breakthrough cancer pain and already receiving an opioid medication for chronic background pain**?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
	No	0 (0.0%)	1 (1.5%)	3 (9.7%)	1 (5.9%)	5 (4.4%)	5 (2.4%)	6 (2.3%)
	95% Confidence Limits							[95.5% - 99.9%]
	Yes	97 (100.0%)	64 (98.5%)	28 (90.3%)	16 (94.1%)	108 (95.6%)	205 (97.6%)	273.1 (97.7%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	No	1 (2.5%)	1 (5.3%)	4 (16.7%)	4 (23.5%)	9 (15.0%)	10 (10.0%)	2 (5.4%)
	Yes	37 (92.5%)	14 (73.7%)	19 (79.2%)	9 (52.9%)	42 (70.0%)	79 (79.0%)	27 (87.8%)
	95% Confidence Limits							[80.8% - 94.9%]
	Do not know/recall	2 (5.0%)	4 (21.1%)	1 (4.2%)	4 (23.5%)	9 (15.0%)	11 (11.0%)	2.1 (6.8%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	No	1 (0.7%)	2 (2.4%)	7 (12.7%)	5 (14.7%)	14 (8.1%)	15 (4.8%)	-
	Yes	134 (97.8%)	78 (92.9%)	47 (85.5%)	25 (73.5%)	150 (86.7%)	284 (91.6%)	-
	Do not know/recall	2 (1.5%)	4 (4.8%)	1 (1.8%)	4 (11.8%)	9 (5.2%)	11 (3.5%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	No	0.6 (0.3%)	0.3 (2.3%)	5.8 (10.2%)	1.2 (6.5%)	7.4 (8.2%)	-	8.0 (2.6%)
	Yes	218.0 (99.2%)	13.4 (93.5%)	50.9 (89.4%)	17.7 (92.7%)	82.0 (90.7%)	-	300.0 (96.8%)
	95% Confidence Limits							[94.7% - 98.9%]
	Do not know/recall	1.1 (0.5%)	0.6 (4.2%)	0.2 (0.3%)	0.2 (0.8%)	1.0 (1.1%)	-	2.1 (0.7%)

Q8 of Section 2 asked: What is the maximum daily dose of Instanyl® in terms of number of puffs per episode and number of episodes per day that should be treated per day:

a. Treat no more than [__] breakthrough pain episodes per day
b. Two breakthrough pain episodes should be separated at least of [__] hours
c. Use no more than [__] doses/puffs per episode
d. Two doses/puffs should be separated at least of [__] minutes

Maximum number of breakthrough pain episodes that could be treated per day

Shown in

Table 0-1 are responses to (a). The recommended number/frequency is to treat no more than 4 episodes per day, and this was answered by 64.3% of physicians. Anesthesiologists (75.2%, n=57) had the highest percentage giving this response and oncologists (52.7%%, n=19) and radiologists (52.9%, n=19) had the lowest, with GPs (63.3%) intermediate between the specialists. These results should be taken with caution because some sample sizes are low and <40.

Overall 72.5% of physicians gave responses that were equal or within the recommended maximum treatments per day, and the proportions were highest among anaesthesiologists (79.1%, n=57) and GPs (73.6%) and lowest among oncologists (56.2%, n=14) and anesthesiologists (53.3%, n=19). These results should be taken with caution because some sample sizes are low and <40.

Among specialist, 34.3% of oncologist and 35.1% of radiologists responded that up to 6 episodes could be treated per day. Relatively few anesthesiologists and GPs responded with number of treatments above the recommended maximum of up to 4 episodes per day.

Table 0-1: Maximum daily dose of Instanyl® - Number of breakthrough pain episodes that a patient could be treated per day

(Basis = Physicians with complete analysable questionnaire)

Q8a. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day:
Treat no more than xx breakthrough pain episodes per day?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	2	4 (4.1%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	5 (2.4%)	8.3 (3.0%)
	3	6 (6.2%)	1 (1.5%)	1 (3.2%)	0 (0.0%)	2 (1.8%)	8 (3.8%)	14.1 (5.0%)
	4	**62 (63.9%)**	**36 (55.4%)**	**24 (77.4%)**	**9 (52.9%)**	**69 (61.1%)**	**131 (62.4%)**	**182.7 (65.4%)**
	95% Confidence Limits							[57.8% - 73.0%]
	5	3 (3.1%)	0 (0.0%)	1 (3.2%)	1 (5.9%)	2 (1.8%)	5 (2.4%)	8.9 (3.2%)
	6	16 (16.5%)	21 (32.3%)	4 (12.9%)	6 (35.3%)	31 (27.4%)	47 (22.4%)	49.5 (17.7%)
	8	4 (4.1%)	3 (4.6%)	0 (0.0%)	1 (5.9%)	4 (3.5%)	8 (3.8%)	9.7 (3.5%)
	10	2 (2.1%)	3 (4.6%)	1 (3.2%)	0 (0.0%)	4 (3.5%)	6 (2.9%)	6.3 (2.2%)
	Mean (SD)	4.5 (1.44)	5.1 (1.64)	4.5 (1.26)	5.0 (1.22)	4.9 (1.50)	4.7 (1.48)	4.6 (1.62)
	Median	4.0	4.0	4.0	4.0	4.0	4.0	4.0
	Q1-Q3	[4.0 - 5.0]	[4.0 - 6.0]	[4.0 - 4.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 5.0]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (1.7%)	1 (1.0%)	0.0 (0.1%)
	1	0 (0.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (1.7%)	1 (1.0%)	0.2 (0.6%)
	2	2 (5.0%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	3 (3.0%)	1.3 (4.2%)
	3	2 (5.0%)	0 (0.0%)	2 (8.3%)	1 (5.9%)	3 (5.0%)	5 (5.0%)	1.5 (5.0%)
	4	**23 (57.5%)**	**8 (42.1%)**	**12 (50.0%)**	**9 (52.9%)**	**29 (48.3%)**	**52 (52.0%)**	**16.8 (54.8%)**
	95% Confidence Limits							[42.8% - 66.9%]
	5	4 (10.0%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	5 (5.0%)	2.4 (7.8%)
	6	4 (10.0%)	8 (42.1%)	7 (29.2%)	5 (29.4%)	20 (33.3%)	24 (24.0%)	5.0 (16.3%)
	8	3 (7.5%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (1.7%)	4 (4.0%)	1.9 (6.1%)
	10	2 (5.0%)	1 (5.3%)	1 (4.2%)	1 (5.9%)	3 (5.0%)	5 (5.0%)	1.5 (4.9%)
	Mean (SD)	4.8 (1.81)	5.1 (1.66)	4.8 (1.82)	4.6 (2.03)	4.9 (1.81)	4.8 (1.80)	4.8 (0.99)
	Median	4.0	5.0	4.0	4.0	4.0	4.0	4.0
	Q1-Q3	[4.0 - 5.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 6.0]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	1 (0.6%)	1 (0.3%)	-
	1	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	1 (0.6%)	1 (0.3%)	-
	2	6 (4.4%)	2 (2.4%)	0 (0.0%)	0 (0.0%)	2 (1.2%)	8 (2.6%)	-
	3	8 (5.8%)	1 (1.2%)	3 (5.5%)	1 (2.9%)	5 (2.9%)	13 (4.2%)	-
	4	**85 (62.0%)**	**44 (52.4%)**	**36 (65.5%)**	**18 (52.9%)**	**98 (56.6%)**	**183 (59.0%)**	**-**
	5	7 (5.1%)	1 (1.2%)	1 (1.8%)	1 (2.9%)	3 (1.7%)	10 (3.2%)	-
	6	20 (14.6%)	29 (34.5%)	11 (20.0%)	11 (32.4%)	51 (29.5%)	71 (22.9%)	-
	8	7 (5.1%)	3 (3.6%)	1 (1.8%)	1 (2.9%)	5 (2.9%)	12 (3.9%)	-
	10	4 (2.9%)	4 (4.8%)	2 (3.6%)	1 (2.9%)	7 (4.0%)	11 (3.5%)	-
	Mean (SD)	4.6 (1.56)	5.1 (1.63)	4.6 (1.52)	4.8 (1.66)	4.9 (1.61)	4.7 (1.59)	-
	Median	4.0	4.0	4.0	4.0	4.0	4.0	-
	Q1-Q3	[4.0 - 5.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 6.0]	[4.0 - 6.0]	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.2%)	0 (0.0%)	-	0.0 (0.0%)
	1	0 (0.0%)	0 (0.0%)	0 (0.3%)	0 (0.0%)	0 (0.2%)	-	0.2 (0.1%)
	2	9 (4.2%)	0 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.4%)	-	9.6 (3.1%)
	3	13 (6.1%)	0 (1.2%)	2 (3.6%)	0 (0.2%)	2 (2.5%)	-	15.6 (5.0%)
	4	**139 (63.3%)**	**8 (52.7%)**	**43 (75.2%)**	**10 (52.9%)**	**60 (66.9%)**	**-**	**199.4 (64.3%)**
	95% Confidence Limits							[57.4% - 71.3%]
	5	8 (3.8%)	0 (1.1%)	2 (3.0%)	1 (5.7%)	3 (3.2%)	-	11.3 (3.6%)
	6	35 (15.8%)	5 (34.3%)	8 (14.2%)	7 (35.1%)	20 (21.8%)	-	54.5 (17.6%)
	8	10 (4.5%)	1 (3.7%)	0 (0.3%)	1 (5.7%)	2 (2.0%)	-	11.6 (3.7%)

Q8a. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day: Treat no more than xx breakthrough pain episodes per day?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
	10	5 (2.4%)	1 (4.7%)	2 (3.3%)	0 (0.2%)	3 (2.9%)	-	7.8 (2.5%)
	Mean (SD)	4.5 (1.88)	5.1 (0.67)	4.5 (1.33)	5.0 (0.93)	4.7 (0.99)	-	4.6 (1.45)
	Median	4.0	4.0	4.0	4.0	4.0	-	4.0
	Q1-Q3	[4.0 - 5.0]	[4.0 - 6.0]	[4.0 - 4.0]	[4.0 - 6.0]	[4.0 - 6.0]	-	[4.0 - 5.0]

Time interval between treatments:

Shown in Table 0-2 are responses to time interval (hours) between Instanyl® treatments. Overall 53.4% of physicians responded that at least 4 hours should separate treatments, as recommended in the SmPC, and 60.2% gave time intervals that were equal to or within the minimum interval between treatments.

It was noted that 34.0% of anesthesiologists (n=19/57) responded that treatments should be separated by at least 1 hour, substantially less than the recommended minimum interval in the SmPC, whereas relatively few GPS oncologists or radiologists answered with a minimum interval of at least 1 hour.

Two physicians gave responses of 0.1 hours between treatments, this most likely reflected misunderstanding of the question and confusing treatment intervals with time between puffs.

Table 0-2: Maximum daily dose of Instanyl® - Number of hours that should separate 2 breakthrough pain episodes

(Basis = Physicians with complete analysable questionnaire)

Q8b. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day: Two breakthrough pain episodes should be separated at least of xx hours?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	0.1	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.5%)	2.0 (0.7%)
	0.5	0 (0.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	1 (0.9%)	1 (0.5%)	1.7 (0.6%)
	1.0	14 (14.4%)	14 (21.5%)	11 (35.5%)	3 (17.6%)	28 (24.8%)	42 (20.0%)	52.7 (18.9%)
	2.0	16 (16.5%)	5 (7.7%)	2 (6.5%)	4 (23.5%)	11 (9.7%)	27 (12.9%)	41.1 (14.7%)
	3.0	6 (6.2%)	3 (4.6%)	0 (0.0%)	0 (0.0%)	3 (2.7%)	9 (4.3%)	12.7 (4.6%)
	4.0	**53 (54.6%)**	**35 (53.8%)**	**16 (51.6%)**	**9 (52.9%)**	**60 (53.1%)**	**113 (53.8%)**	**150.7 (53.9%)**
	95% Confidence Limits							[46.0% - 61.9%]
	5.0	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.5%)	2.0 (0.7%)
	6.0	6 (6.2%)	7 (10.8%)	1 (3.2%)	0 (0.0%)	8 (7.1%)	14 (6.7%)	15.1 (5.4%)
	15.0	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.5%)	0.2 (0.1%)
	24.0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (0.9%)	1 (0.5%)	1.1 (0.4%)
	Mean (SD)	3.3 (1.39)	3.5 (2.11)	2.8 (1.59)	4.2 (5.26)	3.4 (2.72)	3.4 (2.20)	3.2 (2.25)
	Median	4.0	4.0	4.0	4.0	4.0	4.0	4.0
	Q1-Q3	[2.0 - 4.0]	[2.0 - 4.0]	[1.0 - 4.0]	[2.0 - 4.0]	[1.0 - 4.0]	[2.0 - 4.0]	[2.0 - 4.0]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	0.0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (1.7%)	1 (1.0%)	0.0 (0.1%)
	1.0	5 (12.5%)	0 (0.0%)	4 (16.7%)	1 (5.9%)	5 (8.3%)	10 (10.0%)	3.6 (11.8%)
	2.0	8 (20.0%)	7 (36.8%)	7 (29.2%)	2 (11.8%)	16 (26.7%)	24 (24.0%)	7.0 (22.8%)
	3.0	4 (10.0%)	2 (10.5%)	0 (0.0%)	0 (0.0%)	2 (3.3%)	6 (6.0%)	2.5 (8.3%)
	4.0	**20 (50.0%)**	**8 (42.1%)**	**11 (45.8%)**	**11 (64.7%)**	**30 (50.0%)**	**50 (50.0%)**	**15.0 (49.0%)**

Q8b. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day:
Two breakthrough pain episodes should be separated at least of xx hours?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
95% Confidence Limits								[36.8% - 61.1%]
	5.0	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.0%)	0.6 (1.8%)
	6.0	2 (5.0%)	1 (5.3%)	2 (8.3%)	1 (5.9%)	4 (6.7%)	6 (6.0%)	1.7 (5.5%)
	8.0	0 (0.0%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (1.0%)	0.2 (0.5%)
	24.0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (1.7%)	1 (1.0%)	0.0 (0.1%)
	Mean (SD)	3.3 (1.32)	3.5 (1.58)	3.1 (1.50)	4.6 (5.18)	3.7 (3.06)	3.5 (2.51)	3.3 (0.86)
	Median	4.0	4.0	4.0	4.0	4.0	4.0	4.0
	Q1-Q3	[2.0 - 4.0]	[2.0 - 4.0]	[2.0 - 4.0]	[4.0 - 4.0]	[2.0 - 4.0]	[2.0 - 4.0]	[2.0 - 4.0]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	0.0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	1 (0.6%)	1 (0.3%)	-
	0.1	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (0.3%)	-
	0.5	0 (0.0%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	1 (0.6%)	1 (0.3%)	-
	1.0	19 (13.9%)	14 (16.7%)	15 (27.3%)	4 (11.8%)	33 (19.1%)	52 (16.8%)	-
	2.0	24 (17.5%)	12 (14.3%)	9 (16.4%)	6 (17.6%)	27 (15.6%)	51 (16.5%)	-
	3.0	10 (7.3%)	5 (6.0%)	0 (0.0%)	0 (0.0%)	5 (2.9%)	15 (4.8%)	-
	4.0	**73 (53.3%)**	**43 (51.2%)**	**27 (49.1%)**	**20 (58.8%)**	**90 (52.0%)**	**163 (52.6%)**	**-**
	5.0	2 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		2 (0.6%)	-
	6.0	8 (5.8%)	8 (9.5%)	3 (5.5%)	1 (2.9%)	12 (6.9%)	20 (6.5%)	-
	8.0	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	1 (0.3%)	-
	15.0	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	1 (0.6%)	1 (0.3%)	-
	24.0	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.9%)	2 (1.2%)	2 (0.6%)	-
	Mean (SD)	3.3 (1.36)	3.5 (1.99)	2.9 (1.54)	4.4 (5.15)	3.5 (2.83)	3.4 (2.30)	-
	Median	4.0	4.0	4.0	4.0	4.0	4.0	-
	Q1-Q3	[2.0 - 4.0]	[2.0 - 4.0]	[1.0 - 4.0]	[2.0 - 4.0]	[2.0 - 4.0]	[2.0 - 4.0]	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	0.0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.2%)	0 (0.0%)	-	0.0 (0.0%)
	0.1	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	2.0 (0.7%)
	0.5	0 (0.0%)	0 (0.0%)	2 (3.0%)	0 (0.0%)	2 (1.9%)	-	1.7 (0.5%)
	1.0	31 (14.2%)	2 (17.2%)	19 (34.0%)	3 (17.2%)	25 (27.8%)	-	56.4 (18.2%)
	2.0	37 (16.9%)	2 (13.6%)	5 (8.3%)	4 (23.1%)	11 (12.3%)	-	48.1 (15.5%)
	3.0	14 (6.6%)	1 (5.8%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	-	15.3 (4.9%)
	4.0	**119 (54.2%)**	**7 (51.5%)**	**29 (51.1%)**	**10 (53.4%)**	**47 (51.7%)**	**-**	**165.7 (53.4%)**
95% Confidence Limits								[46.2% - 60.7%]
	5.0	3 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	2.6 (0.8%)
	6.0	13 (6.1%)	1 (9.7%)	2 (3.6%)	0 (0.2%)	3 (3.9%)	-	16.8 (5.4%)
	8.0	0 (0.0%)	0 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.2%)	-	0.2 (0.0%)
	15.0	0 (0.0%)	0 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.2%)	-	0.2 (0.1%)
	24.0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (1.2%)	-	1.1 (0.4%)
	Mean (SD)	3.3 (1.74)	3.5 (0.83)	2.8 (1.60)	4.2 (3.88)	3.2 (2.05)	-	3.2 (1.92)
	Median	4.0	4.0	4.0	4.0	4.0	-	4.0
	Q1-Q3	[2.0 - 4.0]	[2.0 - 4.0]	[1.0 - 4.0]	[2.0 - 4.0]	[1.0 - 4.0]	-	[2.0 - 4.0]

Maximum doses/puffs per episode

Shown in Table 0-3 are responses to maximum number of doses/puffs per episodes. Overall 71.5% of physicians responded that a maximum of 2 puffs per episode should be used, which corresponded with the recommendation in the SmPC, and 86.4% gave responses that were equal or within the maximum number of puffs per episode.

Relatively few physicians gave responses above the recommended maximum number of puffs per dose.

At country level, 11.3% of physicians in the Netherlands and 13.7% in France gave responses that were higher than the recommended maximum number of puffs per episode (Table 0-2).

Table 0-3: Maximum daily dose of Instanyl® - Number of doses/puffs that could be used per breakthrough pain episode

(Basis = Physicians with complete analysable questionnaire)

Q8c. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day:
Use no more than xx doses/puffs per episodes?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	1	17 (17.5%)	7 (10.8%)	4 (12.9%)	1 (5.9%)	12 (10.6%)	29 (13.8%)	43.6 (15.6%)
	2	**66 (68.0%)**	**52 (80.0%)**	**23 (74.2%)**	**14 (82.4%)**	**89 (78.8%)**	**155 (73.8%)**	**197.3 (70.6%)**
95% Confidence Limits								[63.3% - 78.0%]
	3	3 (3.1%)	2 (3.1%)	3 (9.7%)	0 (0.0%)	5 (4.4%)	8 (3.8%)	11.5 (4.1%)
	4	9 (9.3%)	4 (6.2%)	1 (3.2%)	1 (5.9%)	6 (5.3%)	15 (7.1%)	21.8 (7.8%)
	5	2 (2.1%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (0.9%)	3 (1.4%)	5.2 (1.8%)
	Mean (SD)	2.1 (0.87)	2.0 (0.62)	2.0 (0.60)	2.2 (0.90)	2.1 (0.66)	2.1 (0.77)	2.1 (0.94)
	Median	2.0	2.0	2.0	2.0	2.0	2.0	2.0
	Q1-Q3	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (1.7%)	1 (1.0%)	0.0 (0.1%)
	1	3 (7.5%)	1 (5.3%)	4 (16.7%)	1 (5.9%)	6 (10.0%)	9 (9.0%)	2.6 (8.6%)
	2	**33 (82.5%)**	**14 (73.7%)**	**17 (70.8%)**	**14 (82.4%)**	**45 (75.0%)**	**78 (78.0%)**	**24.4 (79.9%)**
95% Confidence Limits								[70.5% - 89.4%]
	3	0 (0.0%)	1 (5.3%)	1 (4.2%)	0 (0.0%)	2 (3.3%)	2 (2.0%)	0.3 (1.1%)
	4	3 (7.5%)	3 (15.8%)	2 (8.3%)	0 (0.0%)	5 (8.3%)	8 (8.0%)	2.5 (8.2%)
	5	1 (2.5%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (1.7%)	2 (2.0%)	0.6 (2.0%)
	Mean (SD)	2.2 (0.77)	2.3 (0.82)	2.0 (0.75)	2.0 (0.94)	2.1 (0.83)	2.1 (0.80)	2.1 (0.43)
	Median	2.0	2.0	2.0	2.0	2.0	2.0	2.0
	Q1-Q3	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	1 (0.6%)	1 (0.3%)	-
	1	20 (14.6%)	8 (9.5%)	8 (14.5%)	2 (5.9%)	18 (10.4%)	38 (12.3%)	-
	2	**99 (72.3%)**	**66 (78.6%)**	**40 (72.7%)**	**28 (82.4%)**	**134 (77.5%)**	**233 (75.2%)**	**-**
	3	3 (2.2%)	3 (3.6%)	4 (7.3%)	0 (0.0%)	7 (4.0%)	10 (3.2%)	-
	4	12 (8.8%)	7 (8.3%)	3 (5.5%)	1 (2.9%)	11 (6.4%)	23 (7.4%)	-
	5	3 (2.2%)	0 (0.0%)	0 (0.0%)	2 (5.9%)	2 (1.2%)	5 (1.6%)	-
	Mean (SD)	2.1 (0.84)	2.1 (0.68)	2.0 (0.67)	2.1 (0.91)	2.1 (0.72)	2.1 (0.78)	-
	Median	2.0	2.0	2.0	2.0	2.0	2.0	-
	Q1-Q3	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.2%)	0 (0.0%)	-	0.0 (0.0%)
	1	36 (16.5%)	1 (9.7%)	8 (13.2%)	1 (5.9%)	10 (11.1%)	-	46.3 (14.9%)
	2	**153 (69.5%)**	**11 (78.7%)**	**42 (73.9%)**	**16 (82.4%)**	**69 (76.5%)**	**-**	**221.8 (71.5%)**
95% Confidence Limits								[64.9% - 78.2%]
	3	6 (2.8%)	1 (3.5%)	5 (9.2%)	0 (0.0%)	6 (6.4%)	-	11.9 (3.8%)
	4	20 (9.1%)	1 (8.1%)	2 (3.6%)	1 (5.7%)	4 (4.8%)	-	24.3 (7.8%)
	5	5 (2.1%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (1.2%)	-	5.8 (1.9%)
	Mean (SD)	2.1 (1.09)	2.1 (0.28)	2.0 (0.62)	2.2 (0.67)	2.1 (0.50)	-	2.1 (0.81)

Q8c. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day: Use no more than xx doses/puffs per episodes?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
	Median	2.0	2.0	2.0	2.0	2.0	-	2.0
	Q1-Q3	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	[2.0 - 2.0]	-	[2.0 - 2.0]

Interval between puffs when treating an episode of breakthrough pain

Shown in Table 0-4 are physicians' responses on the minimum number of minutes between puffs. Overall, 56.8% of physicians responded that puffs should be a minimum of 10 minutes apart, which is the time recommended between two doses, and 73.1% gave responses that were equal to or within the recommended time interval. There was little variation between physician specialties.

Table 0-4: Maximum daily dose of Instanyl® - Time that should separate doses/puffs of Instanyl®

(Basis = Physicians with complete analysable questionnaire)

Q8d. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day: Two doses/puffs should be separated at least of xx minutes?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	0	2 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.0%)	4.1 (1.5%)
	1	4 (4.1%)	4 (6.2%)	0 (0.0%)	0 (0.0%)	4 (3.5%)	8 (3.8%)	8.8 (3.2%)
	2	4 (4.1%)	0 (0.0%)	1 (3.2%)	0 (0.0%)	1 (0.9%)	5 (2.4%)	9.8 (3.5%)
	3	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	2.0 (0.7%)
	4	2 (2.1%)	2 (3.1%)	1 (3.2%)	0 (0.0%)	3 (2.7%)	5 (2.4%)	6.1 (2.2%)
	5	4 (4.1%)	2 (3.1%)	3 (9.7%)	1 (5.9%)	6 (5.3%)	10 (4.8%)	14.6 (5.2%)
	10	**55 (56.7%)**	**36 (55.4%)**	**20 (64.5%)**	**8 (47.1%)**	**64 (56.6%)**	**119 (56.7%)**	**160.6 (57.5%)**
95% Confidence Limits								[49.6% - 65.4%]
	15	12 (12.4%)	14 (21.5%)	1 (3.2%)	4 (23.5%)	19 (16.8%)	31 (14.8%)	32.9 (11.8%)
	20	2 (2.1%)	2 (3.1%)	1 (3.2%)	1 (5.9%)	4 (3.5%)	6 (2.9%)	7.2 (2.6%)
	30	6 (6.2%)	3 (4.6%)	3 (9.7%)	2 (11.8%)	8 (7.1%)	14 (6.7%)	20.0 (7.1%)
	40	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	2.0 (0.7%)
	60	2 (2.1%)	1 (1.5%)	0 (0.0%)	1 (5.9%)	2 (1.8%)	4 (1.9%)	5.3 (1.9%)
	100	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.5%)	2.0 (0.7%)
	120	1 (1.0%)	1 (1.5%)	1 (3.2%)	0 (0.0%)	2 (1.8%)	3 (1.4%)	3.9 (1.4%)
	Mean (SD)	14.2 (17.18)	13.9 (15.72)	15.0 (20.67)	16.8 (13.10)	14.6 (16.77)	14.4 (16.92)	14.5 (20.18)
	Median	10.0	10.0	10.0	10.0	10.0	10.0	10.0
	Q1-Q3	[10.0 - 15.0]	[10.0 - 15.0]	[10.0 - 10.0]	[10.0 - 15.0]	[10.0 - 15.0]	[10.0 - 15.0]	[10.0 - 15.0]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	0	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	1 (1.7%)	1 (1.0%)	0.0 (0.1%)
	1	2 (5.0%)	1 (5.3%)	0 (0.0%)	1 (5.9%)	2 (3.3%)	4 (4.0%)	1.3 (4.3%)
	5	4 (10.0%)	2 (10.5%)	5 (20.8%)	0 (0.0%)	7 (11.7%)	11 (11.0%)	3.5 (11.5%)
	10	**20 (50.0%)**	**9 (47.4%)**	**13 (54.2%)**	**11 (64.7%)**	**33 (55.0%)**	**53 (53.0%)**	**15.5 (50.7%)**
95% Confidence Limits								[38.5% - 62.9%]
	15	4 (10.0%)	1 (5.3%)	3 (12.5%)	1 (5.9%)	5 (8.3%)	9 (9.0%)	3.0 (9.8%)
	20	2 (5.0%)	3 (15.8%)	1 (4.2%)	0 (0.0%)	4 (6.7%)	6 (6.0%)	1.8 (5.8%)
	30	4 (10.0%)	2 (10.5%)	0 (0.0%)	1 (5.9%)	3 (5.0%)	7 (7.0%)	2.6 (8.5%)
	50	1 (2.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0.6 (1.8%)

Q8d. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day:
Two doses/puffs should be separated at least of xx minutes?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
	60	2 (5.0%)	0 (0.0%)	2 (8.3%)	1 (5.9%)	3 (5.0%)	5 (5.0%)	1.5 (5.0%)
	120	1 (2.5%)	1 (5.3%)	0 (0.0%)	1 (5.9%)	2 (3.3%)	3 (3.0%)	0.8 (2.5%)
	Mean (SD)	18.3 (21.55)	18.7 (25.72)	14.2 (14.57)	19.8 (29.14)	17.2 (22.83)	17.6 (22.22)	17.8 (11.68)
	Median	10.0	10.0	10.0	10.0	10.0	10.0	10.0
	Q1-Q3	[10.0 - 17.5]	[10.0 - 20.0]	[10.0 - 12.5]	[10.0 - 10.0]	[10.0 - 15.0]	[10.0 - 15.0]	[10.0 - 15.0]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	0	2 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.9%)	1 (0.6%)	3 (1.0%)	-
	1	6 (4.4%)	5 (6.0%)	0 (0.0%)	1 (2.9%)	6 (3.5%)	12 (3.9%)	-
	2	4 (2.9%)	0 (0.0%)	1 (1.8%)	0 (0.0%)	1 (0.6%)	5 (1.6%)	-
	3	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	-
	4	2 (1.5%)	2 (2.4%)	1 (1.8%)	0 (0.0%)	3 (1.7%)	5 (1.6%)	-
	5	8 (5.8%)	4 (4.8%)	8 (14.5%)	1 (2.9%)	13 (7.5%)	21 (6.8%)	-
	10	**75 (54.7%)**	**45 (53.6%)**	**33 (60.0%)**	**19 (55.9%)**	**97 (56.1%)**	**172 (55.5%)**	**-**
	15	16 (11.7%)	15 (17.9%)	4 (7.3%)	5 (14.7%)	24 (13.9%)	40 (12.9%)	-
	20	4 (2.9%)	5 (6.0%)	2 (3.6%)	1 (2.9%)	8 (4.6%)	12 (3.9%)	-
	30	10 (7.3%)	5 (6.0%)	3 (5.5%)	3 (8.8%)	11 (6.4%)	21 (6.8%)	-
	40	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	-
	50	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	-
	60	4 (2.9%)	1 (1.2%)	2 (3.6%)	2 (5.9%)	5 (2.9%)	9 (2.9%)	-
	100	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	-
	120	2 (1.5%)	2 (2.4%)	1 (1.8%)	1 (2.9%)	4 (2.3%)	6 (1.9%)	-
	Mean (SD)	15.4 (18.57)	15.0 (18.39)	14.7 (18.11)	18.3 (22.30)	15.5 (19.06)	15.5 (18.82)	-
	Median	10.0	10.0	10.0	10.0	10.0	10.0	-
	Q1-Q3	[10.0 - 15.0]	[10.0 - 15.0]	[10.0 - 10.0]	[10.0 - 15.0]	[10.0 - 15.0]	[10.0 - 15.0]	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	0	4 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.2%)	0 (0.0%)	-	4.1 (1.3%)
	1	9 (4.2%)	1 (6.0%)	0 (0.0%)	0 (0.2%)	1 (1.0%)	-	10.1 (3.3%)
	2	8 (3.7%)	0 (0.0%)	2 (3.0%)	0 (0.0%)	2 (1.9%)	-	9.8 (3.2%)
	3	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	2.0 (0.7%)
	4	4 (1.9%)	0 (2.5%)	2 (3.0%)	0 (0.0%)	2 (2.3%)	-	6.1 (2.0%)
	5	10 (4.7%)	1 (4.6%)	6 (10.6%)	1 (5.7%)	8 (8.6%)	-	18.1 (5.8%)
	10	**123 (56.0%)**	**8 (53.8%)**	**36 (63.7%)**	**9 (47.7%)**	**53 (58.7%)**	**-**	**176.1 (56.8%)**
95% Confidence Limits								[49.6% - 64.0%]
	15	27 (12.1%)	3 (18.3%)	2 (4.0%)	4 (22.9%)	9 (10.2%)	-	35.9 (11.6%)
	20	5 (2.4%)	1 (5.6%)	2 (3.3%)	1 (5.7%)	4 (4.2%)	-	9.0 (2.9%)
	30	14 (6.6%)	1 (5.8%)	5 (8.9%)	2 (11.6%)	8 (9.0%)	-	22.5 (7.3%)
	40	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	2.0 (0.7%)
	50	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	0.6 (0.2%)
	60	5 (2.4%)	0 (1.2%)	0 (0.7%)	1 (5.9%)	2 (1.9%)	-	6.9 (2.2%)
	100	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	2.0 (0.7%)
	120	3 (1.2%)	0 (2.3%)	2 (3.0%)	0 (0.2%)	2 (2.3%)	-	4.6 (1.5%)
	Mean (SD)	14.6 (22.38)	14.9 (7.49)	15.0 (20.44)	16.9 (10.34)	15.3 (13.38)	-	14.8 (17.89)
	Median	10.0	10.0	10.0	10.0	10.0	-	10.0
	Q1-Q3	[10.0 - 15.0]	[10.0 - 15.0]	[10.0 - 10.0]	[10.0 - 15.0]	[10.0 - 15.0]	-	[10.0 - 15.0]

Use in contraindicated patients

Q9 of Section 2 asked: In the last 6 months, have you prescribed Instanyl® to the following:

a. Patients with recurrent episodes of epistaxis
b. Patients with severe respiratory depression /obstructive lung disease

c. Patients without current maintenance opioid therapy
d. Patients with previous facial radiotherapy.

Epistaxis

Table 0-5 presents the proportion of physicians who recently prescribed to patients with epistaxis. 97.2% did not prescribe Instanyl to patients with recurrent epistaxis or nasal discomfort or other conditions that could impair a nasal use. This high compliance was seen in all physician types.

Table 0-5: Prescription of Instanyl® to patients with recurrent episodes of epistaxis (or nasal discomfort while using the spray)

(Basis = Physicians with complete analysable questionnaire)

Q9a. In the last 6 months, have you prescribed Instanyl® to the following patients: With recurrent episodes of epistaxis (or nasal discomfort while using the spray), conditions impairing accurate treatment?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	No	94 (96.9%)	52 (80.0%)	28 (90.3%)	16 (94.1%)	96 (85.0%)	190 (90.5%)	265 (94.8%)
	Yes	1 (1.0%)	11 (16.9%)	2 (6.5%)	0 (0.0%)	13 (11.5%)	14 (6.7%)	7.3 (2.6%)
	95% Confidence Limits							[0.4% - 4.9%]
	Do not know/recall	2 (2.1%)	2 (3.1%)	1 (3.2%)	1 (5.9%)	4 (3.5%)	6 (2.9%)	7.2 (2.6%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	No	35 (87.5%)	19 (100.0%)	20 (83.3%)	15 (88.2%)	54 (90.0%)	89 (89.0%)	27 (88.1%)
	Yes	2 (5.0%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (1.7%)	3 (3.0%)	1.3 (4.3%)
	95% Confidence Limits							[0.0% - 9.5%]
	Do not know/recall	3 (7.5%)	0 (0.0%)	3 (12.5%)	2 (11.8%)	5 (8.3%)	8 (8.0%)	2.3 (7.6%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	(N=310)
	No	129 (94.2%)	71 (84.5%)	48 (87.3%)	31 (91.2%)	150 (86.7%)	279 (90.0%)	292 (94.1%)
	Yes	3 (2.2%)	11 (13.1%)	3 (5.5%)	0 (0.0%)	14 (8.1%)	17 (5.5%)	9 (2.8%)
	Do not know/recall	5 (3.6%)	2 (2.4%)	4 (7.3%)	3 (8.8%)	9 (5.2%)	14 (4.5%)	10 (3.1%)
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	No	210.7 (95.9%)	12.0 (84.0%)	51.1 (89.8%)	18.0 (93.9%)	81.1 (89.7%)	-	291.8 (94.1%)
	Yes	3.2 (1.4%)	1.9 (13.5%)	3.6 (6.3%)	0.0 (0.0%)	5.5 (6.1%)	-	8.7 (2.8%)
	95% Confidence Limits							[0.7% - 4.9%]
	Do not know/recall	5.7 (2.6%)	0.4 (2.5%)	2.3 (4.0%)	1.2 (6.1%)	3.8 (4.2%)	-	9.5 (3.1%)

Severe Respiratory depression / obstructive lung disease

Table 0-6 presents responses in relation to prescribing to patients with severe respiratory depression or severe obstructive lung disease. Overall 91.9% of physicians reported they had not prescribed Instanyl® to patients with severe respiratory depression or severe obstructive lung disease, in accordance with the recommended prescribing information. There was little variation between physician specialties.

Table 0-6: Prescription of Instanyl® to patients with severe respiratory depression (or severe obstructive lung conditions)

(Basis = Physicians with complete analysable questionnaire)

Q9b. In the last 6 months, have you prescribed Instanyl® to the following patients: with severe respiratory depression (or severe obstructive lung conditions)?

Country	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
Q9b. In the last 6 months, have you prescribed Instanyl® to the following patients: with severe respiratory depression (or severe obstructive lung conditions)?								
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	No	90 (92.8%)	56 (86.2%)	25 (80.6%)	16 (94.1%)	97 (85.8%)	187 (89.0%)	252.4 (90.3%)
	Yes	5 (5.2%)	8 (12.3%)	6 (19.4%)	1 (5.9%)	15 (13.3%)	20 (9.5%)	22.8 (8.2%)
	95% Confidence Limits							[3.9% - 12.4%]
	Do not know/recall	2 (2.1%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	3 (1.4%)	4.2 (1.5%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	No	29 (72.5%)	18 (94.7%)	20 (83.3%)	15 (88.2%)	53 (88.3%)	82 (82.0%)	23.4 (76.6%)
	Yes	8 (20.0%)	1 (5.3%)	3 (12.5%)	2 (11.8%)	6 (10.0%)	14 (14.0%)	5.3 (17.3%)
	95% Confidence Limits							[7.7% - 26.9%]
	Do not know/recall	3 (7.5%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (1.7%)	4 (4.0%)	1.9 (6.1%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	No	119 (86.9%)	74 (88.1%)	45 (81.8%)	31 (91.2%)	150 (86.7%)	269 (86.8%)	-
	Yes	13 (9.5%)	9 (10.7%)	9 (16.4%)	3 (8.8%)	21 (12.1%)	34 (11.0%)	-
	Do not know/recall	5 (3.6%)	1 (1.2%)	1 (1.8%)	0 (0.0%)	2 (1.2%)	7 (2.3%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	No	199.2 (90.7%)	12.6 (87.9%)	46.0 (80.9%)	18.0 (93.9%)	76.6 (84.7%)	-	275.8 (89.0%)
	Yes	14.7 (6.7%)	1.6 (10.9%)	10.7 (18.8%)	1.2 (6.1%)	13.4 (14.9%)	-	28.1 (9.1%)
	95% Confidence Limits							[5.1% - 13.0%]
	Do not know/recall	5.7 (2.6%)	0.2 (1.2%)	0.2 (0.3%)	0.0 (0.0%)	0.4 (0.4%)	-	6.1 (2.0%)

Absence of background maintenance opioid therapy

Table 0-7 presents responses pertaining to recent use of Instanyl® without current maintenance opioid maintenance therapy. Overall, 85.8% of physicians had not prescribed Instanyl® in this situation, which is in accordance with the recommended prescribing information.

Highest compliance was seen in oncologists (91.4%, n=14) and lowest, although still relatively high, in radiologists (82.6%, n=19). These results should be taken with caution because some sample sizes are low: <40.

Table 0-7: Prescription of Instanyl® to patients without current maintenance opioid therapy

(Basis = Physicians with complete analysable questionnaire)

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
Q9c. In the last 6 months, have you prescribed Instanyl® to the following patients: Without current maintenance opioid therapy?								
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	No	82 (84.5%)	58 (89.2%)	28 (90.3%)	14 (82.4%)	100 (88.5%)	182 (86.7%)	239.4 (85.7%)
	Yes	15 (15.5%)	6 (9.2%)	3 (9.7%)	3 (17.6%)	12 (10.6%)	27 (12.9%)	39.9 (14.3%)
	95% Confidence Limits							[8.6% - 19.9%]
	Do not know/recall	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	1 (0.5%)	0.2 (0.1%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	No	35 (87.5%)	19 (100.0%)	19 (79.2%)	15 (88.2%)	53 (88.3%)	88 (88.0%)	26.7 (87.4%)
	Yes	5 (12.5%)	0 (0.0%)	3 (12.5%)	2 (11.8%)	5 (8.3%)	10 (10.0%)	3.5 (11.3%)
	95% Confidence Limits							[3.4% - 19.2%]
	Do not know/recall	0 (0.0%)	0 (0.0%)	2 (8.3%)	0 (0.0%)	2 (3.3%)	2 (2.0%)	0.4 (1.2%)
Overall -		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
Q9c. In the last 6 months, have you prescribed Instanyl® to the following patients: Without current maintenance opioid therapy?								
unweighted results	No	117 (85.4%)	77 (91.7%)	47 (85.5%)	29 (85.3%)	153 (88.4%)	270 (87.1%)	-
	Yes	20 (14.6%)	6 (7.1%)	6 (10.9%)	5 (14.7%)	17 (9.8%)	37 (11.9%)	-
	Do not know/recall	0 (0.0%)	1 (1.2%)	2 (3.6%)	0 (0.0%)	3 (1.7%)	3 (1.0%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	No	186.3 (84.8%)	13.1 (91.4%)	50.9 (89.4%)	15.8 (82.6%)	79.8 (88.3%)	-	266.1 (85.8%)
	Yes	33.3 (15.2%)	1.1 (7.4%)	5.6 (9.9%)	3.3 (17.4%)	10.0 (11.1%)	-	43.3 (14.0%)
	95% Confidence Limits							[8.9% - 19.1%]
	Do not know/recall	0.0 (0.0%)	0.2 (1.2%)	0.4 (0.7%)	0.0 (0.0%)	0.6 (0.6%)	-	0.6 (0.2%)

Previous Facial Radiotherapy

Table 0-8 presents data on prescribing to patients with previous facial radiotherapy. Overall 85.0% of physicians had not prescribed to patients with previous facial radiotherapy, and a further 4.9% responded they do not know/recall.

10.1% responded that they had used Instanyl® in the previous 6 months in patients with previous facial radiotherapy. This was most frequent in oncologists (20.9%, n=3/14) and radiologists (23.7%, n=4.5/19) and least frequent in GPs (8.3%, n=18/220). These results should be taken with caution because some sample sizes are low: <40

Interpretation:
The radiologists and oncologists who used nasal Instanyl® in patients with facial radiotherapy probably felt the benefits outweighed the risk in delivering rapid pain relief via a nasal route and that oral administration may not have been appropriate or preferred in such patients.

Table 0-8: Prescription of Instanyl® to patients who had a previous facial radiotherapy

(Basis = Physicians with complete analysable questionnaire)

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
Q9d. In the last 6 months, have you prescribed Instanyl® to the following patients: Patients who had a previous facial radiotherapy?								
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	No	84 (86.6%)	45 (69.2%)	27 (87.1%)	13 (76.5%)	85 (75.2%)	169 (80.5%)	238.4 (85.3%)
	Yes	9 (9.3%)	17 (26.2%)	3 (9.7%)	4 (23.5%)	24 (21.2%)	33 (15.7%)	30.7 (11.0%)
	95% Confidence Limits							[6.2% - 15.8%]
	Do not know/recall	4 (4.1%)	3 (4.6%)	1 (3.2%)	0 (0.0%)	4 (3.5%)	8 (3.8%)	10.3 (3.7%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	No	33 (82.5%)	19 (100.0%)	18 (75.0%)	11 (64.7%)	48 (80.0%)	81 (81.0%)	25.3 (82.6%)
	Yes	0 (0.0%)	0 (0.0%)	2 (8.3%)	5 (29.4%)	7 (11.7%)	7 (7.0%)	0.6 (1.9%)
	95% Confidence Limits							[0.0% - 3.8%]
	Do not know/recall	7 (17.5%)	0 (0.0%)	4 (16.7%)	1 (5.9%)	5 (8.3%)	12 (12.0%)	4.7 (15.5%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	No	117 (85.4%)	64 (76.2%)	45 (81.8%)	24 (70.6%)	133 (76.9%)	250 (80.6%)	-
	Yes	9 (6.6%)	17 (20.2%)	5 (9.1%)	9 (26.5%)	31 (17.9%)	40 (12.9%)	-
	Do not know/recall	11 (8.0%)	3 (3.6%)	5 (9.1%)	1 (2.9%)	9 (5.2%)	20 (6.5%)	-

Q9d. In the last 6 months, have you prescribed Instanyl® to the following patients: Patients who had a previous facial radiotherapy?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	No	189.3 (86.2%)	10.8 (75.4%)	49.0 (86.1%)	14.5 (76.1%)	74.4 (82.3%)	-	263.6 (85.0%)
	Yes	18.3 (8.3%)	3.0 (20.9%)	5.4 (9.6%)	4.5 (23.7%)	13.0 (14.4%)	-	31.3 (10.1%)
95% Confidence Limits								[5.8% - 14.4%]
	Do not know/recall	12.1 (5.5%)	0.5 (3.7%)	2.5 (4.3%)	0.0 (0.2%)	3.0 (3.3%)	-	15.1 (4.9%)

Potential substance abuse or dependence

Table 0-9 presents data on the prescription of Instanyl® to patients at risk of potential substance abuse and/or dependence within the last six months prior to the survey. Overall, 91.0% of physicians had not prescribed to patients at risk of possible substance abuse or dependence. Anesthesiologists, who probably are the most highly trained and experienced in pain control, were the most frequent prescribers (15.5%) and radiologists (0.2%) least frequent prescribers to patients in this situation, with other physician types intermediate.

Table 0-9: Prescription of Instanyl® to patients at risks of potential substance abuse and/or dependence

(Basis = Physicians with complete analysable questionnaire)

Q10. In the last 6 months, have you prescribed Instanyl® to patients at risks of potential substance abuse and/or dependence?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	No	89 (91.8%)	59 (90.8%)	26 (83.9%)	17 (100.0%)	102 (90.3%)	191 (91.0%)	253.7 (90.8%)
	Yes	8 (8.2%)	6 (9.2%)	5 (16.1%)	0 (0.0%)	11 (9.7%)	19 (9.0%)	25.8 (9.2%)
95% Confidence Limits								[4.6% - 13.9%]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	No	37 (92.5%)	19 (100.0%)	22 (91.7%)	16 (94.1%)	57 (95.0%)	94 (94.0%)	28.5 (93.1%)
	Yes	3 (7.5%)	0 (0.0%)	2 (8.3%)	1 (5.9%)	3 (5.0%)	6 (6.0%)	2.1 (6.9%)
95% Confidence Limits								[0.5% - 13.2%]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	No	126 (92.0%)	78 (92.9%)	48 (87.3%)	33 (97.1%)	159 (91.9%)	285 (91.9%)	-
	Yes	11 (8.0%)	6 (7.1%)	7 (12.7%)	1 (2.9%)	14 (8.1%)	25 (8.1%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	(N=310)	(N=310)
	No	201.7 (91.8%)	13.3 (92.6%)	48.1 (84.5%)	19.1 (99.8%)	80.4 (89.0%)	-	282.1 (91.0%)
	Yes	17.9 (8.2%)	1.1 (7.4%)	8.8 (15.5%)	0.08 (0.2%)	9.9 (11.0%)	28 (9.0%)	27.9 (9.0%)
95% Confidence Limits								[4.8% - 13.2%]

Factors taken into consideration before prescribing Instanyl® to patients at risks of potential substance abuse and/or dependence

Table 0-10 and Table 0-11 show responses to Q10a of Section 2: main factors taken into consideration when prescribing of Instanyl® to patients at risk of potential substance abuse and/or dependence The most frequent considerations were the accuracy of use according to the indication (patients presenting

with cancer breakthrough pain (42.0%) and the level of addiction/abuse/dependence risks (41.3%). Other considerations included the fact that Instanyl® can be use safely (14.1%), the patient's frequency of pain episodes (7.9%) and need for effective pain control in palliative care (7.9%).

As the number of respondents who stated Yes to Q10 is very low, the results per country and per specialty should be interpreted with caution.

Table 0-10: Factors taken into consideration before prescribing Instanyl® to patients at risks of potential substance abuse and/or dependence

(Basis = Physicians with complete analysable questionnaire and who have prescribed Instanyl® to patients at risks of addiction: substance abuse and/or dependence)

Q10a. If yes, which factors did you take into consideration?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
France	.	(N=8)		(N=6)		(N=5)		(N=0)		(N=11)		(N=19)		(N=26)	
	Breakthrough pain: Indication	3 (37.5%)	[2]	2 (33.3%)	[1]	3 (60.0%)	[1]		-	5 (45.5%)	[1]	8 (42.1%)	[1]	11.5 (44.7%)	[1]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	5 (62.5%)	[1]	0 (0.0%)	-	0 (0.0%)	-		-		-	5 (26.3%)	[2]	10.2 (39.5%)	[2]
	Safe use	0 (0.0%)	-	2 (33.3%)	[1]	2 (40.0%)	[2]		-	4 (36.4%)	[2]	4 (21.1%)	[3]	3.7 (14.5%)	[3]
	Frequency of pain episodes	1 (12.5%)	[3]	1 (16.7%)	[4]	0 (0.0%)	-		-	1 (9.1%)	[5]	2 (10.5%)	[4]	2.2 (8.6%)	[4]
	Palliative treatment	1 (12.5%)	[3]	1 (16.7%)	[4]	0 (0.0%)	-		-	1 (9.1%)	[5]	2 (10.5%)	[4]	2.2 (8.6%)	[4]
	Efficient	1 (12.5%)	[3]	0 (0.0%)	-	0 (0.0%)	-		-		-	1 (5.3%)	[8]	2.0 (7.9%)	[6]
	Compliance	0 (0.0%)	-	1 (16.7%)	[4]	1 (20.0%)	[3]		-	2 (18.2%)	[3]	2 (10.5%)	[4]	1.9 (7.2%)	[7]
	Route of administration: nasal	0 (0.0%)	-	2 (33.3%)	[1]	0 (0.0%)	-		-	2 (18.2%)	[3]	2 (10.5%)	[4]	0.4 (1.4%)	[8]
The Netherlands	.	(N=3)		(N=0)		(N=2)		(N=1)		(N=3)		(N=6)		(N=2)	
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	2 (66.7%)	[1]		-	1 (50.0%)	[1]	1 (100.0%)	[1]	2 (66.7%)	[1]	4 (66.7%)	[1]	1.4 (64.3%)	[1]
	Route of administration: nasal	1 (33.3%)	[2]		-	0 (0.0%)	-	0 (0.0%)	-		-	1 (16.7%)	[2]	0.6 (26.7%)	[2]
	Breakthrough pain: Indication	0 (0.0%)	-		-	1 (50.0%)	[1]	0 (0.0%)	-	1 (33.3%)	[2]	1 (16.7%)	[2]	0.2 (9.1%)	[3]
	Safe use	0 (0.0%)	-		-	1 (50.0%)	[1]	0 (0.0%)	-	1 (33.3%)	[2]	1 (16.7%)	[2]	0.2 (9.1%)	[3]
Overall - unweighted results	.	(N=11)		(N=6)		(N=7)		(N=1)		(N=14)		(N=25)		-	
	Breakthrough pain: Indication	3 (27.3%)	[2]	2 (33.3%)	[1]	4 (57.1%)	[1]	0 (0.0%)	-	6 (42.9%)	[1]	9 (36.0%)	[1]	-	-
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	7 (63.6%)	[1]	0 (0.0%)	-	1 (14.3%)	[3]	1 (100.0%)	[1]	2 (14.3%)	[3]	9 (36.0%)	[1]	-	-
	Safe use	0 (0.0%)	-	2 (33.3%)	[1]	3 (42.9%)	[2]	0 (0.0%)	-	5 (35.7%)	[2]	5 (20.0%)	[3]	-	-
	Frequency of pain episodes	1 (9.1%)	[3]	1 (16.7%)	[4]	0 (0.0%)	-	0 (0.0%)	-	1 (7.1%)	[6]	2 (8.0%)	[5]	-	-
	Palliative treatment	1 (9.1%)	[3]	1 (16.7%)	[4]	0 (0.0%)	-	0 (0.0%)	-	1 (7.1%)	[6]	2 (8.0%)	[5]	-	-
	Efficient	1 (9.1%)	[3]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (4.0%)	[8]	-	-
	Compliance	0 (0.0%)	-	1 (16.7%)	[4]	1 (14.3%)	[3]	0 (0.0%)	-	2 (14.3%)	[3]	2 (8.0%)	[5]	-	-
	Route of administration: nasal	1 (9.1%)	[3]	2 (33.3%)	[1]	0 (0.0%)	-	0 (0.0%)	-	2 (14.3%)	[3]	3 (12.0%)	[4]	-	-

Q10a. If yes, which factors did you take into consideration?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
Overall - weighted results	.	(N=18)		(N=1)		(N=9)		(N=0.08)		(N=10)		-		(N=28)	
	Breakthrough pain: Indication	6.1 (34.0%)	[2]	0.4 (33.3%)	[1]	5.3 (59.6%)	[1]	0.0 (0.0%)	-	5.6 (56.5%)	[1]	-	-	11.7 (42.0%)	[1]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	11.3 (62.9%)	[1]	0.0 (0.0%)	-	0.2 (2.2%)	[4]	0.008 (100.0%)	[1]	0.2 (2.3%)	[5]	-	-	11.5 (41.3%)	[2]
	Safe use	0.0 (0.0%)	-	0.4 (33.3%)	[1]	3.6 (40.4%)	[2]	0.0 (0.0%)	-	3.9 (39.5%)	[2]	-	-	3.9 (14.1%)	[3]
	Frequency of pain episodes	2.0 (11.3%)	[3]	0.2 (16.7%)	[4]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.8%)	[6]	-	-	2.2 (7.9%)	[4]
	Palliative treatment	2.0 (11.3%)	[3]	0.2 (16.7%)	[4]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.2 (1.8%)	[6]	-	-	2.2 (7.9%)	[4]
	Efficient	2.0 (11.3%)	[3]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	2.0 (7.3%)	[6]
	Compliance	0.0 (0.0%)	-	0.2 (16.7%)	[4]	1.7 (19.1%)	[3]	0.0 (0.0%)	-	1.9 (18.8%)	[3]	-	-	1.9 (6.7%)	[7]
	Route of administration: nasal	0.6 (3.1%)	[6]	0.4 (33.3%)	[1]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.4 (3.5%)	[4]	-	-	0.9 (3.3%)	[8]

Notes: The factor(s) which were taken into consideration by the physician when she/he prescribed Instanyl® among patients at risks of potential substance abuse and/or dependence are displayed in the column 'Response'. Since it is an open-ended question, multiple answers were possible. Therefore, the total exceeds 100%.

Table 0-11 summarizes the above overall weighted values and their 95% confidence intervals, per country and overall.

Table 0-11: Factors taken into consideration before prescribing Instanyl® to patients at risks of potential substance abuse and/or dependence - 95% CI for weighted percentages

Q10a. If yes, which factors did you take into consideration?

Country		Weighted percent	95% Confidence Limits, Weighted percent
France	Breakthrough pain: Indication	44.7%	[16.0% - 73.4%]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	39.5%	[10.7% - 68.2%]
	Safe use	14.5%	[0.0% - 33.4%]
	Frequency of pain episodes	8.6%	[0.0% - 24.9%]
	Palliative treatment	8.6%	[0.0% - 24.9%]
	Efficient	7.9%	[0.0% - 24.2%]
	Compliance	7.2%	[0.0% - 21.0%]
	Route of administration: nasal	1.4%	[0.0% - 3.6%]
The Netherlands	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	64.3%	[0.1% - 100.0%]
	Route of administration: nasal	26.7%	[0.0% - 89.3%]
	Breakthrough pain: Indication	9.1%	[0.0% - 35.2%]
	Safe use	9.1%	[0.0% - 35.2%]
Overall - weighted results	Breakthrough pain: Indication	42.0%	[15.9% - 68.1%]
	Risk of addiction: abuse and dependence: Spe. Warnings, prec. for use	41.3%	[15.2% - 67.5%]
	Safe use	14.1%	[0.0% - 31.2%]
	Frequency of pain episodes	7.9%	[0.0% - 22.7%]
	Palliative treatment	7.9%	[0.0% - 22.7%]
	Efficient	7.3%	[0.0% - 22.0%]
	Compliance	6.7%	[0.0% - 19.1%]

Q10a. If yes, which factors did you take into consideration?			
Country		**Weighted percent**	**95% Confidence Limits, Weighted percent**
	Route of administration: nasal	3.3%	[0.0% - 8.1%]

9.3.4 Information given to the Patients when prescribing Instanyl®

Brochure "How to use your Instanyl"

Q11 of Section 2 asked: When first prescribing Instanyl, what proportion of patients do you give the brochure "How to use your Instanyl®? Responses are presented in Table 9.3.4-1. Overall, 55.8% of physicians had given the brochure to at least some of their patients when first prescribing Instanyl® The proportion of physicians who gave the brochure to their patients was slightly higher in France (57.3%) than in the Netherlands (44.0%), and was higher among specialists (73.8%) than GPs (48.8%).

Interpretation:

The reason why patients were not given the brochure was not collected in the survey. Nevertheless, differences across countries could be due to the fact that the brochure is not delivered in the package in France; the physicians tend to give it to their patients when explaining how to use Instanyl®. In contrast, the brochure is present in the package in the Netherlands.

Table 9.3.4-1: Proportion of patients to whom the physicians gave the brochure "How to use your Instanyl®"

(Basis = Physicians with complete analysable questionnaire who prescribe Instanyl®)

Q11. When first prescribing Instanyl® to a patient, what proportion of patients do you give the brochure "How to use your Instanyl®?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=70)	(N=60)	(N=18)	(N=16)	(N=94)	(N=164)	(N=201)
	100%	5 (7.1%)	14 (23.3%)	3 (16.7%)	2 (12.5%)	19 (20.2%)	24 (14.6%)	19.9 (9.9%)
	75-99%	5 (7.1%)	9 (15.0%)	6 (33.3%)	4 (25.0%)	19 (20.2%)	24 (14.6%)	26.2 (13.1%)
	50-74%	6 (8.6%)	11 (18.3%)	1 (5.6%)	3 (18.8%)	15 (16.0%)	21 (12.8%)	19.1 (9.5%)
	25-49%	10 (14.3%)	3 (5.0%)	2 (11.1%)	1 (6.3%)	6 (6.4%)	16 (9.8%)	25.3 (12.6%)
	<24%	9 (12.9%)	7 (11.7%)	1 (5.6%)	3 (18.8%)	11 (11.7%)	20 (12.2%)	24.5 (12.2%)
	[1-100%]						64.0%	57.3%
	None	35 (50.0%)	16 (26.7%)	5 (27.8%)	3 (18.8%)	24 (25.5%)	59 (36.0%)	85.7 (42.7%)
Netherlands		(N=35)	(N=15)	(N=13)	(N=12)	(N=40)	(N=75)	(N=25)
	100%	2 (5.7%)	2 (13.3%)	2 (15.4%)	0 (0.0%)	4 (10.0%)	6 (8.0%)	1.8 (7.3%)
	75-99%	4 (11.4%)	2 (13.3%)	1 (7.7%)	0 (0.0%)	3 (7.5%)	7 (9.3%)	2.7 (11.0%)
	50-74%	2 (5.7%)	2 (13.3%)	2 (15.4%)	0 (0.0%)	4 (10.0%)	6 (8.0%)	1.8 (7.3%)
	25-49%	4 (11.4%)	0 (0.0%)	2 (15.4%)	0 (0.0%)	2 (5.0%)	6 (8.0%)	2.6 (10.6%)
	<24%	2 (5.7%)	0 (0.0%)	4 (30.8%)	2 (16.7%)	6 (15.0%)	8 (10.7%)	2.0 (7.9%)
	[1-100%]						44.0%	44.0%
	None	21 (60.0%)	9 (60.0%)	2 (15.4%)	10 (83.3%)	21 (52.5%)	42 (56.0%)	13.9 (56.0%)
Overall - unweighted results		(N=105)	(N=75)	(N=31)	(N=28)	(N=134)	(N=239)	-
	100%	7 (6.7%)	16 (21.3%)	5 (16.1%)	2 (7.1%)	23 (17.2%)	30 (12.6%)	-
	75-99%	9 (8.6%)	11 (14.7%)	7 (22.6%)	4 (14.3%)	22 (16.4%)	31 (13.0%)	-
	50-74%	8 (7.6%)	13 (17.3%)	3 (9.7%)	3 (10.7%)	19 (14.2%)	27 (11.3%)	-
	25-49%	14 (13.3%)	3 (4.0%)	4 (12.9%)	1 (3.6%)	8 (6.0%)	22 (9.2%)	-
	<24%	11 (10.5%)	7 (9.3%)	5 (16.1%)	5 (17.9%)	17 (12.7%)	28 (11.7%)	-
	[1-100%]						57.7%	-
	None	56 (53.3%)	25 (33.3%)	7 (22.6%)	13 (46.4%)	45 (33.6%)	101 (42.3%)	-
Overall -		(N=162)	(N=13)	(N=33)	(N=18)	(N=64)	-	(N=225)

Q11. When first prescribing Instanyl® to a patient, what proportion of patients do you give the brochure "How to use your Instanyl®?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
weighted results	100%	11.3 (7.0%)	2.8 (21.6%)	5.4 (16.6%)	2.2 (12.2%)	10.4 (16.3%)	-	21.7 (9.6%)
	75-99%	12.4 (7.7%)	1.9 (14.7%)	10.3 (31.4%)	4.3 (24.3%)	16.5 (26.0%)	-	29.0 (12.8%)
	50-74%	13.3 (8.2%)	2.2 (17.4%)	2.1 (6.3%)	3.3 (18.2%)	7.6 (11.9%)	-	20.9 (9.3%)
	25-49%	22.6 (13.9%)	0.5 (4.1%)	3.8 (11.4%)	1.1 (6.1%)	5.4 (8.5%)	-	27.9 (12.4%)
	<24%	19.4 (12.0%)	1.2 (9.6%)	2.5 (7.5%)	3.3 (18.7%)	7.0 (11.0%)	-	26.4 (11.7%)
	1-100%	48.8%	67.4%	73.2%	81.3%	73.8%	-	55.8%
	None	82.9 (51.2%)	4.2 (32.6%)	8.8 (26.8%)	3.7 (20.5%)	16.7 (26.2%)	-	99.6 (44.2%)

Table 9.3.4-2 summarizes the above overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.4-2: Proportion of patients to whom the physicians gave the brochure "How to use your Instanyl®" - 95% CI for weighted percentages

Q11. When first prescribing Instanyl® to a patient, what proportion of patients do you give the brochure "How to use your Instanyl®?			
Country	Response	**Weighted percent**	**95% Confidence Limits, Weighted percent**
France	100%	9.9%	[4.6% - 15.2%]
	75-99%	13.1%	[7.0% - 19.1%]
	50-74%	9.5%	[4.2% - 14.8%]
	25-49%	12.6%	[6.2% - 19.0%]
	<24%	12.2%	[6.1% - 18.3%]
	None	42.7%	[33.4% - 52.1%]
The Netherlands	100%	7.3%	[0.5% - 14.0%]
	75-99%	11.0%	[2.2% - 19.8%]
	50-74%	7.3%	[0.5% - 14.0%]
	25-49%	10.6%	[1.8% - 19.3%]
	<24%	7.9%	[1.0% - 14.8%]
	None	56.0%	[42.3% - 69.7%]
Overall - weighted results	100%	9.6%	[4.8% - 14.4%]
	75-99%	12.8%	[7.4% - 18.3%]
	50-74%	9.3%	[4.5% - 14.0%]
	25-49%	12.4%	[6.6% - 18.1%]
	<24%	11.7%	[6.2% - 17.2%]
	None	44.2%	[35.7% - 52.6%]

Safe Use and Storage

Q12 of Section 2 asked: What would you advise or explain to your patient with regards to the safe use and storage of Instanyl®? This was an open-ended question with a free text response box. A large number of responses and variations of similar responses were received, and are presented in Table 9.3.4-3 and Table 9.3.4-4.

Overall 94.3% of physicians reported they gave patients information on safe use and storage of Instanyl. The remaining 5.7% responded they did not know or not applicable.

The leading responses were:

- Safe use of Instanyl® (52.6%)
- Not to over use the drug (24.7%)
- General instructions about safe storage (13.7%)
- Keep away from children (13.2%)
- Store in dry and safe place (11.8%)
- Instructions explained in the leaflet/brochure or by a nurse and at the pharmacy (11.3%).

There was also a long list of responses on specific components of safe use not included in the above percentages.

Table 9.3.4-3: Advice or explanations given to patients about the safety use and storage of Instanyl®

(Basis = Physicians with complete analysable questionnaire)

Q12. What would you advise or explain to your patient with regards to the safe use and storage of Instanyl® when prescribing it?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest)

Country	n (%) [rank]	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France	.	(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Instructions for Safe use explained by physician: mainly about dosage and frequency	47 (48.5%) [1]	40 (61.5%) [1]	21 (67.7%) [1]	14 (82.4%) [1]	75 (66.4%) [1]	122 (58.1%) [1]	153.2 (54.8%) [1]
	Do not over use	21 (21.6%) [2]	20 (30.8%) [2]	11 (35.5%) [2]	9 (52.9%) [2]	40 (35.4%) [2]	61 (29.0%) [2]	74.5 (26.7%) [2]
	Safe storage: in general	13 (13.4%) [4]	5 (7.7%) [6]	5 (16.1%) [3]	4 (23.5%) [3]	14 (12.4%) [5]	27 (12.9%) [3]	40.1 (14.3%) [3]
	Store in dry and safe place: safe storage	15 (15.5%) [3]	5 (7.7%) [6]	3 (9.7%) [6]	0 (0.0%) -	8 (7.1%) [7]	23 (11.0%) [6]	36.4 (13.0%) [4]
	Keep away from children: safe storage	11 (11.3%) [5]	6 (9.2%) [5]	4 (12.9%) [5]	4 (23.5%) [3]	14 (12.4%) [5]	25 (11.9%) [4]	34.5 (12.4%) [5]
	Instructions explained in the leaflet/brochure/nurse/at the pharmacy	9 (9.3%) [6]	10 (15.4%) [3]	5 (16.1%) [3]	1 (5.9%) [8]	16 (14.2%) [3]	25 (11.9%) [4]	29.6 (10.6%) [6]
	Breakthrough pain: Indication	7 (7.2%) [7]	10 (15.4%) [3]	3 (9.7%) [6]	2 (11.8%) [5]	15 (13.3%) [4]	22 (10.5%) [7]	23.2 (8.3%) [7]
	Patient should sit or stand in upright position: Method of administration	6 (6.2%) [8]	3 (4.6%) [10]	1 (3.2%) [12]	2 (11.8%) [5]	6 (5.3%) [10]	12 (5.7%) [8]	16.6 (5.9%) [8]
	Recurrent episodes of epistaxis: Contraindications	6 (6.2%) [8]	3 (4.6%) [10]	0 (0.0%) -	1 (5.9%) [8]	4 (3.5%) [12]	10 (4.8%) [10]	13.8 (4.9%) [9]
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	6 (6.2%) [8]	1 (1.5%) [14]	0 (0.0%) -	1 (5.9%) [8]	2 (1.8%) [15]	8 (3.8%) [11]	13.5 (4.8%) [10]
	Call/contact the physician if any question	4 (4.1%) [11]	4 (6.2%) [8]	2 (6.5%) [9]	1 (5.9%) [8]	7 (6.2%) [8]	11 (5.2%) [9]	13.3 (4.8%) [11]

Q12. What would you advise or explain to your patient with regards to the safe use and storage of Instanyl® when prescribing it?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest)

Country	n (%) [rank]	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	3 (3.1%) [14]	1 (1.5%) [14]	2 (6.5%) [9]	0 (0.0%) -	3 (2.7%) [13]	6 (2.9%) [13]	9.7 (3.5%) [12]
	Risk of misuse/overuse	2 (2.1%) [16]	0 (0.0%) -	3 (9.7%) [6]	0 (0.0%) -	3 (2.7%) [13]	5 (2.4%) [16]	9.1 (3.3%) [13]
	Do not know	4 (4.1%) [11]	2 (3.1%) [13]	0 (0.0%) -	0 (0.0%) -	2 (1.8%) [15]	6 (2.9%) [13]	8.5 (3.0%) [14]
	Dosage: possible dose control / dosage easy	4 (4.1%) [11]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	4 (1.9%) [17]	8.1 (2.9%) [15]
	Not applicable	2 (2.1%) [16]	0 (0.0%) -	2 (6.5%) [9]	0 (0.0%) -	2 (1.8%) [15]	4 (1.9%) [17]	7.4 (2.7%) [16]
	Risk of common adverse reactions	1 (1.0%) [20]	4 (6.2%) [8]	1 (3.2%) [12]	2 (11.8%) [5]	7 (6.2%) [8]	8 (3.8%) [11]	6.6 (2.4%) [17]
	Stop treatment if adverse events	3 (3.1%) [14]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	3 (1.4%) [19]	6.1 (2.2%) [18]
	Do not drive/Effects on ability to drive and use machines	1 (1.0%) [20]	3 (4.6%) [10]	1 (3.2%) [12]	1 (5.9%) [8]	5 (4.4%) [11]	6 (2.9%) [13]	5.3 (1.9%) [19]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	2 (2.1%) [16]	1 (1.5%) [14]	0 (0.0%) -	0 (0.0%) -	1 (0.9%) [19]	3 (1.4%) [19]	4.2 (1.5%) [20]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	2 (2.1%) [16]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	2 (1.0%) [21]	4.1 (1.5%) [21]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	1 (1.0%) [20]	0 (0.0%) -	1 (3.2%) [12]	0 (0.0%) -	1 (0.9%) [19]	2 (1.0%) [21]	3.7 (1.3%) [22]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	1 (1.0%) [20]	0 (0.0%) -	1 (3.2%) [12]	0 (0.0%) -	1 (0.9%) [19]	2 (1.0%) [21]	3.7 (1.3%) [22]
	Close vial after utilisation: safe storage	1 (1.0%) [20]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	1 (0.5%) [25]	2.0 (0.7%) [24]
	Efficient	1 (1.0%) [20]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	1 (0.5%) [25]	2.0 (0.7%) [24]
	Quick action: rapid/fast response	1 (1.0%) [20]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	1 (0.5%) [25]	2.0 (0.7%) [24]
	Reassure against risk of addition if used correctly	0 (0.0%) -	0 (0.0%) -	1 (3.2%) [12]	0 (0.0%) -	1 (0.9%) [19]	1 (0.5%) [25]	1.7 (0.6%) [27]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	0 (0.0%) -	1 (1.5%) [14]	0 (0.0%) -	1 (5.9%) [8]	2 (1.8%) [15]	2 (1.0%) [21]	1.3 (0.5%) [28]
	Previous facial radiotherapy: Contraindications	0 (0.0%) -	1 (1.5%) [14]	0 (0.0%) -	0 (0.0%) -	1 (0.9%) [19]	1 (0.5%) [25]	0.2 (0.1%) [29]

Q12. What would you advise or explain to your patient with regards to the safe use and storage of Instanyl® when prescribing it?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	Risk of overdose	0 (0.0%)	-	1 (1.5%)	[14]	0 (0.0%)	-	0 (0.0%)	-	1 (0.9%)	[19]	1 (0.5%)	[25]	0.2 (0.1%)	[29]
	Store in dry, cool and safe place: safe storage	0 (0.0%)	-	1 (1.5%)	[14]	0 (0.0%)	-	0 (0.0%)	-	1 (0.9%)	[19]	1 (0.5%)	[25]	0.2 (0.1%)	[29]
The Netherlands	.	(N=40)		(N=19)		(N=24)		(N=17)		(N=60)		(N=100)		(N=31)	
	Instructions for Safe use explained by physician: mainly about dosage and frequency	11 (27.5%)	[1]	9 (47.4%)	[1]	11 (45.8%)	[1]	7 (41.2%)	[1]	27 (45.0%)	[1]	38 (38.0%)	[1]	9.9 (32.4%)	[1]
	Keep away from children: safe storage	9 (22.5%)	[2]	2 (10.5%)	[4]	5 (20.8%)	[2]	0 (0.0%)	-	7 (11.7%)	[4]	16 (16.0%)	[2]	6.3 (20.6%)	[2]
	Instructions explained in the leaflet/brochure/nurse/at the pharmacy	8 (20.0%)	[3]	3 (15.8%)	[3]	3 (12.5%)	[4]	1 (5.9%)	[3]	7 (11.7%)	[4]	15 (15.0%)	[3]	5.6 (18.2%)	[3]
	Patient should sit or stand in upright position: Method of administration	8 (20.0%)	[3]	0 (0.0%)	-	0 (0.0%)	-	1 (5.9%)	[3]	1 (1.7%)	[11]	9 (9.0%)	[6]	4.5 (14.8%)	[4]
	Safe storage: in general	4 (10.0%)	[5]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	4 (4.0%)	[8]	2.2 (7.3%)	[5]
	Do not over use	1 (2.5%)	[8]	4 (21.1%)	[2]	4 (16.7%)	[3]	1 (5.9%)	[3]	9 (15.0%)	[2]	10 (10.0%)	[4]	2.0 (6.5%)	[6]
	Breakthrough pain: Indication	3 (7.5%)	[6]	1 (5.3%)	[6]	0 (0.0%)	-	1 (5.9%)	[3]	2 (3.3%)	[6]	5 (5.0%)	[7]	1.9 (6.1%)	[7]
	Close vial after utilisation: safe storage	2 (5.0%)	[7]	2 (10.5%)	[4]	0 (0.0%)	-	0 (0.0%)	-	2 (3.3%)	[6]	4 (4.0%)	[8]	1.4 (4.7%)	[8]
	Not applicable	1 (2.5%)	[8]	0 (0.0%)	-	2 (8.3%)	[5]	7 (41.2%)	[1]	9 (15.0%)	[2]	10 (10.0%)	[4]	1.2 (4.0%)	[9]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	1 (2.5%)	[8]	0 (0.0%)	-	1 (4.2%)	[8]	1 (5.9%)	[3]	2 (3.3%)	[6]	3 (3.0%)	[10]	0.8 (2.6%)	[10]
	Quick action: rapid/fast response	1 (2.5%)	[8]	0 (0.0%)	-	1 (4.2%)	[8]	0 (0.0%)	-	1 (1.7%)	[11]	2 (2.0%)	[11]	0.8 (2.5%)	[11]
	Do not know	1 (2.5%)	[8]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (1.0%)	[14]	0.6 (1.8%)	[12]
	Reassure against risk of addition if used correctly	1 (2.5%)	[8]	0 (0.0%)	-	0 (0.0%)	-	0 (0.0%)	-		-	1 (1.0%)	[14]	0.6 (1.8%)	[12]
	Dosage: possible dose control / dosage easy	0 (0.0%)	-	0 (0.0%)	-	2 (8.3%)	[5]	0 (0.0%)	-	2 (3.3%)	[6]	2 (2.0%)	[11]	0.4 (1.2%)	[14]
	Risk of common adverse reactions	0 (0.0%)	-	0 (0.0%)	-	2 (8.3%)	[5]	0 (0.0%)	-	2 (3.3%)	[6]	2 (2.0%)	[11]	0.4 (1.2%)	[14]
	Do not drive/Effects on ability to drive and use machines	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[8]	0 (0.0%)	-	1 (1.7%)	[11]	1 (1.0%)	[14]	0.2 (0.6%)	[16]
	Efficient	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[8]	0 (0.0%)	-	1 (1.7%)	[11]	1 (1.0%)	[14]	0.2 (0.6%)	[16]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	0 (0.0%)	-	0 (0.0%)	-	1 (4.2%)	[8]	0 (0.0%)	-	1 (1.7%)	[11]	1 (1.0%)	[14]	0.2 (0.6%)	[16]

Q12. What would you advise or explain to your patient with regards to the safe use and storage of Instanyl® when prescribing it?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest)

Country	n (%) [rank]	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	0 (0.0%) -	0 (0.0%) -	1 (4.2%) [8]	0 (0.0%) -	1 (1.7%) [11]	1 (1.0%) [14]	0.2 (0.6%) [16]
	Risk of overdose	0 (0.0%) -	1 (5.3%) [6]	0 (0.0%) -	0 (0.0%) -	1 (1.7%) [11]	1 (1.0%) [14]	0.2 (0.5%) [20]
	Store in dry and safe place: safe storage	0 (0.0%) -	1 (5.3%) [6]	0 (0.0%) -	0 (0.0%) -	1 (1.7%) [11]	1 (1.0%) [14]	0.2 (0.5%) [20]
Overall - unweighted results	.	(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Instructions for Safe use explained by physician: mainly about dosage and frequency	58 (42.3%) [1]	49 (58.3%) [1]	32 (58.2%) [1]	21 (61.8%) [1]	102 (59.0%) [1]	160 (51.6%) [1]	- -
	Do not over use	22 (16.1%) [2]	24 (28.6%) [2]	15 (27.3%) [2]	10 (29.4%) [2]	49 (28.3%) [2]	71 (22.9%) [2]	- -
	Safe storage: in general	17 (12.4%) [4]	5 (6.0%) [7]	5 (9.1%) [5]	4 (11.8%) [4]	14 (8.1%) [6]	31 (10.0%) [5]	- -
	Keep away from children: safe storage	20 (14.6%) [3]	8 (9.5%) [5]	9 (16.4%) [3]	4 (11.8%) [4]	21 (12.1%) [4]	41 (13.2%) [3]	- -
	Store in dry and safe place: safe storage	15 (10.9%) [6]	6 (7.1%) [6]	3 (5.5%) [7]	0 (0.0%) -	9 (5.2%) [8]	24 (7.7%) [7]	- -
	Instructions explained in the leaflet/brochure/nurse/at the pharmacy	17 (12.4%) [4]	13 (15.5%) [3]	8 (14.5%) [4]	2 (5.9%) [8]	23 (13.3%) [3]	40 (12.9%) [4]	- -
	Breakthrough pain: Indication	10 (7.3%) [8]	11 (13.1%) [4]	3 (5.5%) [7]	3 (8.8%) [6]	17 (9.8%) [5]	27 (8.7%) [6]	- -
	Patient should sit or stand in upright position: Method of administration	14 (10.2%) [7]	3 (3.6%) [10]	1 (1.8%) [16]	3 (8.8%) [6]	7 (4.0%) [10]	21 (6.8%) [8]	- -
	Recurrent episodes of epistaxis: Contraindications	6 (4.4%) [9]	3 (3.6%) [10]	0 (0.0%) -	1 (2.9%) [10]	4 (2.3%) [13]	10 (3.2%) [11]	- -
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	6 (4.4%) [9]	1 (1.2%) [16]	0 (0.0%) -	1 (2.9%) [10]	2 (1.2%) [17]	8 (2.6%) [13]	- -
	Call/contact the physician if any question	4 (2.9%) [12]	4 (4.8%) [8]	2 (3.6%) [11]	1 (2.9%) [10]	7 (4.0%) [10]	11 (3.5%) [10]	- -
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	3 (2.2%) [14]	1 (1.2%) [16]	2 (3.6%) [11]	0 (0.0%) -	3 (1.7%) [14]	6 (1.9%) [16]	- -
	Risk of misuse/overuse	2 (1.5%) [18]	0 (0.0%) -	3 (5.5%) [7]	0 (0.0%) -	3 (1.7%) [14]	5 (1.6%) [18]	- -
	Do not know	5 (3.6%) [11]	2 (2.4%) [13]	0 (0.0%) -	0 (0.0%) -	2 (1.2%) [17]	7 (2.3%) [14]	- -

Q12. What would you advise or explain to your patient with regards to the safe use and storage of Instanyl® when prescribing it?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest)

Country	n (%) [rank]	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
	Not applicable	3 (2.2%) [14]	0 (0.0%) -	4 (7.3%) [6]	7 (20.6%) [3]	11 (6.4%) [7]	14 (4.5%) [9]	- -
	Dosage: possible dose control / dosage easy	4 (2.9%) [12]	0 (0.0%) -	2 (3.6%) [11]	0 (0.0%) -	2 (1.2%) [17]	6 (1.9%) [16]	- -
	Risk of common adverse reactions	1 (0.7%) [22]	4 (4.8%) [8]	3 (5.5%) [7]	2 (5.9%) [8]	9 (5.2%) [8]	10 (3.2%) [11]	- -
	Stop treatment if adverse events	3 (2.2%) [14]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	3 (1.0%) [20]	- -
	Do not drive/Effects on ability to drive and use machines	1 (0.7%) [22]	3 (3.6%) [10]	2 (3.6%) [11]	1 (2.9%) [10]	6 (3.5%) [12]	7 (2.3%) [14]	- -
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	2 (1.5%) [18]	1 (1.2%) [16]	0 (0.0%) -	0 (0.0%) -	1 (0.6%) [24]	3 (1.0%) [20]	- -
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	2 (1.5%) [18]	0 (0.0%) -	0 (0.0%) -	0 (0.0%) -	-	2 (0.6%) [26]	- -
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	1 (0.7%) [22]	0 (0.0%) -	2 (3.6%) [11]	0 (0.0%) -	2 (1.2%) [17]	3 (1.0%) [20]	- -
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	1 (0.7%) [22]	0 (0.0%) -	1 (1.8%) [16]	0 (0.0%) -	1 (0.6%) [24]	2 (0.6%) [26]	- -
	Close vial after utilisation: safe storage	3 (2.2%) [14]	2 (2.4%) [13]	0 (0.0%) -	0 (0.0%) -	2 (1.2%) [17]	5 (1.6%) [18]	- -
	Quick action: rapid/fast response	2 (1.5%) [18]	0 (0.0%) -	1 (1.8%) [16]	0 (0.0%) -	1 (0.6%) [24]	3 (1.0%) [20]	- -
	Reassure against risk of addition if used correctly	1 (0.7%) [22]	0 (0.0%) -	1 (1.8%) [16]	0 (0.0%) -	1 (0.6%) [24]	2 (0.6%) [26]	- -
	Efficient	1 (0.7%) [22]	0 (0.0%) -	1 (1.8%) [16]	0 (0.0%) -	1 (0.6%) [24]	2 (0.6%) [26]	- -
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	0 (0.0%) -	1 (1.2%) [16]	1 (1.8%) [16]	1 (2.9%) [10]	3 (1.7%) [14]	3 (1.0%) [20]	- -
	Risk of Respiratory depression: Spe. Warnings, prec. for use	1 (0.7%) [22]	0 (0.0%) -	1 (1.8%) [16]	1 (2.9%) [10]	2 (1.2%) [17]	3 (1.0%) [20]	- -
	Risk of overdose	0 (0.0%) -	2 (2.4%) [13]	0 (0.0%) -	0 (0.0%) -	2 (1.2%) [17]	2 (0.6%) [26]	- -
	Previous facial radiotherapy: Contraindications	0 (0.0%) -	1 (1.2%) [16]	0 (0.0%) -	0 (0.0%) -	1 (0.6%) [24]	1 (0.3%) [31]	- -
	Store in dry, cool and safe place: safe storage	0 (0.0%) -	1 (1.2%) [16]	0 (0.0%) -	0 (0.0%) -	1 (0.6%) [24]	1 (0.3%) [31]	- -

Q12. What would you advise or explain to your patient with regards to the safe use and storage of Instanyl® when prescribing it?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
Overall - weighted results	.	(N=220)		(N=14)		(N=57)		(N=19)		(N=90)		-		(N=310)	
	Instructions for Safe use explained by physician: mainly about dosage and frequency	101.7 (46.3%)	[1]	8.4 (58.7%)	[1]	37.5 (66.0%)	[1]	15.5 (80.9%)	[1]	61.4 (68.0%)	[1]	-	-	163.1 (52.6%)	[1]
	Do not over use	43.3 (19.7%)	[2]	4.1 (28.8%)	[2]	19.3 (34.0%)	[2]	9.8 (51.3%)	[2]	33.3 (36.8%)	[2]	-	-	76.5 (24.7%)	[2]
	Safe storage: in general	28.7 (13.1%)	[4]	0.9 (6.1%)	[7]	8.4 (14.8%)	[4]	4.3 (22.7%)	[3]	13.7 (15.1%)	[3]	-	-	42.3 (13.7%)	[3]
	Keep away from children: safe storage	27.4 (12.5%)	[5]	1.4 (9.5%)	[5]	7.7 (13.5%)	[5]	4.3 (22.7%)	[3]	13.4 (14.8%)	[4]	-	-	40.8 (13.2%)	[4]
	Store in dry and safe place: safe storage	30.5 (13.9%)	[3]	1.0 (7.2%)	[6]	5.1 (8.9%)	[6]	0.0 (0.0%)	-	6.1 (6.7%)	[7]	-	-	36.6 (11.8%)	[5]
	Instructions explained in the leaflet/brochure/nurse/at the pharmacy	22.8 (10.4%)	[6]	2.2 (15.5%)	[3]	9.0 (15.8%)	[3]	1.1 (5.9%)	[8]	12.4 (13.7%)	[5]	-	-	35.1 (11.3%)	[6]
	Breakthrough pain: Indication	15.9 (7.2%)	[8]	1.9 (13.3%)	[4]	5.1 (8.9%)	[6]	2.2 (11.6%)	[5]	9.2 (10.2%)	[6]	-	-	25.1 (8.1%)	[7]
	Patient should sit or stand in upright position: Method of administration	16.7 (7.6%)	[7]	0.5 (3.7%)	[10]	1.7 (3.0%)	[15]	2.2 (11.6%)	[5]	4.4 (4.9%)	[11]	-	-	21.1 (6.8%)	[8]
	Recurrent episodes of epistaxis: Contraindications	12.2 (5.6%)	[9]	0.5 (3.7%)	[10]	0.0 (0.0%)	-	1.1 (5.7%)	[9]	1.6 (1.8%)	[18]	-	-	13.8 (4.5%)	[9]
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	12.2 (5.6%)	[9]	0.2 (1.2%)	[16]	0.0 (0.0%)	-	1.1 (5.7%)	[9]	1.3 (1.4%)	[20]	-	-	13.5 (4.3%)	[10]
	Call/contact the physician if any question	8.1 (3.7%)	[12]	0.7 (4.9%)	[8]	3.4 (5.9%)	[10]	1.1 (5.7%)	[9]	5.2 (5.7%)	[8]	-	-	13.3 (4.3%)	[11]
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	6.1 (2.8%)	[14]	0.2 (1.2%)	[16]	3.4 (5.9%)	[10]	0.0 (0.0%)	-	3.6 (3.9%)	[13]	-	-	9.7 (3.1%)	[12]
	Risk of misuse/overuse	4.1 (1.9%)	[17]	0.0 (0.0%)	-	5.1 (8.9%)	[6]	0.0 (0.0%)	-	5.1 (5.6%)	[9]	-	-	9.1 (2.9%)	[13]
	Do not know	8.7 (4.0%)	[11]	0.4 (2.5%)	[13]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.4 (0.4%)	[22]	-	-	9.0 (2.9%)	[14]
	Not applicable	4.6 (2.1%)	[16]	0.0 (0.0%)	-	3.8 (6.6%)	[9]	0.3 (1.5%)	[14]	4.0 (4.5%)	[12]	-	-	8.7 (2.8%)	[15]
	Dosage: possible dose control / dosage easy	8.1 (3.7%)	[12]	0.0 (0.0%)	-	0.4 (0.7%)	[18]	0.0 (0.0%)	-	0.4 (0.4%)	[21]	-	-	8.5 (2.7%)	[16]
	Risk of common adverse reactions	2.0 (0.9%)	[22]	0.7 (4.9%)	[8]	2.1 (3.6%)	[12]	2.2 (11.3%)	[7]	4.9 (5.5%)	[10]	-	-	7.0 (2.3%)	[17]
	Stop treatment if adverse events	6.1 (2.8%)	[14]	0.0 (0.0%)	-	0.0 (0.0%)	-	0.0 (0.0%)	-		-	-	-	6.1 (2.0%)	[18]

Q12. What would you advise or explain to your patient with regards to the safe use and storage of Instanyl® when prescribing it?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest)

Country	n (%) [rank]	GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
	Do not drive/Effects on ability to drive and use machines	2.0 (0.9%) [22]	0.5 (3.7%) [10]	1.9 (3.3%) [13]	1.1 (5.7%) [9]	3.5 (3.9%) [14]	- -	5.5 (1.8%) [19]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	4.1 (1.9%) [17]	0.2 (1.2%) [16]	0.0 (0.0%) -	0.0 (0.0%) -	0.2 (0.2%) [28]	- -	4.2 (1.4%) [20]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	4.1 (1.9%) [17]	0.0 (0.0%) -	0.0 (0.0%) -	0.0 (0.0%) -	-	- -	4.1 (1.3%) [21]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	2.0 (0.9%) [22]	0.0 (0.0%) -	1.9 (3.3%) [13]	0.0 (0.0%) -	1.9 (2.1%) [15]	- -	3.9 (1.3%) [22]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	2.0 (0.9%) [22]	0.0 (0.0%) -	1.7 (3.0%) [15]	0.0 (0.0%) -	1.7 (1.9%) [16]	- -	3.7 (1.2%) [23]
	Close vial after utilisation: safe storage	3.2 (1.4%) [20]	0.3 (2.1%) [15]	0.0 (0.0%) -	0.0 (0.0%) -	0.3 (0.3%) [24]	- -	3.5 (1.1%) [24]
	Quick action: rapid/fast response	2.6 (1.2%) [21]	0.0 (0.0%) -	0.2 (0.3%) [19]	0.0 (0.0%) -	0.2 (0.2%) [26]	- -	2.8 (0.9%) [25]
	Reassure against risk of addition if used correctly	0.6 (0.3%) [27]	0.0 (0.0%) -	1.7 (3.0%) [15]	0.0 (0.0%) -	1.7 (1.9%) [16]	- -	2.2 (0.7%) [26]
	Efficient	2.0 (0.9%) [22]	0.0 (0.0%) -	0.2 (0.3%) [19]	0.0 (0.0%) -	0.2 (0.2%) [26]	- -	2.2 (0.7%) [27]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	0.0 (0.0%) -	0.2 (1.2%) [16]	0.2 (0.3%) [19]	1.1 (5.7%) [9]	1.5 (1.6%) [19]	- -	1.5 (0.5%) [28]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	0.6 (0.3%) [27]	0.0 (0.0%) -	0.2 (0.3%) [19]	0.0 (0.2%) [15]	0.2 (0.3%) [25]	- -	0.8 (0.3%) [29]
	Risk of overdose	0.0 (0.0%) -	0.3 (2.3%) [14]	0.0 (0.0%) -	0.0 (0.0%) -	0.3 (0.4%) [23]	- -	0.3 (0.1%) [30]
	Previous facial radiotherapy: Contraindications	0.0 (0.0%) -	0.2 (1.2%) [16]	0.0 (0.0%) -	0.0 (0.0%) -	0.2 (0.2%) [28]	- -	0.2 (0.1%) [31]
	Store in dry, cool and safe place: safe storage	0.0 (0.0%) -	0.2 (1.2%) [16]	0.0 (0.0%) -	0.0 (0.0%) -	0.2 (0.2%) [28]	- -	0.2 (0.1%) [31]

Note: The explanations given by the physicians to their patients about the safety use and storage of Instanyl® are displayed in the column 'Response'. Since it is an open-ended question, multiple answers were possible. Therefore, the total exceeds 100%.

Table 9.3.4-4 summarizes the above overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.4-4: Advice or explanations given to patients about the safety use and storage of Instanyl® - 95% CI for weighted percentages

Q12. What would you advise or explain to your patient with regards to the safety use and storage of Instanyl® when prescribing it?

Country		Weighted percent	95% Confidence Limits, Weighted percent
France	Instructions for Safe use explained by physician: mainly about dosage and frequency	54.8%	[46.9% - 62.8%]
	Do not over use	26.7%	[19.7% - 33.6%]
	Safe storage: in general	14.3%	[8.8% - 19.9%]
	Store in dry and safe place: safe storage	13.0%	[7.5% - 18.6%]
	Keep away from children: safe storage	12.4%	[7.1% - 17.6%]
	Instructions explained in the leaflet/brochure/nurse/at the pharmacy	10.6%	[5.7% - 15.5%]
	Breakthrough pain: Indication	8.3%	[4.0% - 12.6%]
	Patient should sit or stand in upright position: Method of administration	5.9%	[2.2% - 9.7%]
	Recurrent episodes of epistaxis: Contraindications	4.9%	[1.4% - 8.5%]
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	4.8%	[1.3% - 8.3%]
	Call/contact the physician if any question	4.8%	[1.4% - 8.1%]
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	3.5%	[0.5% - 6.4%]
	Risk of misuse/overuse	3.3%	[0.4% - 6.1%]
	Do not know	3.0%	[0.2% - 5.9%]
	Dosage: possible dose control / dosage easy	2.9%	[0.1% - 5.7%]
	Not applicable	2.7%	[0.1% - 5.3%]
	Risk of common adverse reactions	2.4%	[0.2% - 4.5%]
	Stop treatment if adverse events	2.2%	[0.0% - 4.6%]
	Do not drive/Effects on ability to drive and use machines	1.9%	[0.0% - 3.9%]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	1.5%	[0.0% - 3.5%]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	1.5%	[0.0% - 3.5%]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	1.3%	[0.0% - 3.2%]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	1.3%	[0.0% - 3.2%]
	Close vial after utilisation: safe storage	0.7%	[0.0% - 2.2%]
	Efficient	0.7%	[0.0% - 2.2%]
	Quick action: rapid/fast response	0.7%	[0.0% - 2.2%]
	Reassure against risk of addition if used correctly	0.6%	[0.0% - 1.8%]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	0.5%	[0.0% - 1.2%]
	Previous facial radiotherapy: Contraindications	0.1%	[0.0% - 0.2%]
	Risk of overdose	0.1%	[0.0% - 0.2%]
	Store in dry, cool and safe place: safe storage	0.1%	[0.0% - 0.2%]
The Netherlands	Instructions for Safe use explained by physician: mainly about dosage and frequency	32.4%	[21.3% - 43.5%]
	Keep away from children: safe storage	20.6%	[10.5% - 30.7%]
	Instructions explained in the leaflet/brochure/nurse/at the pharmacy	18.2%	[8.5% - 27.8%]
	Patient should sit or stand in upright position: Method of administration	14.8%	[5.4% - 24.2%]
	Safe storage: in general	7.3%	[0.3% - 14.3%]
	Do not over use	6.5%	[1.7% - 11.2%]
	Breakthrough pain: Indication	6.1%	[0.0% - 12.3%]

Q12. What would you advise or explain to your patient with regards to the safety use and storage of Instanyl® when prescribing it?

Country		Weighted percent	95% Confidence Limits, Weighted percent
	Close vial after utilisation: safe storage	4.7%	[0.0% - 9.9%]
	Not applicable	4.0%	[0.0% - 8.1%]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	2.6%	[0.0% - 6.4%]
	Quick action: rapid/fast response	2.5%	[0.0% - 6.3%]
	Do not know	1.8%	[0.0% - 5.4%]
	Reassure against risk of addition if used correctly	1.8%	[0.0% - 5.4%]
	Dosage: possible dose control / dosage easy	1.2%	[0.0% - 3.0%]
	Risk of common adverse reactions	1.2%	[0.0% - 3.0%]
	Do not drive/Effects on ability to drive and use machines	0.6%	[0.0% - 1.9%]
	Efficient	0.6%	[0.0% - 1.9%]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	0.6%	[0.0% - 1.9%]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	0.6%	[0.0% - 1.9%]
	Risk of overdose	0.5%	[0.0% - 1.5%]
	Store in dry and safe place: safe storage	0.5%	[0.0% - 1.5%]
Overall - weighted results	Instructions for Safe use explained by physician: mainly about dosage and frequency	52.6%	[45.4% - 59.9%]
	Do not over use	24.7%	[18.4% - 31.0%]
	Safe storage: in general	13.7%	[8.6% - 18.7%]
	Keep away from children: safe storage	13.2%	[8.4% - 18.0%]
	Store in dry and safe place: safe storage	11.8%	[6.8% - 16.8%]
	Instructions explained in the leaflet/brochure/nurse/at the pharmacy	11.3%	[6.8% - 15.8%]
	Breakthrough pain: Indication	8.1%	[4.2% - 12.0%]
	Patient should sit or stand in upright position: Method of administration	6.8%	[3.3% - 10.3%]
	Recurrent episodes of epistaxis: Contraindications	4.5%	[1.3% - 7.6%]
	Respiratory, thoracic and mediastinal disorders (Throat irritation, resp. depression, epistaxis, nasal septum perforation,etc.): A. reactions	4.3%	[1.2% - 7.5%]
	Call/contact the physician if any question	4.3%	[1.3% - 7.3%]
	Patients without maintenance opioid therapy (increased risk of respiratory depression): Contraindications	3.1%	[0.5% - 5.8%]
	Risk of misuse/overuse	2.9%	[0.4% - 5.5%]
	Do not know	2.9%	[0.3% - 5.5%]
	Not applicable	2.8%	[0.4% - 5.2%]
	Dosage: possible dose control / dosage easy	2.7%	[0.2% - 5.3%]
	Risk of common adverse reactions	2.3%	[0.3% - 4.2%]
	Stop treatment if adverse events	2.0%	[0.0% - 4.2%]
	Do not drive/Effects on ability to drive and use machines	1.8%	[0.0% - 3.6%]
	Gastrointestinal disorders (Nausea, vomiting, constipation, stomatitis, diarrhoea, etc.): Adverse reactions	1.4%	[0.0% - 3.2%]
	Nervous system disorders (somnolence, dizziness, headache, paraesthesia, convulsion, etc.): Adverse reactions	1.3%	[0.0% - 3.1%]
	Risk of addiction: Abuse potential and dependence (physical/psychological): Spe. Warnings, prec. for use	1.3%	[0.0% - 2.9%]
	Severe respiratory depression or severe obstructive lung conditions: Contraindications	1.2%	[0.0% - 2.9%]
	Close vial after utilisation: safe storage	1.1%	[0.0% - 2.5%]
	Quick action: rapid/fast response	0.9%	[0.0% - 2.2%]
	Reassure against risk of addition if used correctly	0.7%	[0.0% - 1.9%]
	Efficient	0.7%	[0.0% - 2.0%]
	Nasal conditions/discomfort: Spe. Warnings, prec. for use	0.5%	[0.0% - 1.2%]
	Risk of Respiratory depression: Spe. Warnings, prec. for use	0.3%	[0.0% - 0.6%]
	Risk of overdose	0.1%	[0.0% - 0.3%]
	Previous facial radiotherapy: Contraindications	0.1%	[0.0% - 0.2%]

Q12. What would you advise or explain to your patient with regards to the safety use and storage of Instanyl® when prescribing it?			
Country		**Weighted percent**	**95% Confidence Limits, Weighted percent**
	Store in dry, cool and safe place: safe storage	0.1%	[0.0% - 0.2%]

Receipt of the updated educational materials:

Q13 of Section 2 asked if the physician had received the Instanyl® educational materials within the 6-12 months prior to the survey. Responses are shown in Table 9.3.4-5. Overall, 20.3% responded Yes they had received it, 38.4% responded they could not remember or were not sure, and 41.3% responded that they had not received it.

Physician specialty with the highest proportion responding that they had received the educational materials were radiologist (45.6%, n=19) and oncologists (31.6%, n=14) whereas GPs (17.4%) and anesthesiologists (19.8%) had the lowest proportions reporting they had received the materials. Conversely, GPs (41.7%) and radiologists (41.0%) had the highest proportions responding that they could not remember or were not sure.

Interpretation:

As is standard practice with effectiveness surveys of educational materials, this survey was conducted 3-12 months after distribution of the educational materials, so the high proportion of responses of not remembering or not being sure is unsurprising. The low positive response rate may also reflect physicians being overwhelmed by materials being distributed by pharmaceutical companies.

Table 9.3.4-5: Receipt of the educational materials on Instanyl® sent by the pharmaceutical company

(Basis = Physicians with complete analysable questionnaire)

Q13. Did you receive any educational materials on Instanyl® sent by the pharmaceutical company in the last 6-12 months?								
Country		**GPs**	**Oncologists**	**Anesthesiologists**	**Radiologists**	**Specialists**	**All - Unweighted sample**	**All - Weighted sample**
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	No	42 (43.3%)	19 (29.2%)	18 (58.1%)	2 (11.8%)	39 (34.5%)	81 (38.6%)	121.3 (43.4%)
	Yes	18 (18.6%)	24 (36.9%)	6 (19.4%)	8 (47.1%)	38 (33.6%)	56 (26.7%)	59.6 (21.3%)
	95% Confidence Limits							[15.0% - 27.7%]
	I cannot remember/ I am not sure	37 (38.1%)	22 (33.8%)	7 (22.6%)	7 (41.2%)	36 (31.9%)	73 (34.8%)	98.5 (35.3%)
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=31)	(N=31)
	No	8 (20.0%)	8 (42.1%)	4 (16.7%)	10 (58.8%)	22 (36.7%)	6.9 (22.5%)	6.9 (22.5%)
	Yes	3 (7.5%)	2 (10.5%)	6 (25.0%)	1 (5.9%)	9 (15.0%)	3.2 (10.4%)	3.2 (10.4%)
	95% Confidence Limits							[3.5% - 17.2%]
	I cannot remember/ I am not sure	29 (72.5%)	9 (47.4%)	14 (58.3%)	6 (35.3%)	29 (48.3%)	58 (58.0%)	20.5 (67.2%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	No	50 (36.5%)	27 (32.1%)	22 (40.0%)	12 (35.3%)	61 (35.3%)	111 (35.8%)	-
	Yes	21 (15.3%)	26 (31.0%)	12 (21.8%)	9 (26.5%)	47 (27.2%)	68 (21.9%)	-
	I cannot remember/ I am not sure	66 (48.2%)	31 (36.9%)	21 (38.2%)	13 (38.2%)	65 (37.6%)	131 (42.3%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	No	89.9 (40.9%)	4.6 (31.8%)	31.1 (54.7%)	2.6 (13.4%)	38.3 (42.4%)	-	128.2 (41.3%)
	Yes	38.3 (17.4%)	4.5 (31.6%)	11.3 (19.8%)	8.7 (45.6%)	24.5 (27.1%)	-	62.8 (20.3%)
	95% Confidence Limits							[14.5% - 26.0%]
	I cannot remember/ I am not sure	91.5 (41.7%)	5.2 (36.6%)	14.5 (25.5%)	7.8 (41.0%)	27.6 (30.5%)	-	119.0 (38.4%)

Awareness about the conditions of safe use of Instanyl recently updated by the MAH:

Q14 of Section 2 asked if physicians were aware of the conditions of safe use of Instanyl® recently updated by the MAH. Responses are shown in Table 9.3.4-5. Overall, only 13.6% of physicians reported they were aware about the conditions of safe use of on Instanyl® recently updated by the pharmaceutical company. While 39.9% of radiologists responded Yes, only 6.6% of GP similarly responded. In total few physicians were aware that the conditions of safe use had recently been updated.

Interpretation:

Unfortunately, in hindsight, this question was poorly phrased, as the conditions of safe use had not been modified, the education materials had just been updated to reinforce the safe use of the drug. This imprecision in the question may have contributed to the low positive response rate.

Table 9.3.4-6: Awareness about the conditions of safe use of Instanyl® recently reiterated

(Basis = Physicians with complete analysable questionnaire)

Q14. Are you aware about the conditions of safe use of Instanyl® recently updated by the pharmaceutical company?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Yes	7 (7.2%)	17 (26.2%)	9 (29.0%)	7 (41.2%)	33 (29.2%)	40 (19.0%)	40.0 (14.3%)
	95% Confidence Limits							[9.0% - 19.6%]
Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Yes	2 (5.0%)	0 (0.0%)	5 (20.8%)	1 (5.9%)	6 (10.0%)	8 (8.0%)	2.1 (6.9%)
	95% Confidence Limits							[1.2% - 12.6%]
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Yes	9 (6.6%)	17 (20.2%)	14 (25.5%)	8 (23.5%)	39 (22.5%)	48 (15.5%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Yes	15.4 (7.0%)	3.0 (20.9%)	16.1 (28.4%)	7.6 (39.9%)	26.8 (29.6%)	-	42 (13.6%)
	95% Confidence Limits							[8.8% - 18.4%]

Sources of information:

Q14a of section 2 asked the physicians (N=48) who responded Yes in Q14, what sources of information did they obtain the safety information on Instanyl. Responses are listed in Table 9.3.4-7.

The leading sources of information were the pharmaceutical company representative (62.5%), the SmPC (49.0%), the National Health Authority's website (37.4%), medical congress/ symposia (31.1%) and the national drug dictionary (29.6%).

Within GPs, the main sources of information were pharmaceutical company representatives (56.6%, n=9/15), national drug dictionaries (56.6%) and the SmPC (53.0%, n=8/15). Within the specialists a slightly set of information sources were used: their main sources were the pharmaceutical company representative (65.8%, n=18/27), the SmPC (46.7% n=12.5/27) and medical congresses/symposia (41.1%, n=11/27). Few physicians reported obtaining information from the MAH's website (12.2%, n=5/42). Results at the country level should be interpreted with caution because of small numbers.

Table 9.3.4-7: Sources of the recent safety information about Instanyl®

(Basis = Physicians with complete analysable questionnaire, who declared to be aware of the safety information about Instanyl® : who answered 'Yes' to Q14)

Q14a. If yes, from which of the following sources did you obtain recently the safety information about Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
France	.	(N=7)		(N=17)		(N=9)		(N=7)		(N=33)		(N=40)		(N=40)	
	Medical/ Pharmaceutical representatives	4 (57.1%)	[1]	13 (76.5%)	[1]	5 (55.6%)	[1]	6 (85.7%)	[1]	24 (72.7%)	[1]	28 (70.0%)	[1]	25.4 (63.4%)	[1]
	Summary of Product Characteristics (SPC updated 07-05-2014).	4 (57.1%)	[1]	7 (41.2%)	[2]	4 (44.4%)	[2]	4 (57.1%)	[2]	15 (45.5%)	[2]	19 (47.5%)	[2]	20.5 (51.1%)	[2]
	National Health Authority website	3 (42.9%)	[4]	3 (17.6%)	[5]	4 (44.4%)	[2]	2 (28.6%)	[4]	9 (27.3%)	[5]	12 (30.0%)	[4]	15.5 (38.9%)	[3]
	Congress/ symposia	1 (14.3%)	[6]	5 (29.4%)	[4]	4 (44.4%)	[2]	3 (42.9%)	[3]	12 (36.4%)	[3]	13 (32.5%)	[3]	12.9 (32.3%)	[4]
	Drugs dictionary	4 (57.1%)	[1]	1 (5.9%)	[8]	2 (22.2%)	[5]	0 (0.0%)	-	3 (9.1%)	[8]	7 (17.5%)	[6]	11.7 (29.2%)	[5]
	Colleagues	2 (28.6%)	[5]	2 (11.8%)	[6]	1 (11.1%)	[7]	1 (14.3%)	[6]	4 (12.1%)	[6]	6 (15.0%)	[7]	7.2 (18.0%)	[6]
	Educational materials	0 (0.0%)	-	6 (35.3%)	[3]	2 (22.2%)	[5]	2 (28.6%)	[4]	10 (30.3%)	[4]	10 (25.0%)	[5]	6.6 (16.5%)	[7]
	Pharmaceutical company website	1 (14.3%)	[6]	2 (11.8%)	[6]	1 (11.1%)	[7]	1 (14.3%)	[6]	4 (12.1%)	[6]	5 (12.5%)	[8]	5.2 (12.9%)	[8]
	Press/ media	1 (14.3%)	[6]	1 (5.9%)	[8]	1 (11.1%)	[7]	0 (0.0%)	-	2 (6.1%)	[9]	3 (7.5%)	[9]	3.9 (9.7%)	[9]
The Netherlands	.	(N=2)		(N=0)		(N=5)		(N=1)		(N=6)		(N=8)		(N=2)	
	Medical/ Pharmaceutical representatives	1 (50.0%)	[1]		-	2 (40.0%)	[1]	0 (0.0%)	-	2 (33.3%)	[1]	3 (37.5%)	[1]	0.9 (44.5%)	[1]
	Drugs dictionary	1 (50.0%)	[1]		-	1 (20.0%)	[2]	1 (100.0%)	[1]	2 (33.3%)	[1]	3 (37.5%)	[1]	0.8 (37.4%)	[2]
	Colleagues	1 (50.0%)	[1]		-	1 (20.0%)	[2]	0 (0.0%)	-	1 (16.7%)	[3]	2 (25.0%)	[3]	0.8 (35.5%)	[3]
	Educational materials	0 (0.0%)	-		-	1 (20.0%)	[2]	0 (0.0%)	-	1 (16.7%)	[3]	1 (12.5%)	[4]	0.2 (9.0%)	[4]
	Summary of Product Characteristics (SPC updated 07-05-2014).	0 (0.0%)	-		-	1 (20.0%)	[2]	0 (0.0%)	-	1 (16.7%)	[3]	1 (12.5%)	[4]	0.2 (9.0%)	[4]
	National Health Authority website	0 (0.0%)	-		-	1 (20.0%)	[2]	0 (0.0%)	-	1 (16.7%)	[3]	1 (12.5%)	[4]	0.2 (9.0%)	[4]
	Congress/ symposia	0 (0.0%)	-		-	1 (20.0%)	[2]	0 (0.0%)	-	1 (16.7%)	[3]	1 (12.5%)	[4]	0.2 (9.0%)	[4]
Overall - unweighted results	.	(N=9)		(N=17)		(N=14)		(N=8)		(N=39)		(N=48)		-	
	Medical/ Pharmaceutical representatives	5 (55.6%)	[1]	13 (76.5%)	[1]	7 (50.0%)	[1]	6 (75.0%)	[1]	26 (66.7%)	[1]	31 (64.6%)	[1]	-	-
	Summary of Product Characteristics (SPC updated 07-05-2014).	4 (44.4%)	[3]	7 (41.2%)	[2]	5 (35.7%)	[2]	4 (50.0%)	[2]	16 (41.0%)	[2]	20 (41.7%)	[2]	-	-

Q14a. If yes, from which of the following sources did you obtain recently the safety information about Instanyl®?
(Several answers are possible - Items sorted by rank (from the highest value to the lowest value of the column All - Weighted sample)

Country	n (%) [rank]	GPs		Oncologists		Anesthesiologists		Radiologists		Specialists		All - Unweighted sample		All - Weighted sample	
	National Health Authority website	3 (33.3%)	[4]	3 (17.6%)	[5]	5 (35.7%)	[2]	2 (25.0%)	[4]	10 (25.6%)	[5]	13 (27.1%)	[4]	-	-
	Congress/ symposia	1 (11.1%)	[6]	5 (29.4%)	[4]	5 (35.7%)	[2]	3 (37.5%)	[3]	13 (33.3%)	[3]	14 (29.2%)	[3]	-	-
	Drugs dictionary	5 (55.6%)	[1]	1 (5.9%)	[8]	3 (21.4%)	[5]	1 (12.5%)	[6]	5 (12.8%)	[6]	10 (20.8%)	[6]	-	-
	Colleagues	3 (33.3%)	[4]	2 (11.8%)	[6]	2 (14.3%)	[7]	1 (12.5%)	[6]	5 (12.8%)	[6]	8 (16.7%)	[7]	-	-
	Educational materials	0 (0.0%)	-	6 (35.3%)	[3]	3 (21.4%)	[5]	2 (25.0%)	[4]	11 (28.2%)	[4]	11 (22.9%)	[5]	-	-
	Pharmaceutical company website	1 (11.1%)	[6]	2 (11.8%)	[6]	1 (7.1%)	[8]	1 (12.5%)	[6]	4 (10.3%)	[8]	5 (10.4%)	[8]	-	-
	Press/ media	1 (11.1%)	[6]	1 (5.9%)	[8]	1 (7.1%)	[8]	0 (0.0%)	-	2 (5.1%)	[9]	3 (6.3%)	[9]	-	-
Overall - weighted results	.	(N=15)		(N=3)		(N=16)		(N=8)		(N=27)		-		(N=42)	
	Medical/ Pharmaceutical representatives	8.7 (56.6%)	[1]	2.3 (76.5%)	[1]	8.8 (54.6%)	[1]	6.5 (85.3%)	[1]	17.6 (65.8%)	[1]	-	-	26.3 (62.5%)	[1]
	Summary of Product Characteristics (SPC updated 07-05-2014).	8.1 (53.0%)	[3]	1.2 (41.2%)	[2]	6.9 (43.0%)	[2]	4.3 (56.8%)	[2]	12.5 (46.7%)	[2]	-	-	20.6 (49.0%)	[2]
	National Health Authority website	6.1 (39.7%)	[4]	0.5 (17.6%)	[5]	6.9 (43.0%)	[2]	2.2 (28.4%)	[4]	9.6 (36.0%)	[4]	-	-	15.7 (37.4%)	[3]
	Congress/ symposia	2.0 (13.2%)	[6]	0.9 (29.4%)	[4]	6.9 (43.0%)	[2]	3.3 (42.6%)	[3]	11.1 (41.4%)	[3]	-	-	13.1 (31.1%)	[4]
	Drugs dictionary	8.7 (56.6%)	[1]	0.2 (5.9%)	[8]	3.6 (22.1%)	[5]	0.0 (0.5%)	[8]	3.8 (14.1%)	[6]	-	-	12.5 (29.6%)	[5]
	Colleagues	4.6 (30.1%)	[5]	0.4 (11.8%)	[6]	1.9 (11.6%)	[7]	1.1 (14.2%)	[6]	3.3 (12.4%)	[7]	-	-	7.9 (18.9%)	[6]
	Educational materials	0.0 (0.0%)	-	1.1 (35.3%)	[3]	3.6 (22.1%)	[5]	2.2 (28.4%)	[4]	6.8 (25.4%)	[5]	-	-	6.8 (16.1%)	[7]
	Pharmaceutical company website	2.0 (13.2%)	[6]	0.4 (11.8%)	[6]	1.7 (10.5%)	[8]	1.1 (14.2%)	[6]	3.1 (11.7%)	[8]	-	-	5.2 (12.2%)	[8]
	Press/ media	2.0 (13.2%)	[6]	0.2 (5.9%)	[8]	1.7 (10.5%)	[8]	0.0 (0.0%)	-	1.9 (7.0%)	[9]	-	-	3.9 (9.3%)	[9]

Notes: The following sources from which the physician obtain recently the safety information about Instanyl® are displayed in the column 'Response'. Multiple answers were possible. Therefore, the total can exceed 100%.

Table 9.3.4-8 summarizes the above overall weighted values and their 95% confidence intervals, per country and overall.

Table 9.3.4-8: Sources of the recent safety information about Instanyl®

Q14a. If yes, from which of the following sources did you obtain recently the safety information about Instanyl®?

Country		Weighted percent	95% Confidence Limits, Weighted percent
France	Medical/ Pharmaceutical representatives	63.4%	[43.4% - 83.4%]

Country		Weighted percent	95% Confidence Limits, Weighted percent
Q14a. If yes, from which of the following sources did you obtain recently the safety information about Instanyl®?			
	Summary of Product Characteristics (SPC updated 07-05-2014).	51.1%	[30.8% - 71.5%]
	National Health Authority website	38.9%	[18.8% - 59.0%]
	Congress/ symposia	32.3%	[13.5% - 51.0%]
	Drugs dictionary	29.2%	[9.6% - 48.8%]
	Colleagues	18.0%	[1.8% - 34.1%]
	Educational materials	16.5%	[2.7% - 30.3%]
	Pharmaceutical company website	12.9%	[0.0% - 26.6%]
	Press/ media	9.7%	[0.0% - 22.5%]
The Netherlands	Medical/ Pharmaceutical representatives	44.5%	[0.0% - 98.4%]
	Drugs dictionary	37.4%	[0.0% - 91.2%]
	Colleagues	35.5%	[0.0% - 89.5%]
	Educational materials	9.0%	[0.0% - 31.8%]
	Summary of Product Characteristics (SPC updated 07-05-2014).	9.0%	[0.0% - 31.8%]
	National Health Authority website	9.0%	[0.0% - 31.8%]
	Congress/ symposia	9.0%	[0.0% - 31.8%]
Overall - weighted results	Medical/ Pharmaceutical representatives	62.5%	[43.5% - 81.4%]
	Summary of Product Characteristics (SPC updated 07-05-2014).	49.0%	[29.7% - 68.4%]
	National Health Authority website	37.4%	[18.3% - 56.4%]
	Congress/ symposia	31.1%	[13.4% - 48.8%]
	Drugs dictionary	29.6%	[11.0% - 48.2%]
	Colleagues	18.9%	[3.4% - 34.3%]
	Educational materials	16.1%	[3.1% - 29.1%]
	Pharmaceutical company website	12.2%	[0.0% - 25.2%]
	Press/ media	9.3%	[0.0% - 21.3%]

Usefulness of the revised educational materials:

Q15 of Section 2 asked if the revised educational materials were useful. Responses are presented in Table 9.3.4-9.

Of the 72 physicians eligible to answer this question (who answered having received the educational materials), 48 left the response unanswered. Of those who did respond, the majority found the information presented in the educational materials very useful (43.7%) or rather useful (28.0%). Because of the high non-response to this question, the interpretation of the responses should be interpreted with caution.

Table 9.3.4-9: Usefulness of the information about Instanyl® presented in the educational materials

(Basis = Physicians with a complete analysable questionnaire and who received the educational materials or read them)

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
Q15. Was the information as received in the educational materials about Instanyl® useful to you?								
France		(N=18)	(N=25)	(N=7)	(N=9)	(N=41)	(N=59)	(N=63)
	Missing	17	13	3	3	19	36	45
	Very useful	0 (0.0%)	6 (50.0%)	2 (50.0%)	3 (50.0%)	11 (50.0%)	11 (47.8%)	7.7 (44.2%)
	Rather useful	0 (0.0%)	5 (41.7%)	1 (25.0%)	2 (33.3%)	8 (36.4%)	8 (34.8%)	4.7 (27.2%)
	*Rather not useful	1 (100.0%)	1 (8.3%)	1 (25.0%)	0 (0.0%)	2 (9.1%)	3 (13.0%)	3.9 (22.4%)

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
	No opinion	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	1 (4.5%)	1 (4.3%)	1.1 (6.2%)
Netherlands		(N=3)	(N=2)	(N=7)	(N=1)	(N=10)	(N=13)	(N=3)
	Missing	3	2	6	1	9	12	3
	Rather useful	0 (0%)	0 (0%)	1 (100.0%)	0 (0%)	1 (100.0%)	1 (100.0%)	0.2 (100.0%)
Overall - unweighted results		(N=21)	(N=27)	(N=14)	(N=10)	(N=51)	(N=72)	-
	Missing	20	15	9	4	28	48	-
	Very useful	0 (0.0%)	6 (50.0%)	2 (40.0%)	3 (50.0%)	11 (47.8%)	11 (45.8%)	-
	Rather useful	0 (0.0%)	5 (41.7%)	2 (40.0%)	2 (33.3%)	9 (39.1%)	9 (37.5%)	-
	*Rather not useful	1 (100.0%)	1 (8.3%)	1 (20.0%)	0 (0.0%)	2 (8.7%)	3 (12.5%)	-
	No opinion	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	1 (4.3%)	1 (4.2%)	-
Overall - weighted results		(N=38)	(N=5)	(N=13)	(N=10)	(N=28)	(N=66)	(N=66)
	Missing	36	3	6	3	12	-	48
	Very useful	0.0 (0.0%)	1.1 (50.0%)	3.4 (48.6%)	3.3 (50.0%)	7.7 (49.4%)	-	7.7 (43.7%)
	Rather useful	0.0 (0.0%)	0.9 (41.7%)	1.9 (27.1%)	2.2 (33.3%)	4.9 (31.7%)	-	4.9 (28.0%)
	*Rather not useful	2.0 (100.0%)	0.2 (8.3%)	1.7 (24.3%)	0.0 (0.0%)	1.9 (12.0%)	-	3.9 (22.1%)
	No opinion	0.0 (0.0%)	0.0 (0.0%)	0.0 (0.0%)	1.1 (16.7%)	1.1 (7.0%)	-	1.1 (6.2%)

Q15. Was the information as received in the educational materials about Instanyl® useful to you?

**The main reason that explains why the French physicians did not find the information useful is: Information already known, found or received.*

10. DISCUSSION

10.1 KEY RESULTS

This study was undertaken to assess the effectiveness of the educational materials in increasing the knowledge of physicians about safe use of Instanyl® and influencing their attitude when prescribing Instanyl®.

10.1.1 Study participation rate

Unsolicited email approaches to HCPs to participate in surveys typically have a low participation rate. In this study we sent out email invitations to participate to 6,565 relevant physicians, and ended up with 310 physicians (4.7%) who agreed to participate and completed a questionnaire. This level of participation was anticipated as per IMS Health experience.

10.1.2 Knowledge of approved indication and safe use

96.8% of participating physicians correctly identified that episodes of breakthrough cancer pain in patients already receiving an opioid medication for chronic background pain as the approved indication, and among GPs this rose to 99.2% (Question 7: Q7). It was also found that 72.5% reported a maximum daily dose at or within the recommended maximum (Q8a), 60% reported an interval between treatments at least as long as recommended (Q8b), 86.4% responded that the maximum number of puffs where no higher than recommended (Q8c), and 84.7% reported the minimum interval between puffs no higher than recommended (Q8d).

There was also a high level of knowledge on which patients should not receive Instanyl®, 97.2% knew not to use it in patients with recurrent epistaxis (Q9a), 91.9% knew not to use in patients with severe respiratory depression or severe obstructive lung disease (Q9b), 85.8% knew not to use Instanyl® without current maintenance opioid therapy (Q9c), 89.9% knew not to use in those with previous facial radiotherapy (Q9d), and 91.0% avoided the use in patients at potential risk of substance abuse or dependence (Q10).

The questions on safety consideration considered when prescribing Instanyl® generated a long list of consideration (Q3). The leading responses were not to use Instanyl® in patients without maintenance opioid therapy and risk of respiratory depression. Q12 similarly asked what would you advise or explain to your patient with regards to the safe use and storage of Instanyl®. Overall 94.3% of physicians reported they gave patients information on safe use and storage of Instanyl, with the majority discussing how to use safely and not to overuse.

10.1.3 Off-label use

The survey found evidence of off-label use: 15.9% of physicians reported using Instanyl® in patients without cancer pain, and there were mostly for a range of other forms of chronic pain (Q5). This was more prevalent among anesthesiologists, 24.7% of whom reported using in patients without cancer pain. Anesthesiologists are highly trained and experienced in pain control, and it is likely this off-label use was felt by these physicians to be appropriate and that the benefits outweighed potential risks for those patients.

Moreover, 14.7% of physicians also reported having using Instanyl in patients® without maintenance opioid therapy (Q6). Their reason for prescribing Instanyl® off-label included its quick action, nasal route and ease of use (Q6b). It thus appears these physicians were knowledgeable of the risk associated with using Instanyl® without a background of opioid therapy (as seen in responses to Questions 7 and 9), but elected to prescribe off-label.

10.1.4 Receipt of the educational materials

The survey was conducted 6-12 months after the distribution of the updated educational materials. Relatively few physicians (20.3%) recalled having received the updated educational materials (Q13).

There are two possible explanations for this low recall. First, physicians receive a large amount of medical and promotional materials from pharmaceutical companies. Physicians may have discarded before reading or may not have remembered receiving or reading the educational material, or may not have recognised the nature of the material.. It is also possible some physicians may not have received the educational material. The MAH provided a list of 816 physicians, 532 in France and 284 in the Netherlands who reported to the Sales Representative they had previously prescribed or were likely to prescribe Instanyl®, and each was given a copy of the updated educational materials. As discussed in the methods, physicians were also recruited from the IMS Medical Radar List of physicians in France and the Netherlands to reach the required number of respondents. The survey screening question S2 asked only if the physician knew of Instanyl®. In hindsight, this question would have been better if it had asked if they had ever prescribed or were likely to prescribe Instanyl®, as the updated educational materials were only distributed to those who have prescribed or were intending to prescribe.

Although the low proportion of physicians who recalled receiving the educational materials was low, the physician knowledge on the indication and safe use of Instanyl® was remarkably high, as indicated from responses to Q7 -12. This is also supported by the responses on sources of information used (Q14a). Sales Representatives, SmPC and national Drug dictionaries were key sources of information, rather than specific educational materials. Importantly, the educational material was primarily distributed by medical and sales representatives, and the discussion with the medical or sales representative on the appropriate use of Instanyl may have been more memorable than receipt of the actual material.

This survey found strong knowledge about the product indication and its safe use, even though only a minority of physicians recalled having received/seen the educational materials. This highlights the importance of including all possible communications measures (SmPC, information presented by the Medical / Pharmaceutical representatives, National Health Authority website, congress/symposia, drug dictionary, etc.) to adequately provide safety information knowing that physician have multiple channels of information and knowledge gathering.

Overall, from this survey, physicians had a strong understanding the key safety factors to take into consideration when prescribing Instanyl, and have received this information from multiple sources, including from the product SmPC and via Medical/Sales representatives.

10.2 LIMITATIONS

10.2.1 Possible selection bias due to voluntary participation

The voluntary participation of physicians in the survey could have been a potential source of bias. It is an inherent limitation to any study based on volunteer participation. The distributions of each stratification criterion of healthcare professional (country and specialty) were compared between participants and non-participants in order to quantify any selection bias. Every effort was undertaken to contact the required specialists in order to reach the target per specialty and per country.

Several actions were taken to maximise the response rate: compensation fee were proposed to physicians for their participation in the survey, all physicians were sent an email or were contacted by operators of IMS Medical Radar with extensive experience in conducting health related surveys. Each physician was emailed or called up to 3-5 times before being considered as “not reachable” (reminders were sent by email when IMS Medical Radar did not received the web questionnaire).

Moreover, it was difficult to recruit radiologists in France for this survey, probably because they did not prescribe Instanyl® frequently and were less concerned or interested in the topic of the survey.

10.2.2 Limitations inherent to web surveys

In surveys, and especially in web surveys, the number of physicians to contact in order to reach the required number of participants is usually higher than 10 times more the expected number. In this

survey, 6565 physicians were invited to participate by email for 310 respondents with a complete analysable questionnaire, i.e. 20 times more the target number.

The generalisation and external validity of the web survey results is restricted to physicians who have an active email address, and were able and willing to answer web questionnaires. These physicians may not be fully representative of the whole targeted physician population (12).

With regard to non-response bias, there are several reasons that may explain the reason why the physicians targeted or contacted would not have received the invitations sent, namely because it may have been blocked as spam or unsolicited email. For these reasons, certain physicians were also contacted by phone to avoid and reduce non-responses.

Web surveys may also promote social desirability bias which refers to the tendency of physicians to give socially desirable or expected responses instead of choosing those reflecting their current knowledge or prescribing behaviour. For example, physicians could provide responses gathered online rather than giving their own opinions (12). Social desirability can affect the validity of the survey research findings, but the use of pre-populated items in the questionnaire, as we did in this survey, tends to reduce this bias (13).

Finally, the access to the web questionnaire interface was strictly limited to those invited, with a single possibility to participate and with a traceability system. Thus stakeholder bias (multiple answers of people who might have had a personal interest in survey results and/or who incite peers to fulfil the survey in order to influence the results) or unverified respondents (when it is not possible to check who has responded) were not applicable.

10.2.4 **Limitations related to open-ended questions**

The questionnaire included general questions followed by specific ones. Since the physicians may have understood the correct answers in subsequent questions, it was not possible to go back and edit the previous answers once given or ticked.

The survey results showed that answers to some open-ended questions were heterogeneous and sometimes irrelevant, suggesting that some physicians did not understand the question, did not know how to answer it, or answered something in order not leave to the space blank (for social desirability).

10.3 INTERPRETATION

The physicians participating in the survey had good knowledge of the approved indication and safety aspects of prescribing and using Instanyl. This finding is likely to be representative of the wider physician population that prescribe Instanyl in France and Netherlands.

Awareness or recall of having received the updated educational materials was disappointing. Physicians have access and use a wide range of information sources on drug safety. All possible communications measures (SmPC, information presented by the Medical / Pharmaceutical pharmaceutical representatives, National Health Authority website, congress/symposia, drug dictionary, etc.) should be considered to maximise spread of the safety information knowing that each physician has multiple channels to get or update their knowledge.

10.4 GENERALISABILITY

The study design presented an over-sampling of oncologists, anaesthesiologists and radiologists in the Netherlands, and an under-sampling of GPs in France. The raw results were ‘weighted’, to reflect the real number of physicians targeted with the educational materials, as per risk minimisation activities. For more transparency and accuracy, both unweighted (i.e. raw data) and weighted results are presented in this study report.

Considering the representativeness of the samples in the two participating countries including GPs and specialists (oncologists, anesthesiologists and radiologists), the weighted results of this survey can be generalised to the population of GPs and oncologists managing or likely to manage adult cancer patients presenting with breakthrough pain in France and Netherlands. However, the low proportion of anesthesiologists and radiologists present in the sample, and their low frequency of prescription of Instanyl® might not reflect the general behaviour of this sub group. Moreover, the two countries surveyed represent both a large and a small population of physicians with different healthcare system nuances. It is not known if the results from this survey are generalisable across the EU region, although there is relatively little use f Instanyl outside of France and Netherlands.

Since the study design presented an over-sampling of oncologists, anaesthesiologists and radiologists in the Netherlands, and an under-sampling of GPs in France, the unweighted survey results were not generalised to the overall target population. For more transparency and accuracy, both unweighted (i.e. unweighted data) and weighted results are presented in the study report.

11. OTHER INFORMATION

11.1 PROTECTION OF HUMAN SUBJECTS

The survey was non-interventional and totally anonymous to the study sponsor. Data collected remained absolutely confidential, and only aggregated data were analysed and communicated in a synthesis.

11.2 REGULATORY AND ETHICS CONSIDERATIONS

11.2.1 Ethical principles, laws and regulations

The survey followed the regulatory and ethical requirements of each country. IMS followed the European Pharmaceutical Marketing Research Association (EphMRA) code of conduct guidelines updated in February 2014 (14) for both countries, and specific local requirements were applied as follows:

- France:
  The LOI Bertrand ("Sunshine Act"), the law of 29 December 2011 on the reinforcement of the safety of medicines and health products (the "Act"), supplemented by a decree dated 21 May 2013 (the "Decree"), regarding transparency of the relations between healthcare companies and, notably, French-registered healthcare professionals will be followed.

  The Act states that companies which manufacture, market, or provide health products or services in relation to health products intended for human use must disclose the existence of the agreements they enter with players in the health sector, as well as any benefits that they grant to the same persons (13,15).

- Netherlands:
  The Dutch CGR (Code Geneesmiddelen Reclame) i.e. code for pharmaceutical advertising, regarding transparency of the relations between healthcare companies will be followed. The CGR Act states that a Dutch healthcare professional who entered into a financial relationship with a pharmaceutical company based abroad, have the obligation to register [the earnings] which lies with the healthcare professional.
  Moreover, the Dutch tax laws make necessary to store the confirmation of receipt of incentives, for the length of time required by law.

11.3 PHYSICIANS INFORMATION

Physicians participating in the survey were informed about: objectives of the study, the nature of the transmitted data, the intended use of data, recipients of these data, and their right of access and rectification to their personal data, as well as their right of objection to use their data or to IMS keeping their data.

11.3.1 Physicians compensations

Physicians were offered a compensation (that they could refuse) in return to the time spent participating in this survey, estimated between 10 to 15 minutes. The amount of this compensation was determined according to the EphMRA recommendations and the Association of Opinion and Behaviour in health field research companies (ASOCS) charter, and which states: "When it is necessary to compensate a physician in return to the time spent during an interview or a group meeting, the compensation must not exceed the fees commonly taken by the physician for his/her advice or consultation and must be proportional to the time provided. The compensations should be clearly stated prior to the physician's participation in the survey. They must be declared to the tax authorities in accordance with applicable laws".

11.4 CONFIDENTIALITY

11.4.1 Patient confidentiality

Not applicable: no patient's data will be collected.

11.4.2 Data confidentiality / Data security

Participating physicians accessed the website using an https secure link. This link was unique to each specific physician. The answers provided were collected in an anonymous way, only aggregated data and presented as a synthesis were transmitted to the MAH. Data were recorded in a central database and tracked using an audit trail. The system enables retrieving all introduced data at any time, and includes security elements to prevent others than authorized staff from accessing data.

Each user had a specific profile that limited his/her use of the database. A security copy of the database and the application files was made outside the server housing the web-based study. Security copies were periodically made and stored outside this server. A copy of the data stored in the database will be transferred to MAH at the end of the study. Description of all elements of security and traceability were available upon request.

11.5 RECORD RETENTION

The study documentation is stored in the electronic-Trial master file. The web questionnaires data were stored on the survey server.

11.6 ADVERSE EVENT / ADVERSE REACTION COLLECTION

11.6.1 Management and reporting of Adverse Events

If an Adverse Event /Adverse Reaction was reported during this survey, physicians had to agree to waive the confidentiality given to them under the studies Codes of Conduct in order to report it to the MAH. All physicians agreed in the Netherlands and 97.0% in France.

Table 11.6.1-1: Management and reporting of adverse events / adverse reactions

(Basis = Physicians with complete analysable questionnaire)

Q16.In the event of an Adverse Event side effect being found during this survey, are you willing to waive the confidentiality given to you under the studies Codes of Conduct specifically in relation to that Adverse Event?

Country		GPs	Oncologists	Anesthesiologists	Radiologists	Specialists	All - Unweighted sample	All - Weighted sample
France		(N=97)	(N=65)	(N=31)	(N=17)	(N=113)	(N=210)	(N=279)
	Yes	96 (99.0%)	60 (92.3%)	29 (93.5%)	15 (88.2%)	104 (92.0%)	200 (95.2%)	271 (97.0%)
The Netherlands		(N=40)	(N=19)	(N=24)	(N=17)	(N=60)	(N=100)	(N=31)
	Yes	40 (100.0%)	19 (100.0%)	24 (100.0%)	17 (100.0%)	60 (100.0%)	100 (100.0%)	31 (100.0%)
Overall - unweighted results		(N=137)	(N=84)	(N=55)	(N=34)	(N=173)	(N=310)	-
	Yes	136 (99.3%)	79 (94.0%)	53 (96.4%)	32 (94.1%)	164 (94.8%)	300 (96.8%)	-
Overall - weighted results		(N=220)	(N=14)	(N=57)	(N=19)	(N=90)	-	(N=310)
	Yes	218 (99.1%)	13 (93.9%)	54 (94.1%)	17 (88.7%)	84 (92.9%)	-	302 (97.3%)

One Adverse Event related to the risk of addiction was reported by a physician in the Netherlands.
The details were collected by IMS Health (Medical Radar division) and the Product Complaint reconciliation was provided to Takeda Drug Safety Department, Details are provided in (Table 11.6.1-2).

Table 11.6.1-2: Description of the Adverse Event(s) reported during the survey

Event No	Vendor reference no for patient/ Respondent ID	Product(s)	Event Details
1	NL // 17675 // 1303215	Instanyl	Risico op verslaving werd pas achteraf duidelijk, doordat afbouwen niet goed ging (te langzaam, of patient durfde niet af te bouwen) [Message from IMS: answer to question "Factors taken into consideration when prescribing Instanyl to patients on substance abuse"] *English translation*: The risk for addiction didn't become clear until afterwards, because the tapering off wasn't working (too slow, or the patient didn't dare to cut down)
Total number of Adverse Event(s) Reported:			**1**

Two physicians refused to waive the confidentiality they were given according to the pharmacovigilance rules for Adverse Events reporting. They were screened out and did not participate into the survey: one GP in France and one oncologist in the Netherlands.

12. CONCLUSION

This survey found participating physicians in France and the Netherlands were knowledgeable of the approved indication and of the safe use of Instanyl®. Some physicians reported they used Instanyl® in patients without cancer, and in patients without background opioid maintenance therapy, even though they were fully knowledgeable of the indication and safe use of the product. It thus seems physicians weigh up benefits versus and risks in deciding in which patients to use Instanyl®.

This survey found strong knowledge about the product indication and its safe use, even though only a minority of physicians recalled having received the educational materials. This highlights the importance of including all possible communications measures (SmPC, information presented by the Medical / Pharmaceutical representatives, National Health Authority website, congress/symposia, drug dictionary, etc.) to adequately provide safety information knowing that physician have multiple channels of information and knowledge gathering.

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14. ANNEX

14.1 SURVEY QUESTIONNAIRE

Evaluation of the Effectiveness of Risk Minimisation Measures:

a Survey among Health Care Professionals to assess their Knowledge and Attitudes on Prescribing Conditions of Instanyl®in France and the Netherlands

SURVEY QUESTIONNAIRE AND GUIDE

Recruitment (by phone)

Survey presentation and arguments

Good morning/good afternoon, I'm Mr. /Mrs. XXXXX from IMS Health, a company specialising in epidemiological and observational studies and surveys in the field of health and drug safety.

IMS Health is currently conducting a Risk Minimisation assessment study among specialists and general practitioners in two European countries (France and the Netherlands).

The survey aims to assess the knowledge of prescribing conditions of Instanyl® (intranasal fentanyl), an opioid analgesic used in the treatment of breakthrough pain episodes in adult patients already receiving opioid background therapy for chronic cancer pain.

The aim of this survey is to assess the effectiveness of the updated educational materials *[to be adapted to the country. 'Guide d'utilisation à destination des professionnels de santé' for France and 'Richtlijn voor artsen bij het voorschrijven' for the Netherlands]* recently provided to healthcare professionals. The survey has been requested by the European Medicines Agency (EMA) and it is funded by the Marketing Authorisation Holder (MAH).

The survey will be conducted in an anonymous way. The information collected will remain absolutely confidential and will only be used for the purposes of this survey. The results obtained will be presented in aggregated form to the MAH and regulatory agencies, mainly the EMA. No connections will be made between your identity and your answers to the survey.

The survey does not involve any promotional material and you will not be contacted for marketing purposes based on your answers to the survey. Neither the survey sponsor nor its contractors will sell or rent your information.

The questionnaire will take 10-15 minutes to complete.

As appreciation for the time you will dedicate to completion of the questionnaire you will be compensated with *[to be adapted to the specialty and country, e.g. XX Euros for Oncologists]*. You may also choose not to accept the monetary compensation.

If you are interested please supply me with an email address so that I may send you more details about the study and your personal link to the survey website.

Thank you,

IMS Health Medical Radar Team

Recruitment (by e-mail)

Survey presentation and arguments

Dear Dr…….

We, IMS Health, a company specialising in epidemiological and observational studies and surveys in the field of health and drug safety, are contacting you on behalf of Takeda Development Centre Europe Ltd.

We are conducting a Risk Minimisation assessment study among specialists and general practitioners in two European countries (France and the Netherlands). The survey aims to assess the knowledge of prescribing conditions of Instanyl® (intranasal fentanyl), an opioid analgesic used in the treatment of breakthrough pain episodes in adult patients already receiving opioid background therapy for chronic cancer pain.

The aim of this survey is to assess the effectiveness of the updated educational materials *[to be adapted to the country. 'Guide d'utilisation à destination des professionnels de santé' for France and 'Richtlijn voor artsen bij het voorschrijven' for the Netherlands]* recently provided to healthcare professionals. The survey has been requested by the European Medicines Agency (EMA) and it is funded by the Marketing Authorisation Holder (MAH).

The survey will be conducted in an anonymous way. The information collected will remain absolutely confidential and will only be used for the purposes of this survey. The results obtained will be presented in aggregated form to the MAH and regulatory agencies, mainly the EMA. No connections will be made between your identity and your answers to the survey.

The survey does not involve any promotional material and you will not be contacted for marketing purposes based on your answers to the survey. Neither the survey sponsor nor its contractors will sell or rent your information.

The questionnaire will take 10-15 minutes to complete.

We would greatly appreciate your participation in this research survey.

For the time you will dedicate to completion of the questionnaire you will be compensated with *[to be adapted to the specialty and country, e.g. XX Euros for Oncologists]*. You may also choose not to accept the monetary compensation.

If you are interested in participating in this survey, please click on the link below:
http://URL

Kind regards,

IMS Health Medical Radar Team

Web questionnaire

Introduction and agreement

The aim of this survey is to assess the effectiveness of the updated educational materials *[to be adapted to the country. 'Guide d'utilisation à destination des professionnels de santé' for France and 'Richtlijn voor artsen bij het voorschrijven' for the Netherlands]* recently provided to healthcare professionals. The survey has been requested by the European Medicines Agency (EMA) and it is funded by the Marketing Authorisation Holder (MAH).
The information will be collected anonymously and will only be used for the purposes of this survey. The results obtained will be presented to the MAH and regulatory agencies in an aggregated form.

We greatly appreciate your participation in this research survey.

The following questionnaire will take 10-15 minutes to complete.

As appreciation for the time you will dedicate to completion of the questionnaire you will be compensated with *[to be adapted to the specialty and country, e.g. XX Euros for Oncologists]*. You may also choose not to accept the monetary compensation.

❒ Please check this box if you do not want to be paid.

Before starting the questionnaire, we have to ensure that you are eligible for this survey by asking the following questions:

S1. Are you currently employed by a pharmaceutical company (e.g. Takeda) or contracted by regulatory bodies (e.g. EMA or *[add the name of the local regulatory agency]*?

No ☐ *Continue*
Yes ☐ Thank you for your interest in participating in this survey, unfortunately you cannot proceed with the survey.
Kind regards,
IMS Health Medical Radar Team

S2. Do you know the opioid analgesic Instanyl® (intranasal fentanyl)?

Yes ☐ *Continue*

No ☐ Thank you for your interest in participating in this survey. As this survey is targeted at physicians who know Instanyl® (intranasal fentanyl), unfortunately you cannot proceed with the survey.

Kind regards,
IMS Health Medical Radar Team

Disclaimer

Start of Interview:
Please be assured that this study will comply with all *[to be adapted to the COUNTRY, e.g. French]* laws in protecting your personal data, and will be in accordance with the EphMRA Code of Conduct and any other local pharmaceutical codes of conduct. Your answers will be treated in confidence. Data will be combined with those of other respondents, and results presented in an aggregated and anonymous format. They will remain confidential and will not be used other than for the purposes of this research, or disclosed to any third party without your approval. Subject as provided below, in the context of your participation in this survey and the answers that you giveyour identity will not be revealed to the company sponsoring this research.

We remind you that you may at all times request a copy of your personal information, have it corrected and object to its processing by contacting *[agency contact details]*. You can withdraw from the survey at any time."

Text for France:
We are required to pass on to our client details of any Adverse Events that are mentioned during the course of the questionnaire. Although, your answers will be treated in confidence, should an Adverse Event in a specific patient be identified we will need to report this even if it has already been reported by you directly to the company or the regulatory authorities. Later in the interview you will be asked whether or not you are willing to waive the confidentiality given to you according to the pharmacovigilance rules specifically in relation to Adverse Events. The answers you gave during the course of the interview will continue to remain confidential.

Are you happy to proceed with this interview on this basis?

Yes ☐ *Continue*
No ☐ *Thank you and close*

In compliance with the French law n°2011-2012 of December 29, 2011 and the French Decree n° 2013-414 of May 21, 2013, IMS will publish the existence of the convention related to the study *[to fill with the name of the survey]*.

IMS will publish the following information, in accordance with the provision of articles L1453-1 and R1453-3 of French Public Health Code:

- Convention signatory's identity (first name; last name; work address; qualification; specialty; title; order inscription number or RPPS number)
- The date of signature of the convention.
- The object of the convention in accordance with secrets protecting by law (as trade secrets for example).

The publication aforementioned will be available on IMS' website: www.imshealth.com

IMS will also publish the possible benefits granted to you for the execution of the convention. Please note that, in compliance with the French Data Protection Act of January 6, 1978 you have a right of access to and rectification of your personal information. This right can be exercised by mail to the following address: IMS HEALTH , Legal Department – Tour Ariane, 5-7 place de la Pyramide, 92088 La Défense - France or by email at dataprivacy@fr.imshealth.com.

As this publication is set forth by French Law, it is specified that you do not have a right of opposition to such publication.

Text for the Netherlands:
We are required to pass on to our client details of Adverse Events that are mentioned during the course of the questionnaire. Although, your answers will be treated in confidence, should an Adverse Event in a specific patient be identified we will need to report this even if it has already been reported by you directly to the company or the regulatory authorities. Later in the interview you will be asked whether or not you are willing to waive the confidentiality given to you according to the pharmacovigilance rules specifically in relation to Adverse Events. The answers you gave during the course of the interview will continue to remain confidential.
Are you happy to proceed with this interview on this basis?

Yes ☐ *Continue*
No ☐ *Thank you and close*

In compliance with the EphMRA Code of Conduct, version updated in February 2014, IMS will publish the existence of the convention related to the survey *[to fill with the name of the survey]*.

IMS will publish the following information:

- Convention signatory's identity (first name; last name; work address; qualification; specialty; title; order inscription number)
- The date of signature of the convention.
- The object of the convention in accordance with secrets protecting by law (as trade secrets for example).

The publication aforementioned will be available on IMS' website: www.imshealth.com

IMS will also publish the possible benefits granted to you for the execution of the convention. Please note that, in compliance with the law you have a right of access to and rectification of your personal information. This right can be exercised by mail to the following address: IMS HEALTH , Legal Department - Tour Ariane, 5-7 place de la Pyramide, 92088 La Défense - France or by email at dataprivacy@fr.imshealth.com.

Questionnaire

Section 1: Demographics and practice information

1. Gender

• Male	( )
• Female	( )

Data: single punch

2. What is your age category?

• ≤ 30 years old	( )
• 31-39 years old	( )
• 40-49 years old	( )
• 50-59 years old	( )
• ≥ 60 years old	( )

Data: single punch

3. What is your primary medical specialty?

• Oncology	( )
• Anesthesiology	( )
• Radiology	( )
• General Practitioner	( )
• Other, please specify:……	( )

Data: single punch

4. In which setting do you spend the majority of your time when practicing?

• Private practice	( )
• Clinic or Hospital practice	( )
• Both: private + Clinic or Hospital practice	( )
• Other, please specify: ……	( )

Data: single punch

5. For how long have you been practicing medicine?

|__|__| years

OR since which date: |__|__|/|__|__|__|__|
Month / year

Data: open numeric, years

6. How many patients with breakthrough cancer pain did you treat / follow-up per month on average in the last 6 months?

|__|__|__| patients/month

Data: open numeric

Section 2: Awareness of the safety information related to Instanyl®

1. Have you prescribed Instanyl® to patients with cancer pain in the last 6 months?

• Yes	( )
• No	( ) *Go to Q3*

Data: single punch

2. In the last 6 months, what proportion of patients with breakthrough cancer pain have you treated with Instanyl®?

   (Please select the answer that applies in the following list).

• <5% (less than 1 out of 20)	( )
• 6-10% (1 or 2 out of 20)	( )
• 11-25% (3 to 5 out of 20)	( )
• 26-50% (6 to 10 out of 20)	( )
• 51-75% (11 to 15 out of 20)	( )
• 76-95% (16 to 19 out of 20)	( )
• 100% (all of them)	( )

Data: single punch

3. What are the main safety considerations / measures of safety when thinking of prescribing Instanyl®?

Please specify: …… ……

Data: open text

4. When you decided to not prescribe Instanyl® in the last 6 months, what were the reasons of non prescription?

Please specify: …… ……

Data: open text

5. In the last 6 months, have you prescribed Instanyl® in patients without cancer pain?

• Yes	( )
• No	( ) *Go to Q6*

Data: single punch

5a. If yes, why did you choose Instanyl® instead of another drug?

Please specify the indication(s): …… ……

Data: open text

5b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?

Please specify the condition(s): …… ……

Data: open text

6. In the last 6 months, have you prescribed Instanyl® in patients without maintenance opioid therapy for chronic cancer pain?

• Yes	( )
• No	( ) *Go to Q7*

Data: single punch

6a. If yes, why did you choose Instanyl® instead of another drug?

Please specify the indication(s): …… ……

Data: open text

6b. What underlying condition(s) did the patient(s) have in whom you used Instanyl® off label?

Please specify the condition(s): …… ……

Data: open text

7. Which of the following condition(s) represent the approved indication(s) of Instanyl®?
(Please select the answer that apply - yes, no or unknown - for each sentence).

Therapeutic indication(s)	**Yes**	**No**	**Ukn**
• acute pain other than breakthrough pain	( )	( )	( )
• any short-term pain or any pain status	( )	( )	( )
• as a maintenance treatment for cancer pain	( )	( )	( )
• all episodes of breakthrough cancer pain	( )	( )	( )
• episodes of breakthrough cancer pain and already receiving an opioid medication for chronic background pain	( )	( )	( )

8. What is the maximum daily dose of Instanyl®, in terms of number of puffs per episode and number of episodes per day that should be treated per day?

• treat no more than |__| breakthrough pain episodes per day
• two breakthrough pain episodes should be separated at least of |__| hours
• use no more than |__| doses/puffs per episodes
• two doses/puffs should be separated at least of |__|__| minutes

Data: semi open text

9. In the last 6 months, have you prescribed Instanyl® to the following patients?
(Please select the answer that apply - yes, no or unknown - for each sentence).

	Yes	No	Ukn
• with recurrent episodes of epistaxis (or nasal discomfort while using the spray): conditions impairing accurate treatment	( )	( )	( )
• with severe respiratory depression (or severe obstructive lung conditions)	( )	( )	( )
• without current maintenance opioid therapy	( )	( )	( )
• patients who had a previous facial radiotherapy	( )	( )	( )

Data: multi punch

10. In the last 6 months, have you prescribed Instanyl® to patients at risks of potential substance abuse and/or dependence?

• Yes	( )
• No	( ) *Go to Q11*

Data: single punch

10a. If yes, which factors did you take into consideration?

Please specify:
……
……

Data: open text

Question for the physicians who prescribe Instanyl® (those who answered it in Q1).

11. When first prescribing Instanyl® to a patient, what proportion of patients do you give the brochure "How to use your Instanyl®?
(Please select the answer that applies).

• 100%	( )
• 75-99%	( )
• 50-74%	( )
• 25-49%	( )
• <24%	( )
• None	

Data: single punch

12. What would you advise or explain to your patient with regards to the safety use and storage of Instanyl® when prescribing it?

Please specify:(answers expected:§ educational materials, Instanyl® physician prescribing checklist) …… ……

Data: open text

13. Did you receive any educational materials *['Guide d'utilisation à destination des professionnels de santé' for France and 'Richtlijn voor artsen bij het voorschrijven' for the Netherlands]* on Instanyl® sent by the pharmaceutical company in the last 6-12 months?

(The pack included the: safety information about Instanyl®, package leaflet, the Instanyl® prescribing checklist, physician's guide to prescribing and pharmacist guide to dispensing).

• Yes	( )
• No	( )
• I cannot remember / I am not sure	( )

Data: single punch

14. Are you aware about the conditions of safe use of Instanyl® recently updated by the pharmaceutical company?

• Yes	( )
• No	( ) *Go to Section 3*

Data: single punch

14a. If yes, from which of the following sources did you obtain recently the safety information about Instanyl®

(Please select the answer(s) that apply in the following list. Several answers are possible).

Information sources	
• Educational materials	( )
• Summary of Product Characteristics (SPC updated 07-05-2014).	( )
• National Health Authority website	( )
• Pharmaceutical company website	( )
• Medical / Pharmaceutical representatives	( )
• Congress / symposia	( )
• Colleagues	( )
• Drugs dictionary	( )
• Press / media	( )
• Other(s), please specify: ……..	( )

Data: multi punch

Question for physicians who received the educational materials or read them.

15. Was the information as received in the educational materials about Instanyl® useful to you?
(Please select the answer that applies).

• Very useful	( ) *Go to Section 3*
• Rather useful	( ) *Go to Section 3*
• Rather not useful	( ) *Go to Q18*
• Not useful	( ) *Go to Q18*
• No opinion	( ) *Go to Section 3*

Data: single punch

16. Please explain why you did not find this information useful?

Please specify: …… ……

Data: open text

Section 3: Management and reporting of adverse events / adverse reactions

In the event of an Adverse Event/side effect being found during this survey, are you willing to waive the confidentiality given to you under the studies Codes of Conduct specifically in relation to that Adverse Event?
Your contact details will be sent to the Pharmaceutical Company. You may in that case be re-contacted by the pharmaceutical company's Drug Safety department for documenting this observation. Please note that if you consent to a follow-up of the Adverse Event, your name will not be linked in any way to your responses given during the survey, other than in relation to the Adverse Event. Your anonymity will be removed only for this reporting, the answers given in this web survey will stay confidential.

• Yes	( )
• No	( )

Data: single punch