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**Janssen Research & Development\***  
**Gilead Sciences Inc.**

**Non-interventional Postauthorization Safety Study – Study Report**

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**EDURANT/EVIPLERA Health Care Professional Survey**

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**Protocol 30 July 2013**

**EDURANT and EVIPLERA (rilpivirine) and (emtricitabine/rilpivirine/tenofovir  
disoproxil fumarate)**

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**EU PAS Register Number:** ENCEPP/SDPP/5565

SPONSOR'S RESPONSIBLE MEDICAL OFFICER: Marita Stevens, MD

DATE STUDY INITIATED: 13 January 2014

DATE STUDY COMPLETED: 18 March 2014

**Status:** Approved

**Report Version:** 1.0

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**Prepared by:** Janssen Infectious Diseases - Diagnostics BVBA

**EDMS no:** EDMS-ERI-88865066

**Compliance:** This study was conducted in compliance with the protocol and applicable regulatory requirements.

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## PASS INFORMATION

|   |  |
|---|--|
| Title:  | EDURANT/EVIPLERA Health Care Professional Survey   |
| Version identifier of the final study report: | 1.0  |
| Date of last version of the protocol:         | 30 July 2013   |
| EU PAS Register No:                           | ENCEPP/SDPP/5565   |
| Active substance (INN common name):           | rilpivirine (RPV) hydrochloride and emtricitabine (FTC)/RPV hydrochloride/tenofovir disoproxil fumarate (TDF)  |
| Pharmacotherapeutic group (ATC Code):         | J05AG05 and J05AR08  |
| Medicinal product(s):                         | EDURANT <sup>®</sup> and EVIPLERA <sup>®</sup>   |
| Product reference:                            | EU/1/11/736/001 and EU/1/11/737/001, EU/1/11/737/002   |
| Procedure number:                             | EMA/H/C/002264 and EMA/H/C/002312  |
| Name of Marketing Authorization Holder(s)     | Janssen-Cilag International NV, and Gilead Sciences International Ltd  |
| Joint PASS                                    | Yes  |
| Research question and objectives              | <p>The survey objective was to gain an understanding of the effectiveness of the current prescribing conditions (human immunodeficiency virus [HIV] health care professional [HCP] understanding and utilization of the EDURANT and EVIPLERA prescribing instructions related to food intake contained within the Summary of Product Characteristics [SmPC]) in minimizing the risk associated with taking the products without a meal/food.</p> <p>Therefore, the survey was specifically designed to focus on the food intake instruction that HCPs provide as part of their therapeutic advice (when prescribing EDURANT or EVIPLERA)</p> |
| Countries of study                            | Austria, Belgium, Denmark, France, Germany, Norway, Sweden, the Netherlands, United Kingdom  |
| Author  | Marita Stevens, Dominique Devogel, Carla Truyers (Janssen Research & Development)  |

## MARKETING AUTHORIZATION HOLDER(S)

Name of Marketing  
Authorization Holder: Janssen-Cilag International NV and  
Gilead Sciences International Ltd

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Address: *Janssen:* Turnhoutseweg 30, 2340 Beerse, Belgium  
*Gilead:* Granta Park, Abington, Cambridge, CB21 6GT, United Kingdom

---

Contact Details: *Janssen:* +32 (0)14 60 21 11  
*Gilead:* +44 (0)1223 897300

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Sponsor's Responsible Medical  
Officer:

Name: Marita Stevens, MD, Janssen Research & Development

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## TABLE OF CONTENTS

|   |           |
|---|-----------|
| <b>PASS INFORMATION .....</b>   | <b>2</b>  |
| <b>MARKETING AUTHORIZATION HOLDER(S) .....</b>  | <b>3</b>  |
| <b>TABLE OF CONTENTS .....</b>  | <b>4</b>  |
| <b>LIST OF IN-TEXT TABLES AND FIGURES .....</b>   | <b>5</b>  |
| <b>1. ABSTRACT .....</b>  | <b>8</b>  |
| <b>2. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS .....</b>  | <b>13</b> |
| <b>3. INVESTIGATORS .....</b>   | <b>14</b> |
| <b>4. OTHER RESPONSIBLE PARTIES .....</b>   | <b>14</b> |
| <b>5. MILESTONES .....</b>  | <b>14</b> |
| <b>6. BACKGROUND AND RATIONALE .....</b>  | <b>14</b> |
| <b>7. RESEARCH QUESTION AND OBJECTIVES .....</b>  | <b>15</b> |
| <b>8. AMENDMENTS AND UPDATES .....</b>  | <b>15</b> |
| <b>9. RESEARCH METHODS .....</b>  | <b>16</b> |
| 9.1. Study Design .....   | 16        |
| 9.1.1. Overview of Study Design .....   | 16        |
| 9.1.2. Changes in Conduct .....   | 16        |
| 9.2. Setting .....  | 16        |
| 9.3. Survey Population .....  | 17        |
| 9.4. Variables .....  | 17        |
| 9.4.1. Evaluation of Effectiveness of the Prescribing Conditions in Minimizing the Risk of<br>Taking EDURANT/EVIPLERA Without a Meal/Food ..... | 17        |
| 9.5. Data Sources and Measurement .....   | 18        |
| 9.6. Bias .....   | 19        |
| 9.7. Study Size .....   | 19        |
| 9.8. Data Transformation .....  | 21        |
| 9.9. Statistical Methods .....  | 21        |
| 9.9.1. Main Summary Measures .....  | 21        |
| 9.9.2. Main Statistical Methods .....   | 22        |
| 9.9.3. Missing Values .....   | 22        |
| 9.9.4. Sensitivity Analyses .....   | 22        |
| 9.9.5. Amendments to the Statistical Analysis Plan .....  | 22        |
| 9.10. Quality Control .....   | 22        |
| <b>10. RESULTS .....</b>  | <b>23</b> |
| 10.1. Participants and Treatment Information .....  | 23        |
| 10.2. Descriptive Data .....  | 27        |
| 10.3. Outcome Data .....  | 27        |
| 10.4. Main Results .....  | 28        |
| 10.4.1. Awareness of the prescribing instructions by the respondents .....  | 28        |
| 10.4.1.1. Question 1 .....  | 28        |
| 10.4.1.2. Question 2 (Key Question) .....   | 31        |
| 10.4.2. Usage of the prescribing instructions by the respondents .....  | 35        |
| 10.4.2.1. Question 3a (Key Question) and Question 4a .....  | 35        |
| 10.4.2.2. Question 3b and Question 4b .....   | 38        |
| 10.4.2.3. Question 7 .....  | 41        |

|   |           |
|---|-----------|
| 10.4.2.4. Question 8 and Question 9.....  | 43        |
| 10.4.3. Sense of importance of the prescribing instructions by the respondents..... | 46        |
| 10.4.3.1. Question 5 and Question 6.....  | 46        |
| 10.5. Other Analyses.....   | 47        |
| 10.6. Adverse Events/Adverse Reactions.....   | 48        |
| <b>11. DISCUSSION.....</b>  | <b>48</b> |
| 11.1. Key Results.....  | 48        |
| 11.2. Limitations.....  | 48        |
| 11.3. Interpretation.....   | 48        |
| 11.4. Generalizability.....   | 49        |
| <b>12. OTHER INFORMATION.....</b>   | <b>49</b> |
| <b>13. CONCLUSION.....</b>  | <b>49</b> |
| <b>14. REFERENCES.....</b>  | <b>49</b> |
| <b>ANNEX 1: STAND-ALONE DOCUMENTS.....</b>  | <b>50</b> |
| <b>ANNEX 2: ADDITIONAL/SUPPORTING INFORMATION.....</b>                              | <b>51</b> |
| <b>SIGNATURE OF SPONSOR'S RESPONSIBLE MEDICAL OFFICER.....</b>                      | <b>59</b> |

## LIST OF IN-TEXT TABLES AND FIGURES

### TABLES

|  |    |
|--|----|
| Table 1: Expected number of HCPs by country in target sample.....  | 20 |
| Table 2: Number of EDURANT HCPs in the survey, by region.....  | 24 |
| Table 3: Number of EDURANT HCPs in the survey, by specialty.....   | 24 |
| Table 4: Number of EDURANT HCPs, cross-tabulation by region and specialty.....   | 24 |
| Table 5: Number of EVIPLERA HCPs in the survey, by region.....   | 24 |
| Table 6: Number of EVIPLERA HCPs in the survey, by specialty.....  | 25 |
| Table 7: Number of EVIPLERA HCPs, cross-tabulation by region and specialty.....  | 25 |
| Table 8: Number of EDURANT and EVIPLERA HCPs, cross-tabulation by number of HIV patients seen per month and specialty.....   | 26 |
| Table 9: Number of EDURANT HCPs, cross-tabulation by number of EDURANT prescriptions in last 3 months and specialty.....   | 26 |
| Table 10: Number of EVIPLERA HCPs, cross-tabulation by number of EVIPLERA prescriptions in last 3 months and specialty.....  | 27 |
| Table 11: Number of EDURANT HCPs spontaneously providing correct prescribing instructions related to intake with a meal (Q1), by region.....   | 28 |
| Table 12: Number of EDURANT HCPs spontaneously providing correct prescribing instructions related to intake with a meal (Q1), by specialty.....  | 29 |
| Table 13: Number of EDURANT HCPs spontaneously providing correct prescribing instructions related to intake with a meal (Q1), by number of HIV patients seen per month.....            | 29 |
| Table 14: Number of EDURANT HCPs spontaneously providing correct prescribing instructions related to intake with a meal (Q1), by number of prescriptions in the last 3 months.....     | 29 |
| Table 15: Number of EVIPLERA HCPs spontaneously providing correct prescribing instructions related to intake with food/with a meal (Q1), by region.....                                | 29 |
| Table 16: Number of EVIPLERA HCPs spontaneously providing correct prescribing instructions related to intake with food/with a meal (Q1), by specialty.....                             | 30 |
| Table 17: Number of EVIPLERA HCPs spontaneously providing correct prescribing instructions related to intake with food/with a meal (Q1), by number of HIV patients seen per month..... | 30 |

|  |    |
|--|----|
| Table 18: Number of EVIPLERA HCPs spontaneously providing correct prescribing instructions related to intake with food/with a meal (Q1), by number of prescriptions in the last 3 months .....                           | 30 |
| Table 19: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed for the first time (Q3a), by region.....  | 36 |
| Table 20: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed for the first time (Q3a), by specialty.....   | 36 |
| Table 21: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed for the first time (Q3a), by number of HIV patients seen per month .....                              | 36 |
| Table 22: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed for the first time (Q3a), by number of prescriptions in the last 3 months .....                       | 36 |
| Table 23: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time (Q3a), by region .....  | 37 |
| Table 24: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time (Q3a), by specialty .....   | 37 |
| Table 25: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time (Q3a), by number of HIV patients seen per month .....                   | 37 |
| Table 26: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time (Q3a), by number of prescriptions in the last 3 months .....            | 37 |
| Table 27: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed during follow-up appointments (Q3b), by region .....  | 39 |
| Table 28: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed during follow-up appointments (Q3b), by specialty .....   | 39 |
| Table 29: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed during follow-up appointments (Q3b), by number of HIV patients seen per month .....                   | 39 |
| Table 30: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed during follow-up appointments (Q3b), by number of prescriptions in the last 3 months .....            | 40 |
| Table 31: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed during follow-up appointments (Q3b), by region.....  | 40 |
| Table 32: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed during follow-up appointments (Q3b), by specialty.....                                     | 40 |
| Table 33: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed during follow-up appointments (Q3b), by number of HIV patients seen per month .....        | 40 |
| Table 34: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed during follow-up appointments (Q3b), by number of prescriptions in the last 3 months ..... | 41 |
| Table 35: Mean proportion of HCPs by rationale for providing instruction that EDURANT must be taken with a meal (Q7), by region.....   | 41 |
| Table 36: Mean proportion of HCPs by rationale for providing instruction that EDURANT must be taken with a meal (Q7), by specialty.....  | 42 |
| Table 37: Mean proportion of HCPs by rationale for providing instruction that EVIPLERA must be taken with food / with a meal (Q7), by region .....   | 42 |
| Table 38: Mean proportion of HCPs by rationale for providing instruction that EVIPLERA must be taken with food / with a meal (Q7), by specialty .....  | 43 |

## FIGURES

|   |    |
|---|----|
| Figure 1: Sample size estimation .....  | 20 |
| Figure 2: Proportion of EDURANT HCPs correctly identifying instruction: "must be taken with a meal" (Q2), by region .....   | 32 |
| Figure 3: Proportion of EDURANT HCPs correctly identifying instruction: "must be taken with a meal" (Q2), by specialty .....  | 32 |
| Figure 4: Proportion of EDURANT HCPs correctly identifying instruction: "must be taken with a meal" (Q2), by number of HIV patients seen per month and by number of prescriptions in the last 3 months .....            | 33 |
| Figure 5: Proportion of EVIPLERA HCPs correctly identifying instruction: "must be taken with food/with a meal" (Q2), by region .....  | 33 |
| Figure 6: Proportion of EVIPLERA HCPs correctly identifying instruction: "must be taken with food/with a meal" (Q2), by specialty .....   | 34 |
| Figure 7: Proportion of EVIPLERA HCPs correctly identifying instruction: "must be taken with food/with a meal" (Q2), by number of HIV patients seen per month and by number of prescriptions in the last 3 months ..... | 34 |
| Figure 8: Mean proportion of HCPs by method for providing instruction that EDURANT must be taken with a meal (Q8), overall and by region .....  | 44 |
| Figure 9: Mean proportion of HCPs by method for providing instruction that EDURANT must be taken with a meal (Q8), overall and by specialty .....   | 44 |
| Figure 10: Mean proportion of HCPs by method for providing instruction that EVIPLERA must be taken with food / with a meal (Q8), overall and by region.....   | 45 |
| Figure 11: Mean proportion of HCPs by method for providing instruction that EVIPLERA must be taken with food / with a meal (Q8), overall and by specialty.....  | 45 |
| Figure 12: Mean proportion of HCPs by importance scale score for providing instruction that EDURANT must be taken with a meal (Q5), overall and by region and specialty .....   | 46 |
| Figure 13: Mean proportion of HCPs by importance scale score for providing instruction that EVIPLERA must be taken with food / with a meal (Q5), overall and by region and specialty .....                              | 47 |

## 1. ABSTRACT

|                                     |  |
|-------------------------------------|--|
| <u>Name of Sponsor/Company</u>      | Janssen Research & Development*<br>Gilead Sciences Inc.  |
| <u>Name of Finished Product</u>     | EDURANT® and EVIPLERA®   |
| <u>Name of Active Ingredient(s)</u> | rilpivirine (RPV) hydrochloride and<br>emtricitabine (FTC)/RPV hydrochloride/tenofovir disoproxil fumarate (TDF) |

\* Janssen Research & Development is a global organization that operates through different legal entities in various countries. Therefore, the legal entity acting as the Sponsor for Janssen Research & Development studies may vary, such as, but not limited to Janssen Biotech, Inc.; Janssen Products, LP; Janssen Biologics, BV; Janssen-Cilag International NV; Janssen, Inc; Janssen Infectious Diseases BVBA; Janssen R&D Ireland; or Janssen Research & Development, LLC. The term "Sponsor" is used to represent these various legal entities as identified on the Sponsor List.

**Protocol No.:** Protocol number is not applicable (protocol date is 30 July 2013)

**Title of Study:** EDURANT/EVIPLERA Health Care Professional Survey

**Sponsor's Responsible Medical Officer:** Marita Stevens, MD, Janssen Research & Development

**Keywords:** Health Care Professional (HCP) Survey, Edurant, Eviplera, meal/food requirements

**EU PAS Register Number:** ENCEPP/SDPP/5565

**NCT No.:** Not applicable

**Clinical Registry No.:** Not applicable

**Marketing Authorization Holder(s):** Janssen-Cilag International NV, and Gilead Sciences International Ltd

**Names and Affiliations of Principal Investigator(s):** Not applicable

**Study Center(s):** Austria/Germany (101), Belgium/the Netherlands (49), Nordic countries (Sweden/Norway/Denmark; 29), France (71), United Kingdom (73)

**Publication (Reference):** None

**Study Period:** 13 January 2014-18 March 2014

**Background and Rationale:** EDURANT (single agent oral tablet of rilpivirine [RPV]), and EVIPLERA (single oral tablet regimen of emtricitabine [FTC]/RPV/tenofovir disoproxil fumarate [TDF]) are both indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection.

In line with the respective Summary of Product Characteristics (SmPCs), EDURANT must be administered with a meal and EVIPLERA must be administered with food/with a meal\*. Adherence to these instructions is important to ensure that adequate RPV levels are maintained in order to optimize a patient's response to RPV treatment.

The study was designed to gain an understanding of the effectiveness of the current prescribing information to minimize the risks associated with taking the product without a meal/food, which could potentially result in lower plasma exposures and subsequent development of drug resistance.

**Research Question and Objectives:** The survey objective was to gain an understanding of the effectiveness of the current prescribing conditions (HIV HCP understanding and utilization of the EDURANT and EVIPLERA prescribing instructions related to food intake contained within the SmPC)

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\* Section 4.2 (posology and method of administration) of the EVIPLERA SmPC was amended from instruction to take EVIPLERA "with a meal" to take EVIPLERA "with food" (Variation EMEA/H/C/002312/II/0017 - CHMP positive opinion January 2013)



in minimizing the risk of potentially decreased exposure and lack of therapeutic effect associated with taking RPV-containing regimens without a meal/food, potentially leading to development of resistance (ie, a safety concern in the risk management plan [RMP]). The survey was specifically designed to focus on the food intake instruction that HCPs provide as part of their therapeutic advice when prescribing/dispensing EDURANT or EVIPLERA.

**Study Design:** An online survey was conducted among 323 HIV HCPs in 9 countries (Austria, Belgium, Denmark, France, Germany, Norway, Sweden, the Netherlands, the United Kingdom [UK]) where both EDURANT and EVIPLERA are launched. A two-phase approach was followed with regard to the development and deployment of the survey: an initial pilot or qualitative phase (including a tele-depth interview, online questionnaire and a phone call to obtain feedback) was followed by the main or quantitative phase (online questionnaire).

**Setting:** All physician respondents were independently recruited through Ipsos Healthcare (Ipsos) panels of HIV prescribers and/or Ipsos' fieldwork partners. Ipsos conducts a regular prescription monitoring survey amongst panels of HIV prescribers and collects this information in the HIV Therapy Monitor Database, which was consulted for this survey. Primarily physicians were targeted to complete the survey. If they indicated that another HCP (ie, nurse or pharmacist) was most involved in providing instructions to the patients, then this HCP was invited to complete the survey.

The survey included screening questions to assess whether the respondent saw at least 10 HIV patients per month, was most involved in providing instructions to the HIV patients, and had prescribed/dispensed/instructed HIV patients to take EDURANT and/or EVIPLERA within the last 3 months. Only if all screening criteria were met (and therefore the HCP selection criteria fulfilled), the respondent continued with the main questionnaire for either EDURANT and/or EVIPLERA dependent on the respondent's prescription profile.

**Survey Population and Study Size:** HCPs involved in the management of HIV patients were invited to complete the survey. A target sample size of 289 HCPs, ie, 2.9% of EDURANT/EVIPLERA prescribers in the countries surveyed, was considered a robust and appropriate representation of HCPs for this survey.

The overall sample size allowed for estimation of responses with a margin of less than  $\pm 5\%$ , assuming the true success rate was at least 80% (see below).

A total of 13,516 invitations were sent to HCPs to complete the survey, 9,583 HCPs did not respond to the survey invitation, 3,610 HCPs did not meet all screening criteria, quit the survey before completing or were excluded from completing the main survey due to sufficient number of respondents from that particular country/region. A total of 323 HCPs completed the main survey (ie, the main, quantitative phase, online questionnaire).

**Variables and Data Sources:** A questionnaire was developed (see HCP survey in [ANNEX 1](#)) to assess usage and understanding of the prescribing instructions for either EDURANT or EVIPLERA, or both. The questionnaire consisted of a screening and a main part, translated in the local language for each relevant country. The screening part allowed for a random selection of HCPs who met prespecified criteria and then progressed to the main part of the questionnaire. The main part included 9 questions related to food intake instructions provided by the HCP to HIV patients. The design of the questionnaire was such that it engendered unbiased answers around the use of the instructions on food intake given by HCPs, as part of their therapeutic advice for EDURANT or EVIPLERA. No personal identifiers of the respondents were collected, ie, the answers were anonymous.

The prescribing conditions would be considered effective in minimizing the risk associated with taking the products without a meal/food, firstly, if the majority of HCPs were aware of the need to take EDURANT/EVIPLERA with a meal/with food and, secondly, if the majority of HIV patients were informed of the food intake requirements of EDURANT/EVIPLERA by their HCPs when being prescribed for the first time. For the prescribing conditions to be considered effective to minimize the risk, at least 80% of HCPs had to correctly identify the instructions related to food intake (Question 2).

Additionally, from those HCPs who correctly identified the food intake instruction (in Question 2), at least 80% of HIV patients, on average, had to be given the correct instructions related to food intake (Question 3a), when the treatment was prescribed for the first time.

**Statistical Methods:** Rigorous automated checks were performed to ensure that the data collected and stored, in real time, was valid and of a high quality. If a respondent was identified as failing one of these checks, they were removed from the data analysis and flagged in the database.

Collected data were aggregated and tabulated. Responses to all questions were analyzed individually as well as cross-tabulated with responses to other survey questions. Most common cross-tabulations included HCP type and prescription level. Answers to open-ended questions were grouped together and assigned to aggregated answer codes.

All data were analyzed at a total level, in addition to a regional level whereby countries were grouped together based on geographic proximity to allow for a statistical comparison between regions. The regions were the UK, France, Germany/Austria, Belgium/the Netherlands, Nordic countries (Norway, Sweden and Denmark).

The statistical analysis was performed by the program Quantum which was also used to create the data tables. Differences between subgroups (subgroups of region, specialty, number of HIV patients seen per month, and number of prescriptions in the last 3 months) were tested using a two-tailed Z-test with an alpha level of 5%. Significant differences between 2 subgroups are highlighted in the statistical output. Significance testing was not conducted on subgroups with a base of less than 30 respondents.

## RESULTS:

**PARTICIPANTS AND TREATMENT INFORMATION:** A total of 323 respondents participated in the HCP survey. There were 230 respondents (71%, 230/323) who prescribed\* EDURANT, mostly in Germany/Austria (84) and France (57). There were 317 respondents (98%, 317/323) who prescribed\* EVIPLERA, amounting to 96-100% in all regions. From the 323 HCPs who completed the survey, 224 HCPs prescribed both EDURANT and EVIPLERA, 6 HCPs prescribed EDURANT only, and 93 HCPs prescribed EVIPLERA only (data on file). Respondents included specialists (HIV/AIDS, infectious disease, and internal medicine specialists) and non-specialists (general practitioners/primary care physicians, nurses, and pharmacists); the majority of respondents consisted of physicians.

**OUTCOME DATA:** The prescribing conditions are to be considered effective in minimizing the risk of patients not being properly instructed to take EDURANT/EVIPLERA with a meal/food based on the results of two prespecified key questions, ie, Questions 2 and 3a.

A total of 230 and 317 HCPs responded that they had prescribed EDURANT and EVIPLERA, respectively, in the last 3 months (ie, the base for Question 2, which is the denominator to calculate the proportion of EDURANT/EVIPLERA HCPs correctly identifying the instruction that the product “must be taken with a meal/with food” [Question 2]). Of these HCPs, 205 and 287 HCPs were aware that EDURANT and EVIPLERA, respectively, need to be taken with a meal/with food (ie, the base for Question 3, from whom data were used to calculate the mean proportion of patients receiving instruction that EDURANT /EVIPLERA must be taken with a meal/with food when prescribed for the first time [Question 3a]).

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\* Note that “prescribed” can also include “dispensed” and/or “instructed”. Given that the vast majority of respondents were prescribing physicians, “prescribed” is used throughout the document to indicate “prescribed/dispensed/instructed”.

**MAIN RESULTS:** For EDURANT, 89% (205/230) of the HCPs correctly identified the meal instruction; for EVIPLERA, 91% (287/317) of the HCPs correctly identified the food/meal instruction (Question 2; see table by region below). In addition, 94%, on average, of the patients of the 205 HCPs who were aware that EDURANT needs to be taken with a meal, received the instruction that EDURANT must be taken with a meal when prescribed for the first time; and 96%, on average, of the patients of the 287 HCPs who were aware that EVIPLERA needs to be taken with food/with a meal, received the instruction that EVIPLERA must be taken with food/with a meal (Question 3a; see table by region below).

| <b>Question 2: Proportion of EDURANT/EVIPLERA HCPs correctly identifying instruction: “must be taken with a meal / with food” (results shown by region)</b> |                          |  |  |                           |                          |
|---|--------------------------|--|--|---------------------------|--------------------------|
| <b>EDURANT</b>  |                          |  |  |                           |                          |
| <b>UK<br/>(n=50)</b>  | <b>France<br/>(n=57)</b> | <b>Germany/<br/>Austria<br/>(n=84)</b> | <b>Belgium/<br/>Netherlands<br/>(n=30)</b> | <b>Nordics<br/>(n=9)</b>  | <b>Total<br/>(n=230)</b> |
| 45 (90%)  | 55 (96%)                 | 71 (85%)                               | 25 (83%)                                   | 9 (100%)                  | 205 (89%)                |
| <b>EVIPLERA</b>   |                          |  |  |                           |                          |
| <b>UK<br/>(n=70)</b>  | <b>France<br/>(n=71)</b> | <b>Germany/<br/>Austria<br/>(n=98)</b> | <b>Belgium/<br/>Netherlands<br/>(n=49)</b> | <b>Nordics<br/>(n=29)</b> | <b>Total<br/>(n=317)</b> |
| 67 (96%)  | 68 (96%)                 | 80 (82%)                               | 43 (88%)                                   | 29 (100%)                 | 287 (91%)                |

n = number of HCPs who prescribed EDURANT/EVIPLERA in the last 3 months

| <b>Question 3a: Mean proportion of patients receiving instruction that EDURANT/EVIPLERA must be taken with a meal / with food when prescribed for the first time (results shown by region)</b> |                          |  |  |                           |                          |
|--|--------------------------|--|--|---------------------------|--------------------------|
| <b>EDURANT</b>   |                          |  |  |                           |                          |
| <b>UK<br/>(n=45)</b>   | <b>France<br/>(n=55)</b> | <b>Germany/<br/>Austria<br/>(n=71)</b> | <b>Belgium/<br/>Netherlands<br/>(n=25)</b> | <b>Nordics<br/>(n=9)</b>  | <b>Total<br/>(n=205)</b> |
| 97%  | 90%                      | 96%                                    | 94%  | 98%                       | 94%                      |
| <b>EVIPLERA</b>  |                          |  |  |                           |                          |
| <b>UK<br/>(n=67)</b>   | <b>France<br/>(n=68)</b> | <b>Germany/<br/>Austria<br/>(n=80)</b> | <b>Belgium/<br/>Netherlands<br/>(n=43)</b> | <b>Nordics<br/>(n=29)</b> | <b>Total<br/>(n=287)</b> |
| 97%  | 94%                      | 96%                                    | 97%  | 100%                      | 96%                      |

n = number of HCPs who prescribed EDURANT/EVIPLERA in the last 3 months and were aware that EDURANT/EVIPLERA needs to be taken with a meal/with food

The results of the survey show that the majority of HCPs are aware of the prescribing instructions for EDURANT/EVIPLERA (Questions 1 and 2), communicate them to the majority of patients the first time the treatments are prescribed and during follow-up appointments (Questions 3 [3a and 3b], 4 [4a and 4b], 7, 8 and 9), and consider it important to communicate the correct food instructions to the patients (Questions 5 and 6). Instructions are communicated verbally and through patient information sheets (Question 8).

## DISCUSSION AND CONCLUSION:

**DISCUSSION:** The SmPCs of EDURANT and EVIPLERA provide instructions on taking the treatments with a meal/with food. For the prescribing conditions of EDURANT/EVIPLERA to be considered effective to minimize the risk of potentially decreased exposure and lack of therapeutic effect associated with taking RPV-containing regimens without a meal/food, potentially leading to development of resistance (ie, a safety concern in the RMP), at least 80% of the HCPs needed to correctly identify the instructions (Question 2) and communicate them to at least 80% of patients, on average of those HCPs

who correctly identified the food intake instruction (Question 2), when prescribing the treatment for the first time (Question 3a). These criteria were met (Question 2: 89% for EDURANT and 91% for EVIPLERA; Question 3a: 94% for EDURANT and 96% for EVIPLERA). Consequently, for both EDURANT and EVIPLERA, the current prescribing information is effective and remains adequate to minimize the risk of taking the treatment without a meal/food.

A limitation of the online quantitative survey approach is that it only provided feedback on HCP behavior with regard to providing the correct instructions. It did not provide an assessment of whether patients actually are compliant with the SmPC instructions.

CONCLUSIONS: The results of the HCP survey indicate that the prescribing conditions for EDURANT/EVIPLERA are effective in minimizing the risk associated with taking the products without a meal/food. Based on the results of this survey, no additional risk minimization measures are warranted. The benefit/risk ratios of both EDURANT and EVIPLERA remain favorable.

## 2. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

### Abbreviations

|         |  |
|---------|--|
| AIDS    | acquired immune deficiency syndrome                    |
| ARV     | antiretroviral   |
| CHMP    | Committee for Medicinal Products for Human Use         |
| EphMRA  | European Pharmaceutical Marketing Research Association |
| ESOMAR  | European Society for Opinion and Marketing Research    |
| GP      | general practitioner                                   |
| GUM     | genitourinary medicine specialist                      |
| FTC     | emtricitabine  |
| HCP     | health care professional                               |
| HIV(-1) | human immunodeficiency virus (type 1)                  |
| ID      | infectious disease specialist                          |
| IM      | internal medicine specialist                           |
| Ipsos   | Ipsos Healthcare                                       |
| MAH     | Marketing Authorization Holder                         |
| NNRTI   | non-nucleoside reverse transcriptase inhibitor         |
| PCP     | primary care physician                                 |
| PRAC    | Pharmacovigilance Risk Assessment Committee            |
| Q       | question   |
| RMP     | risk management plan                                   |
| RNA     | ribonucleic acid                                       |
| RPV     | rilpivirine  |
| SmPC    | Summary of Product Characteristics                     |
| TDF     | tenofovir disoproxil fumarate                          |
| UK      | United Kingdom   |

### Definition of Term(s)

|  |  |
|--|--|
| Crossing                               | Analyzing responses to certain questions from the HCP survey based on answers given to other questions, eg, number of patients seen per month.   |
| Post Authorization Safety Study (PASS) | Any study relating to an authorized medicinal product conducted with the aim of identifying, characterizing or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures. |
| Study                                  | The term “study” indicates the collection of data for research purposes only. The use of this term in no way implies that any interventional treatments or procedures, planned or otherwise, have been provided or performed.                                      |

### 3. INVESTIGATORS

Not applicable

### 4. OTHER RESPONSIBLE PARTIES

The Marketing Authorization Holders for this Joint PASS were Janssen-Cilag International NV and Gilead Sciences International Ltd.

|   |  |
|---|--|
| Sponsor's Responsible:                      |  |
| Medical Officer:                            | Marita Stevens*, MD  |
| Statistician:                               | Carla Truysers*, PhD   |
| Medical Writer:                             | Dominique Devogel*, MSc  |
| Ipsos Healthcare (a division of Ipsos MORI) | Kings House, Kymberley Road, HA1 1PT Harrow, United Kingdom (UK), responsible for: project management, development of questionnaire (including translations), recruitment of HCPs, data analysis |

\* Considered an author of this report

### 5. MILESTONES

The dates for key milestones in this study are outlined below.

| Milestone:                          | Planned Date:                         | Actual Date:    | Comments: |
|-------------------------------------|---------------------------------------|-----------------|-----------|
| Start of data collection            | Last quarter 2013/ First quarter 2014 | 13 January 2014 | -         |
| End of data collection              | First quarter 2014                    | 18 March 2014   | -         |
| Registration in the EU PAS register | Last quarter 2013/ First quarter 2014 | 7 February 2014 | -         |
| Final report of study results       | 16 October 2014                       |                 |           |

### 6. BACKGROUND AND RATIONALE

EDURANT (single agent oral tablet of rilpivirine [RPV]), in combination with other antiretroviral (ARV) medicinal products, is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in ARV treatment-naïve adult patients with a viral load  $\leq 100,000$  HIV-1 ribonucleic acid (RNA) copies/ml.

At the time of protocol writing, EVIPLERA (single oral tablet regimen of emtricitabine [FTC]/RPV/tenofovir disoproxil fumarate [TDF]) was indicated for the treatment of HIV-1 infection in antiretroviral treatment-naïve adult patients with a viral load  $\leq 100,000$  HIV-1 RNA copies/ml. Currently, EVIPLERA is indicated for the treatment of adults infected with HIV-1 without known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class, tenofovir or FTC, and with a viral load  $\leq 100,000$  HIV-1 RNA copies/mL.

In line with the respective Summaries of Product Characteristics (SmPCs), EDURANT must be administered with a meal and EVIPLERA must be administered with food/with a meal\*. Adherence to these instructions is important to ensure that adequate RPV levels are maintained in order to optimize a patient's response to RPV treatment.

The study was designed to gain an understanding of the effectiveness of the current prescribing information with regard to the instruction on intake of the treatments with a meal/food.

## 7. RESEARCH QUESTION AND OBJECTIVES

The survey objective was to gain an understanding of the effectiveness of the current prescribing conditions (HIV HCP understanding and utilization of the EDURANT and EVIPLERA prescribing instructions related to food intake contained within the SmPC) in minimizing the risk of potentially decreased exposure and lack of therapeutic effect associated with taking RPV-containing regimens without a meal/food, potentially leading to development of resistance (ie, a safety concern in the risk management plan [RMP]).

The survey was specifically designed to focus on the food intake instruction that HCPs provide as part of their therapeutic advice when prescribing/dispensing/instructing for EDURANT or EVIPLERA.

The hypothesis is that the current prescribing conditions are effective (see also Section 9.4.1).

## 8. AMENDMENTS AND UPDATES

No amendments to the HCP survey protocol were implemented. However, the Committee for Medicinal Products for Human Use (CHMP) final outcome fax for the acceptability of the protocol requested the following items to be taken into account:

- *Question:* Around the questionnaire (see [ANNEX 1](#)), the Pharmacovigilance Risk Assessment Committee (PRAC) queried the question on pharmaceutical affiliations and suggested that the Marketing Authorization Holder (MAH) would limit these kind of questions to the minimum required. *Response:* The survey was brief compared to typical marketing research studies with HCPs and, therefore, this additional question was not considered to be an issue with regard to the length of the questionnaire. The question on pharmaceutical affiliations was required to ensure there was no potential bias in the results by interviewing HCPs who were affiliated to pharmaceutical companies, potentially Janssen and/or Gilead, thus no changes to the questionnaire were made.
- *Question:* Around the recruitment and screening criteria the PRAC commented that the so-called "stratification" of the MAH was not clear and the MAH should clarify if these were selection criteria or grouping criteria. Furthermore, the PRAC requested that a

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\* Section 4.2 (posology and method of administration) of the EVIPLERA SmPC was amended from instruction to take EVIPLERA "with a meal" to take EVIPLERA "with food" (Variation EMEA/H/C/002312/II/0017 - CHMP positive opinion January 2013)

participant flow diagram would be included. *Response:* These points are addressed under Section 9.2 and Section 9.3.

- *Question:* Around the data analysis, the PRAC understood that groups of HCPs (nurses, pharmacists, physicians) would be compared, as well as groups based on prescription levels. The PRAC requested that these groups would clearly be defined in the protocol and that the MAH would define in the protocol which analyses would be done with which groups. *Response:* These points are addressed in Section 9.9.1. *Question:* Furthermore, the PRAC noted that a lot of "crossings" were included in the specification plan and that the MAH should explain what is meant by crossing. *Response:* This has been defined in the definitions section (Section 2).

## 9. RESEARCH METHODS

### 9.1. Study Design

#### 9.1.1. Overview of Study Design

An online survey was conducted with a two-phase approach for the development and deployment of the survey: an initial pilot or qualitative phase (including a tele-depth interview, online questionnaire and a phone call to obtain feedback) was followed by the main or quantitative phase (online questionnaire) (see Section 9.5).

The survey was conducted in 9 countries (Austria, Belgium, Denmark, France, Germany, Norway, Sweden, the Netherlands, the UK) where both EDURANT and EVIPLERA are launched.

A total of 289 HCPs involved in the management of HIV patients were targeted as responders (see Section 9.7) and the survey was completed by a total of 323 HIV HCPs (ie, the survey was completed by 34 more HCPs than targeted). HCPs could include prescribing physicians, nurses and pharmacists; the majority of respondents consisted of physicians (see Sections 9.2 and 10.1).

The results of the survey are presented in Section 10. Additional detailed summary tables are included in the statistical output in ANNEX 1.

#### 9.1.2. Changes in Conduct

There were no changes in the conduct of the study.

### 9.2. Setting

All physician respondents were independently recruited through Ipsos Healthcare (Ipsos) panels of HIV prescribers and/or Ipsos' fieldwork partners. Ipsos conducts a regular prescription monitoring survey amongst panels of HIV prescribers and collects this information in the HIV Therapy Monitor Database, which was consulted for this survey.

Primarily physicians were targeted to complete the survey. If they indicated that another HCP (ie, nurse or pharmacist) was most involved in providing instructions to the patients, then this HCP was invited to complete the survey.



Prescribing physicians were a mix of HIV/acquired immune deficiency syndrome (AIDS), infectious disease, internal medicine, genitourinary medicine specialists, and general practitioners/primary care physicians, reflective of the medical specialties treating HIV-infected patients in the different participating countries.

The survey included screening questions to assess whether the respondent saw at least 10 HIV patients per month, was most involved in providing instructions to the HIV patients, and had prescribed\* HIV patients to take EDURANT and/or EVIPLERA within the last 3 months. Only if all screening criteria were met (and therefore the HCP selection criteria fulfilled), the respondent continued with the main questionnaire for either EDURANT and/or EVIPLERA. The respondent's selection of either EDURANT or EVIPLERA or both determined the route they followed to answer the questionnaire (ie, depending on the respondent's answers to the screening questions whether he/she prescribed patients to take EDURANT or EVIPLERA or both, he/she completed the main questionnaire for either EDURANT and/or EVIPLERA).

### 9.3. Survey Population

HCPs involved in the management of HIV patients were invited to complete the survey (see Sections 9.1 and 9.2).

A sample size of 289 HCPs, ie, 2.9% of EDURANT/EVIPLERA prescribers in the countries surveyed, was targeted (see Section 9.7).

A total of 13,516 invitations were sent to HCPs to complete the survey, 9,583 HCPs did not respond to the survey invitation, 3,610 HCPs did not meet all screening criteria (see Section 9.2), quit the survey before completing or were excluded from completing the main survey due to sufficient number of respondents from that particular country/region. A total of 323 HCPs completed the main survey (ie, the main, quantitative phase, online questionnaire) (see Section 10.1).

### 9.4. Variables

#### 9.4.1. Evaluation of Effectiveness of the Prescribing Conditions in Minimizing the Risk of Taking EDURANT/EVIPLERA Without a Meal/Food

In order to evaluate the effectiveness of the prescribing conditions, related to food intake, a questionnaire (see ANNEX 1) was developed (see Section 9.5) to assess usage and understanding of the prescribing instructions for either EDURANT or EVIPLERA, or both (if relevant to the respondent, in which case each product was assessed separately).

The questionnaire consisted of a screening and a main part, translated in the local language for each relevant country. The screening part allowed for a random selection of HCPs who met

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\* Note that “prescribed” can also include “dispensed” and/or “instructed”. Given that the vast majority of respondents were prescribing physicians, “prescribed” is used throughout the document to indicate “prescribed/dispensed/instructed”.

prespecified criteria (see Section 9.2) and then progressed to the main part of the questionnaire. The main part included 9 questions related to food intake instructions provided by the HCP to HIV patients.

The prescribing conditions would be considered effective in minimizing the risk of potentially decreased exposure and lack of therapeutic effect associated with taking RPV-containing regimens without a meal/food, potentially leading to development of resistance, firstly, if the majority of HCPs were aware of the need to take EDURANT/EVIPLERA with a meal/with food and, secondly, if the majority of HIV patients were informed of the food intake requirements of EDURANT/EVIPLERA by their HCPs when being prescribed for the first time. For the prescribing conditions to be considered effective to minimize the risk, at least 80% of HCPs had to correctly identify the instructions related to food intake (as listed in Question 2 below). Additionally, from those HCPs who correctly identified the food intake instruction (in Question 2), at least 80% of HIV patients, on average, had to be given the correct instructions related to food intake (as listed in Question 3a), when the treatment was prescribed for the first time.

The following key questions were therefore selected to address these measures of effectiveness, respectively (as described in the HCP survey proposal in [ANNEX 1](#)):

- *Q2. Please indicate which of the following instructions / restrictions written below applies to the following HIV treatment (Edurant / Eviplera)*
  - *Must be taken with food / with a meal*
  - *Must be taken without food / without a meal*
  - *Can be taken with or without food / a meal*
  - *Must be taken on an empty stomach*
  - *Don't know*
- *Q3a. To what proportion of patients that you prescribe / dispense / instruct to take the following treatment do you communicate the following instruction when prescribing it for the first time?*
  - *Eviplera must taken with food / with a meal: \_\_\_\_\_%*
  - *Edurant must be taken with a meal: \_\_\_\_\_%*

## 9.5. Data Sources and Measurement

The optimal approach for the development and deployment of this survey was considered to be a two-phase approach; an initial small qualitative pilot phase followed by a main quantitative phase.

In the qualitative phase, the survey was piloted with prescribing physicians in France, Germany and the UK. Tele-depth interviews of 45 minutes were conducted with 2 HIV prescribing physicians in each country (thus 6 HIV prescribing physicians in total). Respondents were asked to complete the online questionnaire. Upon completion of the questionnaire a short follow-up phone call was made to gauge reaction to the survey and obtain feedback on suggested improvements. Based on the provided feedback, the survey was updated to be clearer and more

user-friendly, prior to its use in a broader audience in the quantitative phase. This mini qualitative survey was conducted prior to the launch of the main quantitative survey to help ensure that the final questionnaire provided data relevant to the objective needing to be addressed.

In the quantitative phase, the online survey (lasting approximately 15 minutes) was conducted in the 9 countries mentioned in Section 9.1.1. The questionnaire was translated into the local language for each relevant country. A larger number of HCPs (including nurses and pharmacists in addition to prescribing physicians) completed the survey than planned: 289 responders were targeted (see Section 9.7) and 323 respondents completed the HCP survey (see Sections 9.3 and 10.1). The online approach allowed respondents the flexibility as to when they completed the survey. The online approach also ensured a wide geographical spread of potential respondents, thus allowing a representative and balanced sample to be achieved within the target countries of the survey.

The questionnaire was scripted and routed in such a way that respondents could only answer questions that were relevant to them and consisted of open, closed and multiple choice questions.

The survey was programmed so that respondents could only progress forward through the questions and were not allowed to go back to previously given answers. The respondents were therefore unable to alter answers once responses had been given. Every question had to be answered for the respondents to progress forward through the survey.

Email invitations were sent to HCPs and once 10% of the total sample of target respondents (see Section 9.7) had completed the survey Ipsos performed checks on this interim data. Following these initial data checks further email invitations were sent out in order to achieve the remaining 90% of the sample.

The survey was conducted in accordance with the European Pharmaceutical Marketing Research Association (EphMRA) and the European Society for Opinion and Marketing Research (ESOMAR) guidelines.

## 9.6. Bias

The design of the questionnaire was such that it engendered unbiased answers around the use of the instructions on food intake given by HCPs, as part of their therapeutic advice for EDURANT or EVIPLERA. Invitations for participation were sent to a random sample of HCPs from the Ipsos' panels of HIV prescribers (see Section 9.2). No personal identifiers of the respondents were collected, ie, the answers were anonymous.

## 9.7. Study Size

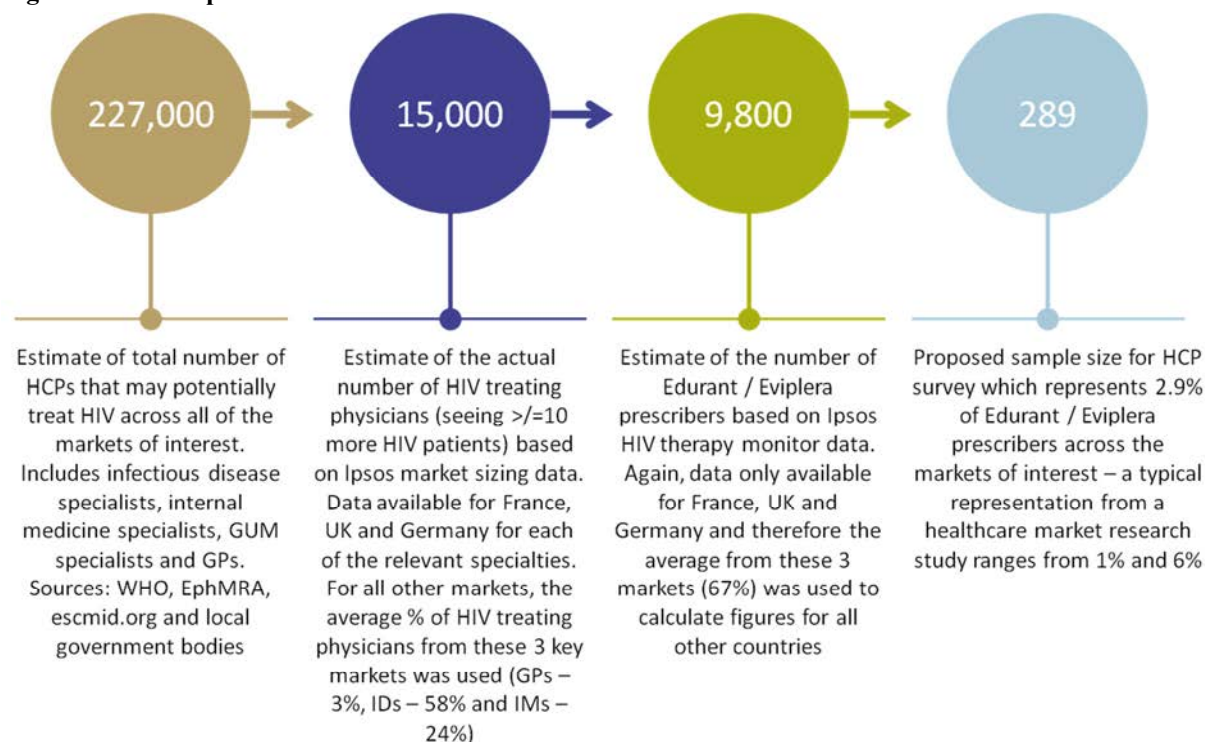
Full details are provided in the HCP survey proposal (Sections 4.2.3 and 4.2.4) in [ANNEX 1](#).

[Figure 1](#) details the sample size estimation. The sample size of 289 HCPs, ie, 2.9% of EDURANT/EVIPLERA prescribers in the selected countries, was considered a robust and appropriate representation of HCPs for this survey. The estimated distribution of the 289 HCPs is shown by country in [Table 1](#). Based on market shares it was anticipated that the sample size of

HCPs would be comprised of approximately 80% EVIPLERA prescribers and 20% EDURANT prescribers.

A sample is considered to be robust if it provides a basis for unbiased estimation of the true target parameter of interest. The proposed sample was designed to be a representative sample of EDURANT/EVIPLERA prescribers, and the overall size allowed for estimation of responses with a margin of less than  $\pm 5\%$ , assuming the true success rate was at least 80% (see Section 9.4.1).

**Figure 1: Sample size estimation**



**Table 1: Expected number of HCPs by country in target sample**

| Country      | Number     |
|--------------|------------|
| France       | 68         |
| Germany      | 68         |
| Austria      | 15         |
| UK           | 60         |
| Belgium      | 20         |
| Netherlands  | 20         |
| Sweden       | 15         |
| Norway       | 15         |
| Denmark      | 8          |
| <b>Total</b> | <b>289</b> |

## 9.8. Data Transformation

Rigorous automated checks were performed to ensure that the data collected and stored, in real time, was valid and of a high quality. These checks involved:

- Reviewing the length of time respondents took to complete sections of the survey, as well as total survey length
- Looking at patterned responses to grid questions
- Looking at verbatim questions for nonsensical answers.

If a respondent was identified as failing one of these checks, they were removed from the data analysis (before providing to the Sponsor) and flagged in the database. In addition, the IP address of respondents completing the survey was closely monitored to ensure that multiple completes did not come from the same computer/device.

## 9.9. Statistical Methods

Statistical analyses were performed under the authority of the Sponsors.

### 9.9.1. Main Summary Measures

Collected data were aggregated and tabulated. Responses to all questions were analyzed individually as well as cross-tabulated with responses to other survey questions. Most common cross-tabulations included HCP type and prescription level. Answers to open-ended questions were grouped together and assigned to aggregated answer codes.

The analysis outputs were provided to the Sponsors. Further details of the planned analysis outputs are provided in the HCP survey proposal (ie, the protocol in [ANNEX 1](#)), and the planned analyses as tabulated in Appendix 1 of the HCP survey proposal are also given in [ANNEX 2](#). These outputs show data based on absolute numbers of respondents and percentages of the total sample. For each question, the base of the respondents answering it is presented.

All data were analyzed at a total level, in addition to a regional level whereby countries were grouped together based on geographic proximity to allow for a statistical comparison between regions. The regions were (with the target sample by region in brackets):

- Germany and Austria (n=83)
- Belgium and the Netherlands (n=40)
- Norway, Sweden and Denmark (n=38)
- UK (n=60)
- France (n=68)

Question 2 and question 3a of the survey were selected per protocol as key questions to address the measures of effectiveness (see Section 9.4.1). To consider the current prescribing conditions effective to minimize the risk of patients taking EDURANT/EVIPLERA without a meal/food, at least 80% of HCPs had to correctly identify (Question 2) the instructions for these products relating to food intake. Additionally, it was necessary that from those HCPs who correctly identified the food intake instruction (in Question 2), at least 80% of patients, on average, were given the instruction that EDURANT must be taken with a meal / EVIPLERA must be taken with food/a meal when prescribed for the first time (Question 3a, see also Section 9.4.1).

### **9.9.2. Main Statistical Methods**

The statistical analysis was performed by the program Quantum which was also used to create the data tables. Differences between subgroups (subgroups of region, specialty, number of HIV patients seen per month, and number of prescriptions in the last 3 months) were tested using a two-tailed Z-test with an alpha level of 5%. Significant differences between 2 subgroups are highlighted. Significance testing was not conducted on subgroups with a base of less than 30 respondents (indicated in the tables/figures with ‘small base’).

Data from open-ended questions within the survey were analyzed through a process of categorizing and grouping responses based on common themes/answers. The process began with a review of all verbatim responses for each open-ended question. Key common themes were identified for each question based on the answers provided, as well as factors associated with each theme. This represented a code frame. Each verbatim response was then analyzed and assigned to its appropriate code. The coding of responses was then checked and verified to ensure accurate interpretation and assignment of all answers provided.

### **9.9.3. Missing Values**

Not applicable.

### **9.9.4. Sensitivity Analyses**

Not applicable.

### **9.9.5. Amendments to the Statistical Analysis Plan**

While per ANNEX 2 the base of the respondents for Question 3, was identified as “All HCPs who have prescribed EVIPLERA/EDURANT in the last 3 months”, in the main analyses the base for this question was taken as “All HCPs who have prescribed EVIPLERA/EDURANT in the last 3 months and who correctly identified the instruction in Question 2”. This was a consequence of the design of the survey, which ended when a particular respondent did not identify the correct instruction in response to Question 2.

### **9.10. Quality Control**

The accuracy and reliability of the study data were assured by the selection of qualifying HCPs and processes outlined in Section 9.8.



## 10. RESULTS

### 10.1. Participants and Treatment Information

A total of 323 respondents completed the HCP survey, ie, 34 more than targeted (see Section 9.1.1). By region, with the exception of the Nordic countries (Denmark, Norway and Sweden), in all countries more HCPs were recruited than targeted. Recruitment challenges relating to Norwegian regulations for HCPs taking part in market research restricted the sample achievable in this region and therefore increased numbers were recruited from other regions to achieve the overall target sample. Germany/Austria had the highest recruitment (as planned) (Table 2, Table 5). There were 230 respondents (71%, 230/323) who prescribed\* EDURANT, mostly in Germany/Austria (83%; 84/101) and France (80%; 57/71) (Table 2). There were 317 respondents (98%, 317/323) who prescribed\* EVIPLERA, amounting to 96-100% of respondents in all regions (Table 5). From the 323 HCPs who completed the survey, 224 HCPs prescribed both EDURANT and EVIPLERA, 6 HCPs prescribed EDURANT only, and 93 HCPs prescribed EVIPLERA only (data on file).

Details on the distribution of the respondents by specialty (overall and by region) is provided for EDURANT in Table 3 and Table 4, respectively and for EVIPLERA in Table 6 and Table 7, respectively.

Due to the overall lower number (and therefore lower % of total number of respondents) of EDURANT prescribing HCPs (230/323) than EVIPLERA prescribing HCPs (317/323), the percentages of EDURANT prescribing specialists (72%) and non-specialists (68%; Table 3) are lower than those of the EVIPLERA prescribing specialists (98%) and non-specialists (97%; Table 6). In the in-text tables of this report, general practitioners/primary care physicians, nurses, and pharmacists are shown pooled as “non-specialists”, because of the small subgroup numbers; details for these subgroups can be found in the statistical output in ANNEX 1.

The numbers of HIV patients seen per month by specialty for EDURANT and EVIPLERA (combined and per product) prescribing HCPs are shown in Table 8. The number of EDURANT and EVIPLERA HCPs by number of prescriptions in the last 3 months and specialty are provided in Table 9 and Table 11, respectively.

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\* Note that “prescribed” can also include “dispensed” and/or “instructed”. Given that the vast majority of respondents were prescribing physicians, “prescribed” is used throughout the document to indicate “prescribed/dispensed/instructed”.

**Table 2: Number of EDURANT HCPs in the survey, by region**

| Region                | UK          | France      | Germany / Austria | Belgium / Netherlands | Nordics countries* | Total         |
|-----------------------|-------------|-------------|-------------------|-----------------------|--------------------|---------------|
| Target sample         | 60          | 68          | 83                | 40                    | 38                 | 289           |
| Total sample achieved | 73          | 71          | 101               | 49                    | 29                 | 323           |
| EDURANT prescribers   | 50/73 (68%) | 57/71 (80%) | 84/101 (83%)      | 30/49 (61%)           | 9/29 (31%)         | 230/323 (71%) |

\* Norway (3), Denmark (0) and Sweden (6); small base

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 4 and page 53)

**Table 3: Number of EDURANT HCPs in the survey, by specialty**

| Specialty             | Specialists | HIV/ AIDS | IDs | IMs | GUMs* | Non-specialists | Total     |
|-----------------------|-------------|-----------|-----|-----|-------|-----------------|-----------|
| Total sample achieved | 258         | 109       | 92  | 49  | 8     | 65              | 323       |
| EDURANT prescribers   | 186 (72%)   | 86        | 51  | 43  | 6     | 44 (68%)        | 230 (71%) |

\* Small base

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

Non-specialists include general practitioners/primary care physicians (20), nurses (9), and pharmacists (15)

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 4 and page 53)

**Table 4: Number of EDURANT HCPs, cross-tabulation by region and specialty**

| Region                                | UK        | France    | Germany / Austria | Belgium / Netherlands | Nordics countries* | Total      |
|---------------------------------------|-----------|-----------|-------------------|-----------------------|--------------------|------------|
| <i>Total sample achieved All HCPs</i> | <i>73</i> | <i>71</i> | <i>101</i>        | <i>49</i>             | <i>29</i>          | <i>323</i> |
| HIV/AIDS Specialist                   | 17        | 28        | 27                | 10                    | 4                  | 86         |
| Infectious Disease Specialist         | 5         | 18        | 20                | 5                     | 3                  | 51         |
| Internal medicine                     | 5         | 11        | 24                | 2                     | 1                  | 43         |
| Genito-Urinary Medicine specialist    | 6         | 0         | 0                 | 0                     | 0                  | 6          |
| GP / PCP                              | 0         | 0         | 9                 | 10                    | 1                  | 20         |
| Nurse                                 | 2         | 0         | 4                 | 3                     | 0                  | 9          |
| Pharmacist                            | 15        | 0         | 0                 | 0                     | 0                  | 15         |
| <b>Total EDURANT prescribers</b>      | <b>50</b> | <b>57</b> | <b>84</b>         | <b>30</b>             | <b>9</b>           | <b>230</b> |

\* Small base

GP: general practitioner, PCP: primary care physician

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 4 and page 53), and data on file

**Table 5: Number of EVIPLERA HCPs in the survey, by region**

| Region                | UK          | France       | Germany / Austria | Belgium / Netherlands | Nordics countries* | Total         |
|-----------------------|-------------|--------------|-------------------|-----------------------|--------------------|---------------|
| Target sample         | 60          | 68           | 83                | 40                    | 38                 | 289           |
| Total sample achieved | 73          | 71           | 101               | 49                    | 29                 | 323           |
| EVIPLERA prescribers  | 70/73 (96%) | 71/71 (100%) | 98/101 (97%)      | 49/49 (100%)          | 29/29 (100%)       | 317/323 (98%) |

\* Norway (6), Denmark (7) and Sweden (16); small base

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 4 and page 53)



**Table 6: Number of EVIPLERA HCPs in the survey, by specialty**

| Specialty             | Specialists | HIV/<br>AIDS | IDs | IMs | GUMs* | Non-<br>specialists | Total     |
|-----------------------|-------------|--------------|-----|-----|-------|---------------------|-----------|
| Total sample achieved | 258         | 109          | 92  | 49  | 8     | 65                  | 323       |
| EVIPLERA prescribers  | 254 (98%)   | 109          | 91  | 46  | 8     | 63 (97%)            | 317 (98%) |

\* Small base

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

Non-specialists include general practitioners/primary care physicians (24), nurses (21), and pharmacists (18)

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 4 and page 53)

**Table 7: Number of EVIPLERA HCPs, cross-tabulation by region and specialty**

| Region                                | UK        | France    | Germany /<br>Austria | Belgium /<br>Netherlands | Nordics<br>countries* | Total      |
|---------------------------------------|-----------|-----------|----------------------|--------------------------|-----------------------|------------|
| <i>Total sample achieved All HCPs</i> | <i>73</i> | <i>71</i> | <i>101</i>           | <i>49</i>                | <i>29</i>             | <i>323</i> |
| HIV/AIDS Specialist                   | 26        | 31        | 32                   | 14                       | 6                     | <b>109</b> |
| Infectious Disease Specialist         | 10        | 25        | 24                   | 13                       | 19                    | <b>91</b>  |
| Internal medicine                     | 4         | 14        | 24                   | 3                        | 1                     | <b>46</b>  |
| Genito-Urinary Medicine<br>specialist | 8         | 0         | 0                    | 0                        | 0                     | <b>8</b>   |
| GP / PCP                              | 0         | 0         | 12                   | 11                       | 1                     | <b>24</b>  |
| Nurse                                 | 6         | 1         | 5                    | 7                        | 2                     | <b>21</b>  |
| Pharmacist                            | 16        | 0         | 1                    | 1                        | 0                     | <b>18</b>  |
| <b>Total EVIPLERA prescribers</b>     | <b>70</b> | <b>71</b> | <b>98</b>            | <b>49</b>                | <b>29</b>             | <b>317</b> |

\* Small base

GP: general practitioner, PCP: primary care physician

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 4 and page 53), and data on file

**Table 8: Number of EDURANT and EVIPLERA HCPs, cross-tabulation by number of HIV patients seen per month and specialty**

|                                    | Number of HIV patients seen per month |                       |                       |                        |                       |                        |                            |                             |
|------------------------------------|---------------------------------------|-----------------------|-----------------------|------------------------|-----------------------|------------------------|----------------------------|-----------------------------|
|                                    | All HCPs (EDURANT and EVIPLERA HCPs)  |                       |                       |                        |                       |                        | Total EDURANT HCPs (n=230) | Total EVIPLERA HCPs (n=317) |
|                                    | 10-20 patients (n=90)                 | 21-40 patients (n=44) | 41-60 patients (n=61) | 61-100 patients (n=58) | ≥ 101 patients (n=70) | Total All HCPs (n=323) |                            |                             |
| HIV/AIDS Specialist                | 4                                     | 8                     | 20                    | 36                     | 41                    | 109                    | 86                         | 109                         |
| Infectious Disease Specialist      | 27                                    | 13                    | 21                    | 12                     | 19                    | 92                     | 51                         | 91                          |
| Internal medicine                  | 18                                    | 10                    | 15                    | 5                      | 1                     | 49                     | 43                         | 46                          |
| Genito-Urinary Medicine specialist | 0                                     | 2                     | 2                     | 3                      | 1                     | 8                      | 6                          | 8                           |
| GP / PCP                           | 22                                    | 2                     | 0                     | 0                      | 0                     | 24                     | 20                         | 24                          |
| Nurse                              | 9                                     | 5                     | 3                     | 0                      | 5                     | 22                     | 9                          | 21                          |
| Pharmacist                         | 10                                    | 4                     | 0                     | 2                      | 3                     | 19                     | 15                         | 18                          |

GP: general practitioner, PCP: primary care physician

Source: Statistical output in [ANNEX 1](#) (EDURANT: pages 12, 13, 53; and EVIPLERA: pages 12, 13, 53)

**Table 9: Number of EDURANT HCPs, cross-tabulation by number of EDURANT prescriptions in last 3 months and specialty**

|  | Number of EDURANT prescriptions in last 3 months |                   |                   |                    |                    |
|--|--|-------------------|-------------------|--------------------|--------------------|
|  | ≥1 prescription                                  | 1-2 prescriptions | 3-5 prescriptions | 6-10 prescriptions | ≥ 11 prescriptions |
| <b>All Respondents who prescribed EDURANT in the last 3 months</b> | <b>230</b>                                       | <b>65</b>         | <b>67</b>         | <b>33</b>          | <b>65</b>          |
| HIV/AIDS Specialist  | 86   | 25                | 24                | 12                 | 25                 |
| Infectious Disease Specialist                                      | 51   | 13                | 13                | 6                  | 19                 |
| Internal medicine  | 43   | 8                 | 12                | 11                 | 12                 |
| Genito-Urinary Medicine specialist                                 | 6  | 4                 | 2                 | 0                  | 0                  |
| GP / PCP   | 20   | 7                 | 10                | 2                  | 1                  |
| Nurse  | 9  | 2                 | 4                 | 0                  | 3                  |
| Pharmacist   | 15   | 6                 | 2                 | 2                  | 5                  |

GP: general practitioner, PCP: primary care physician

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 12, 13, and 53)

**Table 10: Number of EVIPLERA HCPs, cross-tabulation by number of EVIPLERA prescriptions in last 3 months and specialty**

|   | Number of EVIPLERA prescriptions in last 3 months |                   |                   |                    |                     |                    |
|---|---|-------------------|-------------------|--------------------|---------------------|--------------------|
|   | ≥1 prescription                                   | 1-2 prescriptions | 3-5 prescriptions | 6-10 prescriptions | 11-20 prescriptions | ≥ 21 prescriptions |
| <b>All Respondents who prescribed EVIPLERA in the last 3 months</b> | <b>317</b>  | <b>34</b>         | <b>75</b>         | <b>59</b>          | <b>64</b>           | <b>85</b>          |
| HIV/AIDS Specialist   | 109   | 4                 | 16                | 23                 | 26                  | 40                 |
| Infectious Disease Specialist                                       | 91  | 12                | 23                | 16                 | 17                  | 23                 |
| Internal medicine   | 46  | 6                 | 14                | 8                  | 8                   | 10                 |
| Genito-Urinary Medicine specialist                                  | 8   | 0                 | 2                 | 2                  | 2                   | 2                  |
| GP / PCP  | 24  | 4                 | 12                | 6                  | 1                   | 1                  |
| Nurse   | 21  | 4                 | 5                 | 0                  | 8                   | 4                  |
| Pharmacist  | 18  | 4                 | 3                 | 4                  | 2                   | 5                  |

GP: general practitioner, PCP: primary care physician

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 12, 13 and 53)

## 10.2. Descriptive Data

The available data of the HCPs (overall and by subgroups) who participated in the survey are described in Section [10.1](#).

## 10.3. Outcome Data

As detailed in Section [9.4.1](#) the prescribing conditions are to be considered effective in minimizing the risk of patients not being properly instructed to take EDURANT/EVIPLERA with a meal/food based on the results of two prespecified key questions, ie, Question 2 and Question 3a. A total of 230 and 317 HCPs responded that they had prescribed EDURANT and EVIPLERA, respectively, in the last 3 months (ie, the base for Question 2, which is the denominator to calculate the proportion of EDURANT/EVIPLERA HCPs correctly identifying the instruction that the product “must be taken with a meal/with food” [Question 2]). Of these HCPs, 205 and 287 HCPs were aware that EDURANT and EVIPLERA, respectively, need to be taken with a meal/with food (ie, the base for Question 3, from whom data were used to calculate the mean proportion of patients receiving instruction that EDURANT /EVIPLERA must be taken with a meal/with food when prescribed for the first time [Question 3a]). The results are discussed in Section [10.4](#).

## 10.4. Main Results

### 10.4.1. Awareness of the prescribing instructions by the respondents

The awareness of the prescribing instructions by the respondents was determined based on responses to Question 1 (open question; see Section 10.4.1.1) and Question 2 (multiple choice question; see Section 10.4.1.2). Question 2 was considered one of the two key questions for evaluation of the effectiveness of the prescribing information.

#### 10.4.1.1. Question 1

Question 1 (Q1) was an open question on the spontaneous awareness of the prescribing instructions:

*Q1: When you prescribe / dispense / instruct patients to take Eviplera/Edurant, what are the instructions that immediately come to your mind that need to be communicated to a patient about taking this medication?*

For EDURANT, on average, 65% of the 230 HCPs spontaneously mention the meal requirement as an instruction. By region, it is mentioned least often in Germany/Austria (56%) (Table 11). By specialty, internal medicine specialists mention it the least (47%) (Table 12) and it is mentioned less often by HCPs seeing fewer HIV patients (53%) compared to those seeing more HIV patients per month (72-77%) (Table 13). Furthermore, it is mentioned more often if prescribed 1-2 times in the last 3 months (82%) than when prescribed in any subcategory of greater volumes (55-64%) (Table 14).

For EVIPLERA, on average, 77% of the 317 HCPs spontaneously mention the food requirement as an instruction. By region, it is mentioned least often in Germany/Austria (63%) (Table 15). By specialty, internal medicine specialists mention it the least (65%) (Table 16) and it is mentioned less often by HCPs seeing fewer HIV patients (66%) compared to those seeing more HIV patients per month (72-88%) (Table 17). For EVIPLERA, the spontaneous mention of the food requirement was not affected by the number of prescriptions in the last 3 months (73-85%; see Table 18).

**Table 11: Number of EDURANT HCPs spontaneously providing correct prescribing instructions related to intake with a meal (Q1), by region**

| UK<br>(n=50) | France<br>(n=57) | Germany/<br>Austria<br>(n=84) | Belgium/<br>Netherlands<br>(n=30) | Nordics*<br>(n=9) | Total<br>(n=230) |
|--------------|------------------|-------------------------------|-----------------------------------|-------------------|------------------|
| 33 (66%)     | 43 (75%)         | 47 (56%)                      | 20 (67%)                          | 7 (78%)           | 150 (65%)        |

\* Small base

n = all respondents who prescribed EDURANT in the last 3 months

**Note: France is significantly different compared to Germany/Austria**

Source: Statistical output in ANNEX 1 (EDURANT, page 53)

**Table 12: Number of EDURANT HCPs spontaneously providing correct prescribing instructions related to intake with a meal (Q1), by specialty**

| Specialists<br>(n=186) | HIV/AIDS<br>(n=86) | IDs<br>(n=51) | IMs<br>(n=43) | GUMs*<br>(n=6) | Non-specialists**<br>(n=44) | Total<br>(n=230) |
|------------------------|--------------------|---------------|---------------|----------------|-----------------------------|------------------|
| 124 (67%)              | 61 (71%)           | 37 (73%)      | 20 (47%)      | 6 (100%)       | 26 (59%)                    | 150 (65%)        |

\* Small base

\*\* Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = all respondents who prescribed EDURANT in the last 3 months

**Note: Specialists, HIV/AIDS, and IDs are significantly different compared to IMs**

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 53)

**Table 13: Number of EDURANT HCPs spontaneously providing correct prescribing instructions related to intake with a meal (Q1), by number of HIV patients seen per month**

| 10-20<br>patients<br>(n=60) | 21-40<br>patients<br>(n=21) | 41-60<br>patients<br>(n=42) | 61-100<br>patients<br>(n=47) | ≥ 101<br>patients<br>(n=60) | Total<br>(n=230) |
|-----------------------------|-----------------------------|-----------------------------|------------------------------|-----------------------------|------------------|
| 32 (53%)                    | 10 (48%)                    | 28 (67%)                    | 34 (72%)                     | 46 (77%)                    | 150 (65%)        |

n = all respondents who prescribed EDURANT in the last 3 months

**Note: 61-100 and ≥ 101 patients seen per month are significantly different compared to 10-20 patients**

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 69)

**Table 14: Number of EDURANT HCPs spontaneously providing correct prescribing instructions related to intake with a meal (Q1), by number of prescriptions in the last 3 months**

| 1-2<br>prescriptions<br>(n=65) | 3-5<br>prescriptions<br>(n=67) | 6-10<br>prescriptions<br>(n=33) | ≥ 11<br>prescriptions<br>(n=65) | Total<br>(n=230) |
|--------------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| 53 (82%)                       | 43 (64%)                       | 18 (55%)                        | 36 (55%)                        | 150 (65%)        |

n = all respondents who prescribed EDURANT in the last 3 months

**Note: 1-2 prescriptions in the last 3 months is significantly different compared to all other subcategories of number of prescriptions in the last 3 months (ie, 3-5, 6-10, and ≥ 11 prescriptions)**

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 69)

**Table 15: Number of EVIPLERA HCPs spontaneously providing correct prescribing instructions related to intake with food/with a meal (Q1), by region**

| UK<br>(n=70) | France<br>(n=71) | Germany/<br>Austria<br>(n=98) | Belgium/<br>Netherlands<br>(n=49) | Nordics*<br>(n=29) | Total<br>(n=317) |
|--------------|------------------|-------------------------------|-----------------------------------|--------------------|------------------|
| 60 (86%)     | 58 (82%)         | 62 (63%)                      | 39 (80%)                          | 25 (86%)           | 244 (77%)        |

\*Small base

n = all respondents who prescribed EVIPLERA in the last 3 months

**Note: UK, France, and Belgium/Netherlands are significantly different compared to Germany/Austria**

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 53)

**Table 16: Number of EVIPLERA HCPs spontaneously providing correct prescribing instructions related to intake with food/with a meal (Q1), by specialty**

| Specialists<br>(n=254) | HIV/AIDS<br>(n=109) | IDs<br>(n=91) | IMs<br>(n=46) | GUMs*<br>(n=8) | Non-specialists**<br>(n=63) | Total<br>(n=317) |
|------------------------|---------------------|---------------|---------------|----------------|-----------------------------|------------------|
| 202 (80%)              | 89 (82%)            | 75 (82%)      | 30 (65%)      | 8 (100%)       | 42 (67%)                    | 244 (77%)        |

\*Small base

\*\* Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = all respondents who prescribed EVIPLERA in the last 3 months

**Note: Specialists, HIV/AIDS, and IDs are significantly different compared to IMs and Non-specialists**

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 53)

**Table 17: Number of EVIPLERA HCPs spontaneously providing correct prescribing instructions related to intake with food/with a meal (Q1), by number of HIV patients seen per month**

| 10-20<br>patients<br>(n=87) | 21-40<br>patients<br>(n=43) | 41-60<br>patients<br>(n=59) | 61-100<br>patients<br>(n=58) | ≥ 101<br>patients<br>(n=70) | Total<br>(n=317) |
|-----------------------------|-----------------------------|-----------------------------|------------------------------|-----------------------------|------------------|
| 57 (66%)                    | 31 (72%)                    | 50 (85%)                    | 51 (88%)                     | 55 (79%)                    | 244 (77%)        |

n = all respondents who prescribed EVIPLERA in the last 3 months

**Note: 41-60 and 61-100 patients seen per month are significantly different compared to 10-20 patients, and 61-100 patients is also significantly different compared to 21-40 patients**

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 71)

**Table 18: Number of EVIPLERA HCPs spontaneously providing correct prescribing instructions related to intake with food/with a meal (Q1), by number of prescriptions in the last 3 months**

| 1-2<br>prescriptions<br>(n=34) | 3-5<br>prescriptions<br>(n=75) | 6-10<br>prescriptions<br>(n=59) | 11-20<br>prescriptions<br>(n=64) | ≥ 21<br>prescriptions<br>(n=85) | Total<br>(n=317) |
|--------------------------------|--------------------------------|---------------------------------|----------------------------------|---------------------------------|------------------|
| 25 (74%)                       | 56 (75%)                       | 50 (85%)                        | 51 (80%)                         | 62 (73%)                        | 244 (77%)        |

n = all respondents who prescribed EVIPLERA in the last 3 months

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 71)

All spontaneously mentioned instructions that need to be communicated to the patient related to food requirements as well as spontaneously communicated instructions related to dosing and safety information (eg, contraindications, side effects) for both EDURANT and EVIPLERA are available in the statistical output in [ANNEX 1](#) (under Q1, starting on page 53 of the output for both EDURANT and EVIPLERA).

#### 10.4.1.2. Question 2 (Key Question)

The awareness of the prescribing instructions by the respondents was determined based on responses to Question 1 (open question; see Section 10.4.1.1) and Question 2 (multiple choice question; see below). Question 2 (Q2) was considered a key question for evaluation of the effectiveness of the prescribing information (see Section 9.4.1):

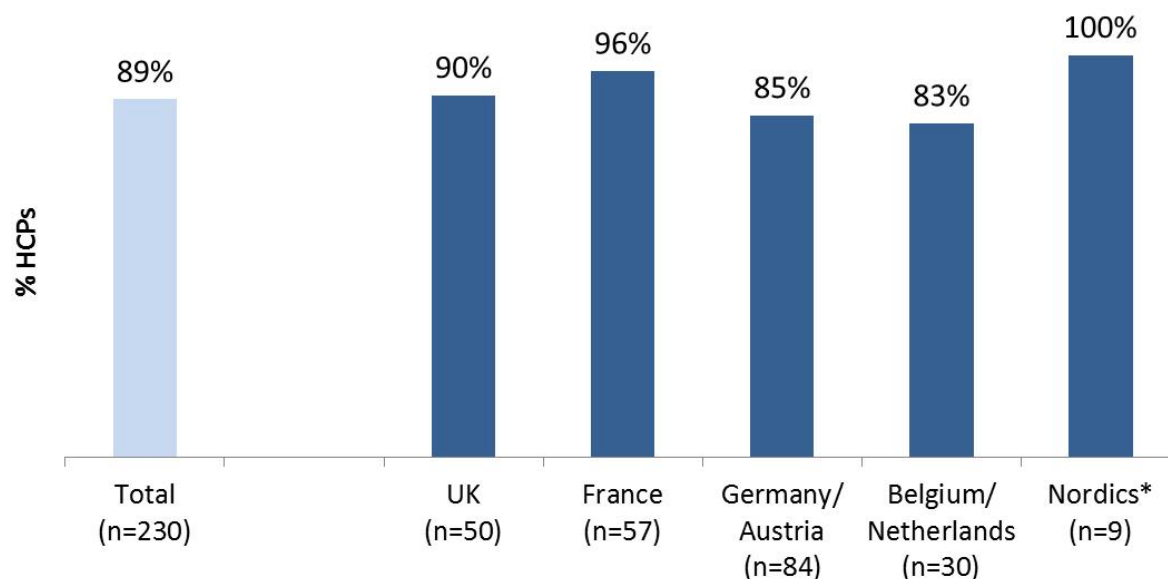
*Q2. Please indicate which of the following instructions / restrictions written below applies to the following HIV treatment (Edurant / Eviplera)*

- *Must be taken with food / with a meal*
- *Must be taken without food / without a meal*
- *Can be taken with or without food / a meal*
- *Must be taken on an empty stomach*
- *Don't know*

For EDURANT, 89% (205/230) of the HCPs correctly identified the meal instruction in their response to Question 2, thereby passing the >80% threshold (see Section 9.4.1) overall, and in all regions (Figure 2) and by all specialties (Figure 3). The correct meal instructions were given less often by HCPs seeing fewer HIV patients per month (10-20 patients: 78%, 21-40 patients: 76%) compared to HCPs seeing more HIV patients per month ( $\geq 41$  patients per month: 92%-100%) (Figure 4). The correct meal instructions were given in >80% for all subcategories of number of prescriptions in the last 3 months, except for the subcategory of 6-10 prescriptions in the last 3 months (79%) (Figure 4).

For EVIPLERA, 91% (287/317) of the HCPs correctly identified the food/meal instruction in their response to Question 2, thereby passing the >80% threshold (see Section 9.4.1) overall, and in all regions (Figure 5) and by all specialties (Figure 6). The correct food/meal instructions were also given in >80% for all subcategories of numbers of HIV patients seen per month and for all subcategories of number of prescriptions in the last 3 months (Figure 7).

**Figure 2: Proportion of EDURANT HCPs correctly identifying instruction: “must be taken with a meal” (Q2), by region**



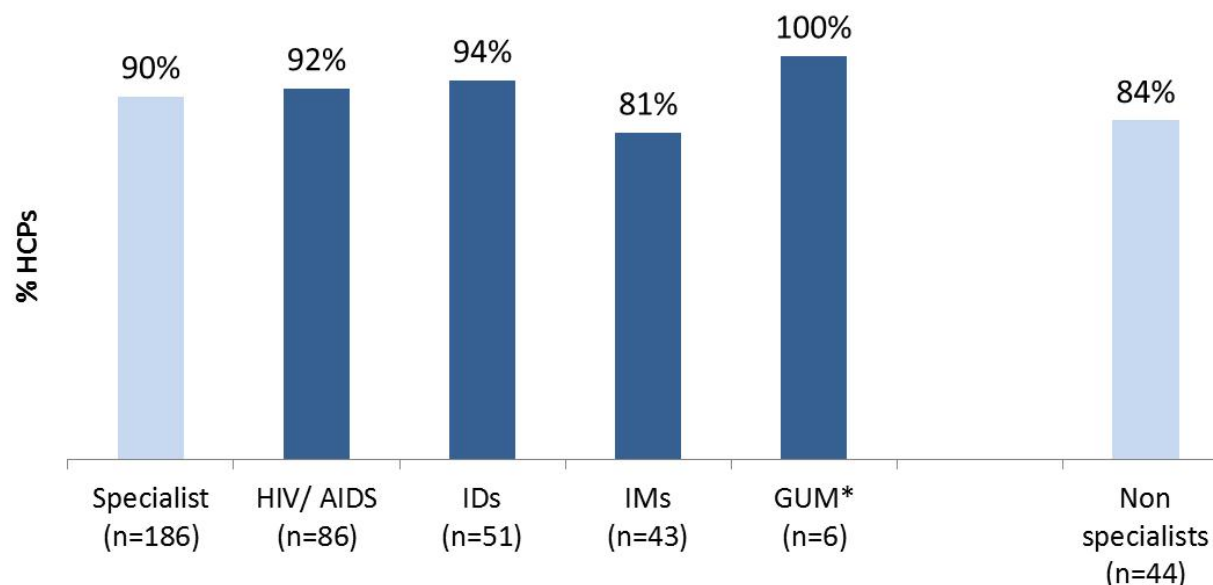
\*Small base

n = number of HCPs who prescribed EDURANT in the last 3 months

**Note: France is significantly different compared to Germany/Austria and Belgium/Netherlands**

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 82)

**Figure 3: Proportion of EDURANT HCPs correctly identifying instruction: “must be taken with a meal” (Q2), by specialty**



\* Small base

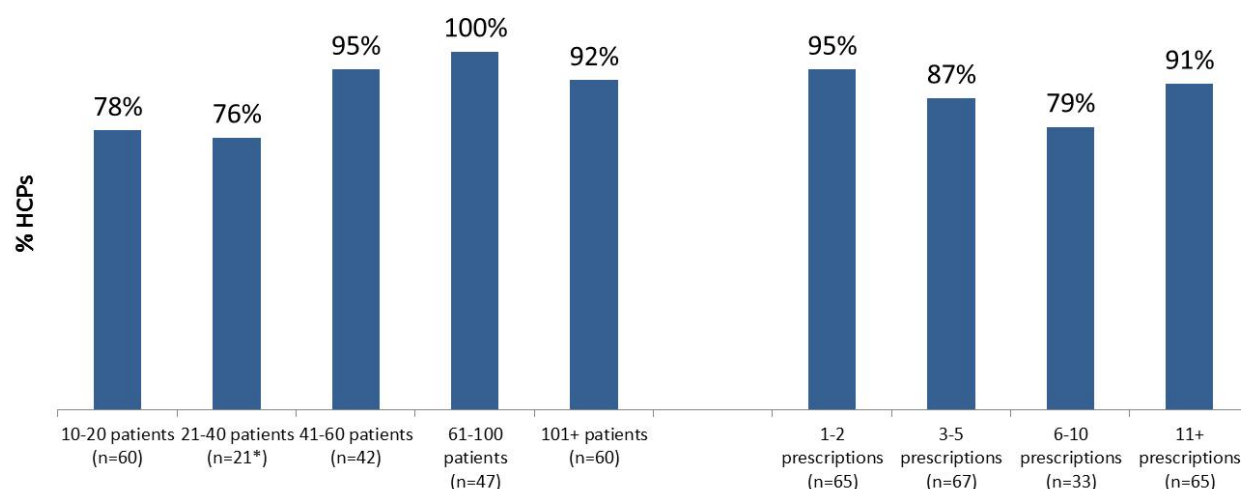
GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EDURANT in the last 3 months

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 82)



**Figure 4: Proportion of EDURANT HCPs correctly identifying instruction: “must be taken with a meal” (Q2), by number of HIV patients seen per month and by number of prescriptions in the last 3 months**



\* Small base

n = number of HCPs who prescribed EDURANT in the last 3 months

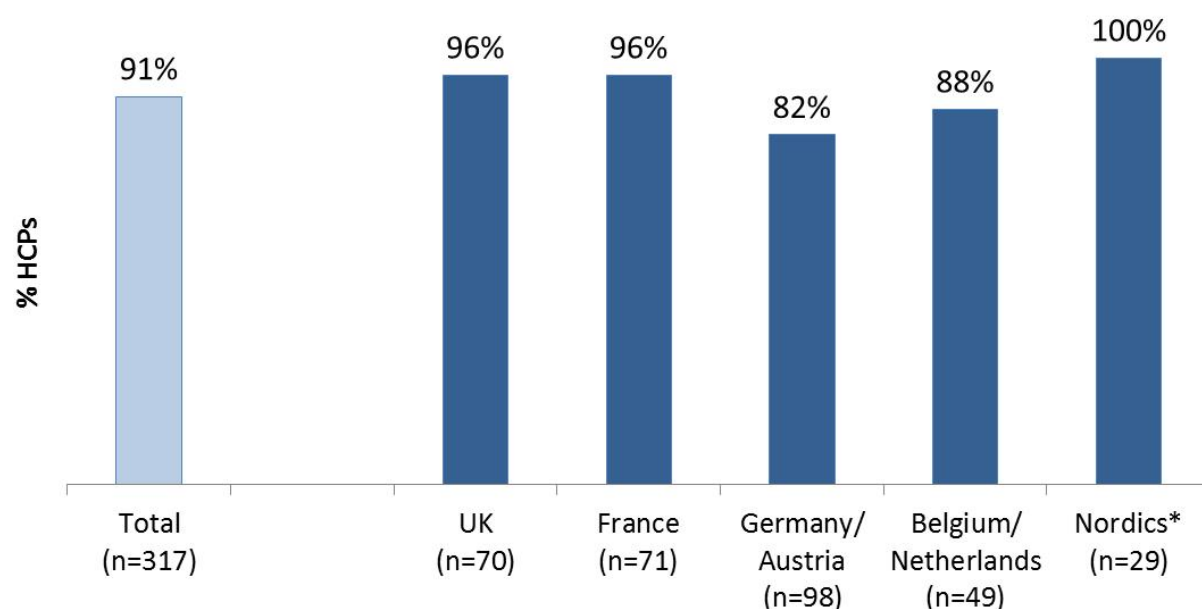
**Note: 41-60, 61-100, and  $\geq 101$  patients seen per month are significantly different compared to 10-20 patients.**

**61-100 patients is also significantly different from  $\geq 101$  patients**

**Note: 1-2 prescriptions is significantly different compared to 6-10 prescriptions**

Source: Statistical output in [ANNEX 1](#) (EDURANT, page 85)

**Figure 5: Proportion of EVIPLERA HCPs correctly identifying instruction: “must be taken with food/with a meal” (Q2), by region**



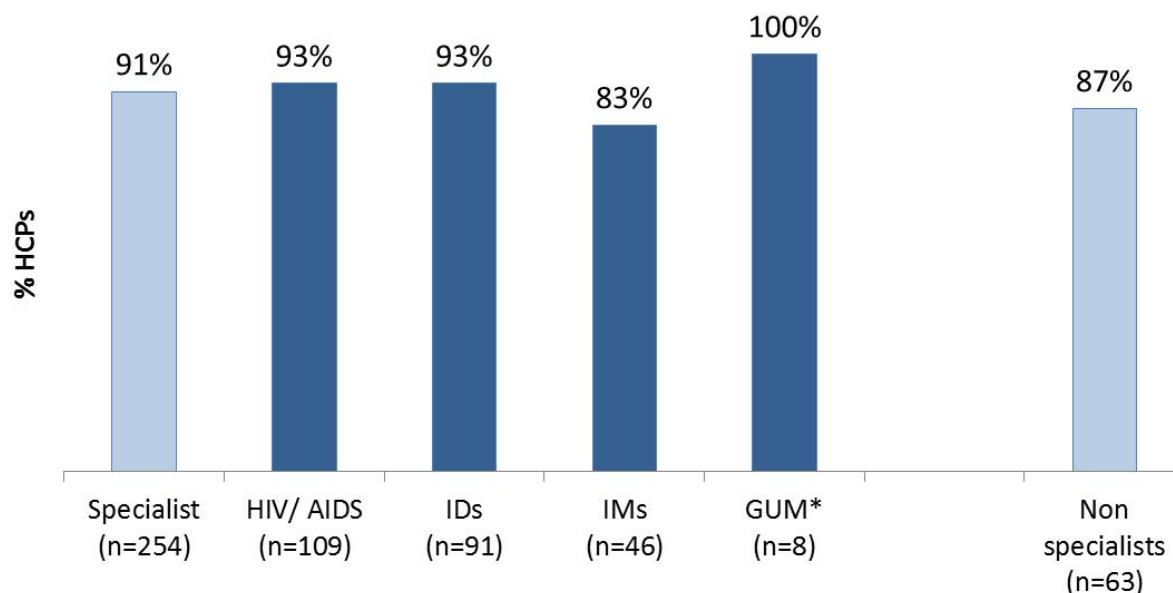
\*Small base

n = number of HCPs who prescribed EVIPLERA in the last 3 months

**Note: UK and France are significantly different compared to Germany/Austria**

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 84)

**Figure 6: Proportion of EVIPLERA HCPs correctly identifying instruction: “must be taken with food/with a meal” (Q2), by specialty**



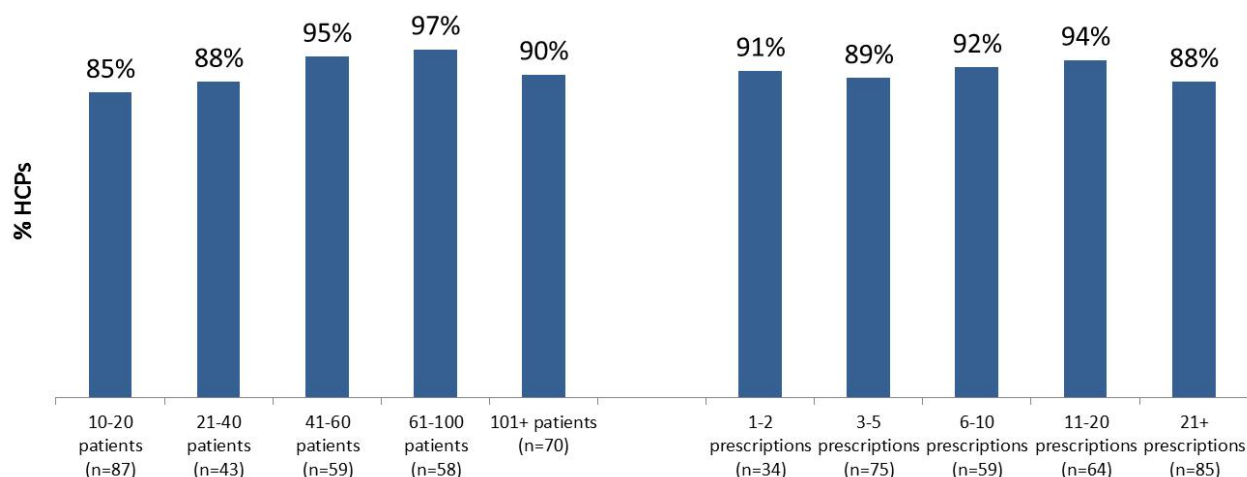
\*Small base

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EVIPLERA in the last 3 months

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 84)

**Figure 7: Proportion of EVIPLERA HCPs correctly identifying instruction: “must be taken with food/with a meal” (Q2), by number of HIV patients seen per month and by number of prescriptions in the last 3 months**



n = number of HCPs who prescribed EVIPLERA in the last 3 months

**Note: 61-100 patients is significantly different compared to 10-20 patients.**

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, page 87)

## 10.4.2. Usage of the prescribing instructions by the respondents

The usage of the prescribing instructions by the respondents was determined based on responses to Questions 3a and 4a (Section 10.4.2.1), Questions 3b and 4b (Section 10.4.2.2), Question 7 (Section 10.4.2.3), and Questions 8 and 9 (Section 10.4.2.4).

### 10.4.2.1. Question 3a (Key Question) and Question 4a

Question 3a (Q3a) was a key question (see Section 9.4.1):

*Q3a. To what proportion of patients that you prescribe / dispense / instruct to take the following treatment do you communicate the following instruction when prescribing it for the first time*

- *Eviplera must be taken with food/with a meal*
- *Edurant must be taken with a meal*

A total of 94%, on average, of the patients of the 205 HCPs who were aware that EDURANT needs to be taken with a meal (see Section 10.4.1.2) received the instruction that EDURANT must be taken with a meal when prescribed for the first time, thereby passing the prespecified >80% threshold (see Section 9.4.1) overall, and in all regions (Table 19), specialties (Table 20), number of HIV patients seen per month (Table 21), and number of prescriptions in the last 3 months (Table 22). Among these HCPs, 87% provided the instruction to all their patients (refer to statistical output in ANNEX 1, output for EDURANT, page 98).

A total of 96%, on average, of the patients of the 287 HCPs who were aware that EVIPLERA needs to be taken with food/with a meal (see Section 10.4.1.2) received the instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time, thereby passing the prespecified >80% threshold (see Section 9.4.1) overall, and in all regions (Table 23), specialties (Table 24), number of HIV patients seen per month (Table 25), and number of prescriptions in the last 3 months (Table 26). Among these HCPs, 91% provided the instruction to all their patients (refer to statistical output in ANNEX 1, output for EVIPLERA, page 101).

As an additional analysis, for Question 3a the average proportion of patients receiving the correct instruction were also calculated taking into account all HCPs who prescribed EDURANT/EVIPLERA in the last 3 months regardless of their response to Question 2 (see Section 10.5).

**Table 19: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed for the first time (Q3a), by region**

| UK<br>(n=45) | France<br>(n=55) | Germany/<br>Austria<br>(n=71) | Belgium/<br>Netherlands<br>(n=25) | Nordics*<br>(n=9) | Total<br>(n=205) |
|--------------|------------------|-------------------------------|-----------------------------------|-------------------|------------------|
| 97%          | 90%              | 96%                           | 94%                               | 98%               | 94%              |

\* Small base

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 97-99)

**Table 20: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed for the first time (Q3a), by specialty**

| Specialists<br>(n=168) | HIV/AIDS<br>(n=79) | IDs<br>(n=48) | IMs<br>(n=35) | GUMs*<br>(n=6) | Non-<br>specialists**<br>(n=37) | Total<br>(n=205) |
|------------------------|--------------------|---------------|---------------|----------------|---------------------------------|------------------|
| 93%                    | 93%                | 94%           | 91%           | 100%           | 99%                             | 94%              |

\* Small base

\*\* Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 97-99)

**Table 21: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed for the first time (Q3a), by number of HIV patients seen per month**

| 10-20<br>patients<br>(n=47) | 21-40<br>patients<br>(n=16) | 41-60<br>patients<br>(n=40) | 61-100<br>patients<br>(n=47) | ≥ 101<br>patients<br>(n=55) | Total<br>(n=205) |
|-----------------------------|-----------------------------|-----------------------------|------------------------------|-----------------------------|------------------|
| 99%                         | 95%                         | 89%                         | 92%                          | 96%                         | 94%              |

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

**Note: 41-60 and 61-100 patients seen per month are significantly different compared to 10-20 patients**

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 100-101)

**Table 22: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed for the first time (Q3a), by number of prescriptions in the last 3 months**

| 1-2<br>prescriptions<br>(n=62) | 3-5<br>prescriptions<br>(n=58) | 6-10<br>prescriptions<br>(n=26) | ≥ 11<br>prescriptions<br>(n=59) | Total<br>(n=205) |
|--------------------------------|--------------------------------|---------------------------------|---------------------------------|------------------|
| 99%                            | 96%                            | 90%                             | 90%                             | 94%              |

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

**Note: 1-2 prescriptions in the last 3 months is significantly different compared to ≥ 11 prescriptions**

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 100-101)

**Table 23: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time (Q3a), by region**

| UK<br>(n=67) | France<br>(n=68) | Germany/<br>Austria<br>(n=80) | Belgium/<br>Netherlands<br>(n=43) | Nordics*<br>(n=29) | Total<br>(n=287) |
|--------------|------------------|-------------------------------|-----------------------------------|--------------------|------------------|
| 97%          | 94%              | 96%                           | 97%                               | 100%               | 96%              |

\*Small base

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 100-102)

**Table 24: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time (Q3a), by specialty**

| Specialists<br>(n=232) | HIV/AIDS<br>(n=101) | IDs<br>(n=85) | IMs<br>(n=38) | GUMs*<br>(n=8) | Non-specialists**<br>(n=55) | Total<br>(n=287) |
|------------------------|---------------------|---------------|---------------|----------------|-----------------------------|------------------|
| 96%                    | 95%                 | 99%           | 92%           | 100%           | 96%                         | 96%              |

\*Small base

\*\* Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

**Note: IMs are significantly different compared to IDs**

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 100-102)

**Table 25: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time (Q3a), by number of HIV patients seen per month**

| 10-20<br>patients<br>(n=74) | 21-40<br>patients<br>(n=38) | 41-60<br>patients<br>(n=56) | 61-100<br>patients<br>(n=56) | ≥ 101<br>patients<br>(n=63) | Total<br>(n=287) |
|-----------------------------|-----------------------------|-----------------------------|------------------------------|-----------------------------|------------------|
| 97%                         | 96%                         | 95%                         | 97%                          | 95%                         | 96%              |

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 103-104)

**Table 26: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed for the first time (Q3a), by number of prescriptions in the last 3 months**

| 1-2<br>prescriptions<br>(n=31) | 3-5<br>prescriptions<br>(n=67) | 6-10<br>prescriptions<br>(n=54) | 11-20<br>prescriptions<br>(n=60) | ≥ 21<br>prescriptions<br>(n=75) | Total<br>(n=287) |
|--------------------------------|--------------------------------|---------------------------------|----------------------------------|---------------------------------|------------------|
| 100%                           | 97%                            | 98%                             | 94%                              | 94%                             | 96%              |

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 103-104)

*Q4a. You stated that you do not always communicate the instructions that patients must take Eviplera/Edurant with food/with a meal when giving this treatment to a patient for the first time. Please explain the reasons for not communicating this instruction to all of your patients taking this treatment for the first time?*

Answers to Question 4a provided insight as to why the respondents did not communicate the EDURANT/EVIPLERA instructions regarding intake with a meal/food to all their patients. Based on the answers provided to Q4a it was determined that upon questioning it appeared that some HCPs who answered they do not always communicate that EDURANT and EVIPLERA must be taken with a meal/with food to patients receiving the treatment for the first time, actually did always provide instructions on intake with a meal or with food during the first consultation. Therefore, their response to Q3a was set to 100%. Refer to Section 10.5 for the recalculated mean proportions of patients receiving the correct food/meal instructions when receiving the treatment for the first time.

#### **10.4.2.2. Question 3b and Question 4b**

*Q3b. To what proportion of patients that you prescribe / dispense / instruct to take the following treatment do you communicate the following instruction during subsequent follow-up appointments*

- *Eviplera must be taken with food/with a meal*
- *Edurant must be taken with a meal*

*Q4b. You stated that you do not always communicate the instructions that patients must take Eviplera/Edurant with food/with a meal during subsequent follow-up appointments. Please explain the reasons for not communicating this instruction to all of your patients taking this treatment during subsequent follow-up appointments?*

On average, 72% of the patients of the 205 HCPs who were aware that EDURANT needs to be taken with a meal, received the instruction that EDURANT must be taken with a meal, at follow-up appointments. Data are presented by region (Table 27), specialty (Table 28), number of HIV patients seen per month (Table 29), and number of prescriptions over the last 3 months (Table 30). Among the respondents, 49% provided the instruction to all their patients (statistical output in ANNEX 1, output for EDURANT, page 103). The main reasons for not providing the instructions at follow-up, was patient compliance/adherence to instructions and the fact that patients are well-informed about the food requirements for EDURANT and that these instructions were provided when EDURANT was prescribed for the first time (Q4b; refer to statistical output in ANNEX 1, output for EDURANT, pages 130-147).

On average, 76% of the patients of the 287 HCPs who were aware that EVIPLERA needs to be taken with food/with a meal, received the instruction that EVIPLERA must be taken with food/with a meal, at follow-up appointments. Data are presented by region (Table 31), specialty (Table 32), number of HIV patients seen per month (Table 33), and number of prescriptions over the last 3 months (Table 34). Among the respondents, 51% provided the instruction to all their

patients (statistical output in [ANNEX 1](#), output for EVIPLERA, page 107). The main reasons for not providing the instructions at follow-up, was patient compliance/adherence to instructions and the fact that patients are well-informed about the food requirements for EVIPLERA and that these instructions were provided when EVIPLERA was prescribed for the first time (Q4b, refer to statistical output in [ANNEX 1](#), output for EVIPLERA, pages 136-153).

**Table 27: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed during follow-up appointments (Q3b), by region**

| UK<br>(n=45) | France<br>(n=55) | Germany/<br>Austria<br>(n=71) | Belgium/<br>Netherlands<br>(n=25) | Nordics*<br>(n=9) | Total<br>(n=205) |
|--------------|------------------|-------------------------------|-----------------------------------|-------------------|------------------|
| 79%          | 70%              | 70%                           | 76%                               | 63%               | 72%              |

\* Small base

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 102-104)

**Table 28: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed during follow-up appointments (Q3b), by specialty**

| Specialists<br>(n=168) | HIV/AIDS<br>(n=79) | IDs<br>(n=48) | IMs<br>(n=35) | GUMs*<br>(n=6) | Non-<br>specialists**<br>(n=37) | Total<br>(n=205) |
|------------------------|--------------------|---------------|---------------|----------------|---------------------------------|------------------|
| 71%                    | 73%                | 69%           | 71%           | 68%            | 77%                             | 72%              |

\* Small base

\*\* Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 102-104)

**Table 29: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed during follow-up appointments (Q3b), by number of HIV patients seen per month**

| 10-20<br>patients<br>(n=47) | 21-40<br>patients<br>(n=16) | 41-60<br>patients<br>(n=40) | 61-100<br>patients<br>(n=47) | ≥ 101<br>patients<br>(n=55) | Total<br>(n=205) |
|-----------------------------|-----------------------------|-----------------------------|------------------------------|-----------------------------|------------------|
| 75%                         | 63%                         | 76%                         | 72%                          | 70%                         | 72%              |

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 105-106)



**Table 30: Mean proportion of patients receiving instruction that EDURANT must be taken with a meal when prescribed during follow-up appointments (Q3b), by number of prescriptions in the last 3 months**

| 1-2 prescriptions<br>(n=62) | 3-5 prescriptions<br>(n=58) | 6-10 prescriptions<br>(n=26) | ≥ 11 prescriptions<br>(n=59) | Total<br>(n=205) |
|-----------------------------|-----------------------------|------------------------------|------------------------------|------------------|
| 73%                         | 78%                         | 79%                          | 63%                          | 72%              |

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

**Note: 3-5 prescriptions in the last 3 months is significantly different compared to ≥ 11 prescriptions**

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 105-106)

**Table 31: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed during follow-up appointments (Q3b), by region**

| UK<br>(n=67) | France<br>(n=68) | Germany/<br>Austria<br>(n=80) | Belgium/<br>Netherlands<br>(n=43) | Nordics*<br>(n=29) | Total<br>(n=287) |
|--------------|------------------|-------------------------------|-----------------------------------|--------------------|------------------|
| 80%          | 72%              | 72%                           | 82%                               | 76%                | 76%              |

\*Small base

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 106-108)

**Table 32: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed during follow-up appointments (Q3b), by specialty**

| Specialists<br>(n=232) | HIV/AIDS<br>(n=101) | IDs<br>(n=85) | IMs<br>(n=38) | GUMs*<br>(n=8) | Non-specialists**<br>(n=55) | Total<br>(n=287) |
|------------------------|---------------------|---------------|---------------|----------------|-----------------------------|------------------|
| 75%                    | 76%                 | 76%           | 70%           | 79%            | 79%                         | 76%              |

\*Small base

\*\* Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 106-108)

**Table 33: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed during follow-up appointments (Q3b), by number of HIV patients seen per month**

| 10-20 patients<br>(n=74) | 21-40 patients<br>(n=38) | 41-60 patients<br>(n=56) | 61-100 patients<br>(n=56) | ≥ 101 patients<br>(n=63) | Total<br>(n=287) |
|--------------------------|--------------------------|--------------------------|---------------------------|--------------------------|------------------|
| 71%                      | 75%                      | 83%                      | 78%                       | 74%                      | 76%              |

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 109-110)



**Table 34: Mean proportion of patients receiving instruction that EVIPLERA must be taken with food/with a meal when prescribed during follow-up appointments (Q3b), by number of prescriptions in the last 3 months**

| 1-2 prescriptions<br>(n=31) | 3-5 prescriptions<br>(n=67) | 6-10 prescriptions<br>(n=54) | 11-20 prescriptions<br>(n=60) | ≥ 21 prescriptions<br>(n=75) | Total<br>(n=287) |
|-----------------------------|-----------------------------|------------------------------|-------------------------------|------------------------------|------------------|
| 84%                         | 74%                         | 76%                          | 74%                           | 76%                          | 76%              |

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 109-110)

### 10.4.2.3. Question 7

*Q7. How do you explain the instruction that Eviplera/Edurant must be taken with food/with a meal to your patients?*

The main 3 explanations provided by the 205 HCPs to their patient for needing to take EDURANT with a meal, are that 1) there is an efficacy gain (31%), 2) it is a dosing requirement (30%), and 3) absorption is improved (24%) ([Table 35](#) [by region] and [Table 36](#) [by specialty]). For EVIPLERA these explanations were provided by 31%, 29% and 24% of 287 HCPs, respectively ([Table 37](#) [by region] and [Table 38](#) [by specialty]).

**Table 35: Mean proportion of HCPs by rationale for providing instruction that EDURANT must be taken with a meal (Q7), by region**

| Rationale                              | Total<br>(n=205) | UK<br>(n=45) | France<br>(n=55) | Germany/<br>Austria<br>(n=71) | Belgium/<br>Netherlands<br>(n=25) | Nordics*<br>(n=9) |
|--|------------------|--------------|------------------|-------------------------------|-----------------------------------|-------------------|
| Efficacy                               | 33%              | 24%          | 38%              | 32%                           | 36%                               | 33%               |
| <i>Provides good/improved efficacy</i> | 31%              | 22%          | 36%              | 31%                           | 36%                               | 33%               |
| Dosing/Administration                  | 33%              | 49%          | 22%              | 23%                           | 60%                               | 22%               |
| <i>Meal/food based dosing</i>          | 30%              | 49%          | 20%              | 18%                           | 56%                               | 22%               |
| Mechanism of action                    | 31%              | 18%          | 33%              | 38%                           | 24%                               | 56%               |
| <i>Improves absorption</i>             | 24%              | 11%          | 27%              | 28%                           | 20%                               | 56%               |

\* Small base

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 175-186)

**Table 36: Mean proportion of HCPs by rationale for providing instruction that EDURANT must be taken with a meal (Q7), by specialty**

| Rationale                              | Total<br>(n=205) | Specialists<br>(n=168) | HIV/AIDS<br>(n=79) | IDs<br>(n=48) | IMs<br>(n=35) | GUMs*<br>(n=6) | Non-specialists**<br>(n=37) |
|--|------------------|------------------------|--------------------|---------------|---------------|----------------|-----------------------------|
| Efficacy                               | 33%              | 32%                    | 33%                | 27%           | 37%           | 17%            | 38%                         |
| <i>Provides good/improved efficacy</i> | 31%              | 30%                    | 30%                | 25%           | 37%           | 17%            | 38%                         |
| Dosing/Administration                  | 33%              | 29%                    | 30%                | 25%           | 29%           | 33%            | 51%                         |
| <i>Meal/food based dosing</i>          | 30%              | 26%                    | 27%                | 25%           | 26%           | 33%            | 49%                         |
| Mechanism of action                    | 31%              | 33%                    | 33%                | 35%           | 34%           | 17%            | 22%                         |
| <i>Improves absorption</i>             | 24%              | 26%                    | 24%                | 29%           | 29%           | 17%            | 16%                         |

\* Small base

\*\* Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT needs to be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 175-186)

**Table 37: Mean proportion of HCPs by rationale for providing instruction that EVIPLERA must be taken with food / with a meal (Q7), by region**

| Rationale                              | Total<br>(n=287) | UK<br>(n=67) | France<br>(n=68) | Germany/<br>Austria<br>(n=80) | Belgium/<br>Netherlands<br>(n=43) | Nordics*<br>(n=29) |
|--|------------------|--------------|------------------|-------------------------------|-----------------------------------|--------------------|
| Efficacy                               | 33%              | 24%          | 34%              | 39%                           | 33%                               | 41%                |
| <i>Provides good/improved efficacy</i> | 31%              | 18%          | 31%              | 39%                           | 30%                               | 38%                |
| Dosing/Administration                  | 32%              | 51%          | 21%              | 15%                           | 58%                               | 28%                |
| <i>Meal/food based dosing</i>          | 29%              | 48%          | 16%              | 12%                           | 56%                               | 24%                |
| Mechanism of action                    | 32%              | 25%          | 31%              | 40%                           | 23%                               | 38%                |
| <i>Improves absorption</i>             | 24%              | 18%          | 22%              | 29%                           | 19%                               | 38%                |

\*Small base

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 182-192)

**Table 38: Mean proportion of HCPs by rationale for providing instruction that EVIPLERA must be taken with food / with a meal (Q7), by specialty**

| Rationale                              | Total<br>(n=287) | Specialists<br>(n=232) | HIV/AIDS<br>(n=101) | IDs<br>(n=85) | IMs<br>(n=38) | GUMs*<br>(n=8) | Non-specialists**<br>(n=55) |
|--|------------------|------------------------|---------------------|---------------|---------------|----------------|-----------------------------|
| Efficacy                               | 33%              | 31%                    | 31%                 | 28%           | 37%           | 38%            | 44%                         |
| <i>Provides good/improved efficacy</i> | 31%              | 28%                    | 26%                 | 27%           | 34%           | 38%            | 42%                         |
| Dosing/Administration                  | 32%              | 29%                    | 33%                 | 28%           | 18%           | 50%            | 45%                         |
| <i>Meal/food based dosing</i>          | 29%              | 27%                    | 28%                 | 28%           | 18%           | 50%            | 38%                         |
| Mechanism of action                    | 32%              | 33%                    | 32%                 | 32%           | 37%           | 50%            | 25%                         |
| <i>Improves absorption</i>             | 24%              | 25%                    | 23%                 | 27%           | 24%           | 25%            | 22%                         |

\* Small base

\*\* Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA needs to be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 182-192)

#### 10.4.2.4. Question 8 and Question 9

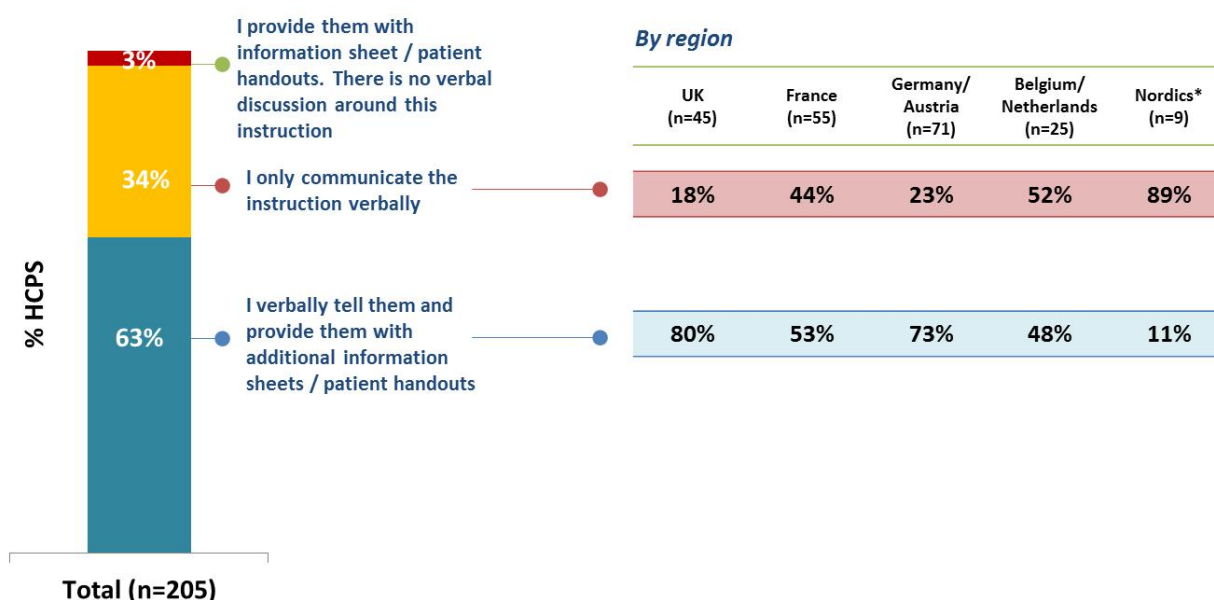
*Q8. Which of the following best describes how you communicate the instruction to your patients that they must take Eviplera/Edurant with food/with a meal?*

*Q9. Which of the following additional information sheets / patient handouts for Eviplera/Edurant do you provide to your patients?*

The preferred means of the HCPs (205 for EDURANT, 287 for EVIPLERA) to communicate to their patients that EDURANT/EVIPLERA must be taken with a meal/food, is to inform them verbally and provide them with additional information sheets/patient handouts, ie, preferred means for 63% ([Figure 8](#) and [Figure 9](#) for EDURANT) and 60% ([Figure 10](#) and [Figure 11](#) for EVIPLERA), respectively.

Half of the respondents who provide information sheets to the patients (136 for EDURANT, 185 for EVIPLERA) make use of information sheets provided by company sales representative, ie, 50% for both EDURANT and EVIPLERA (Q9, refer to statistical output in [ANNEX 1](#), output for EDURANT, pages 209-212; output for EVIPLERA, pages 216-220).

**Figure 8: Mean proportion of HCPs by method for providing instruction that EDURANT must be taken with a meal (Q8), overall and by region**

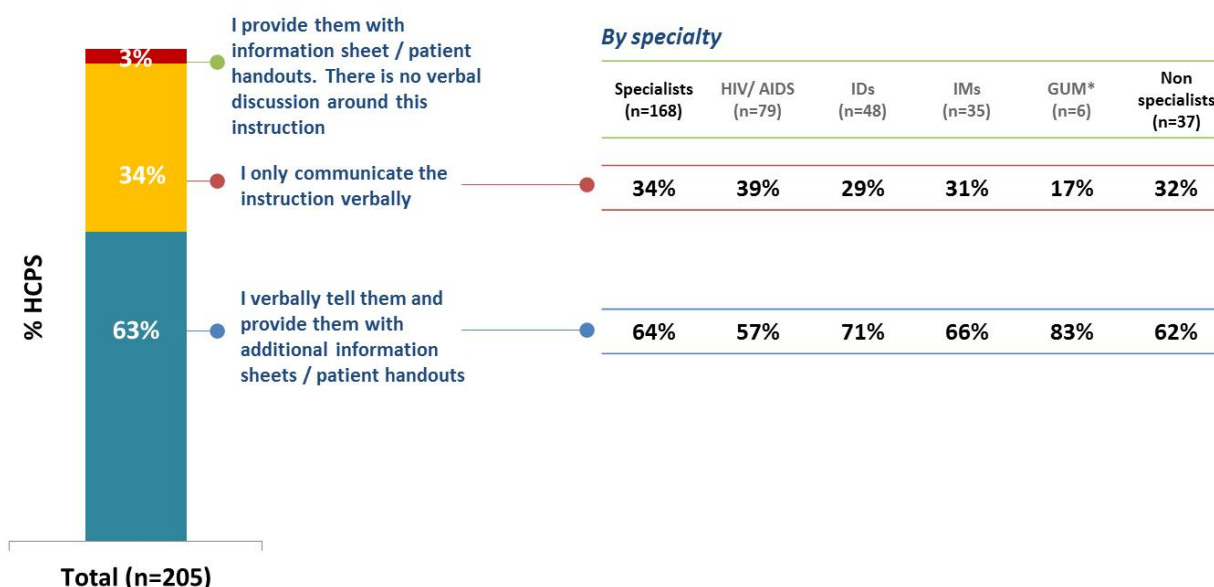


\* Small base

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT must be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 202-204)

**Figure 9: Mean proportion of HCPs by method for providing instruction that EDURANT must be taken with a meal (Q8), overall and by specialty**



\* Small base

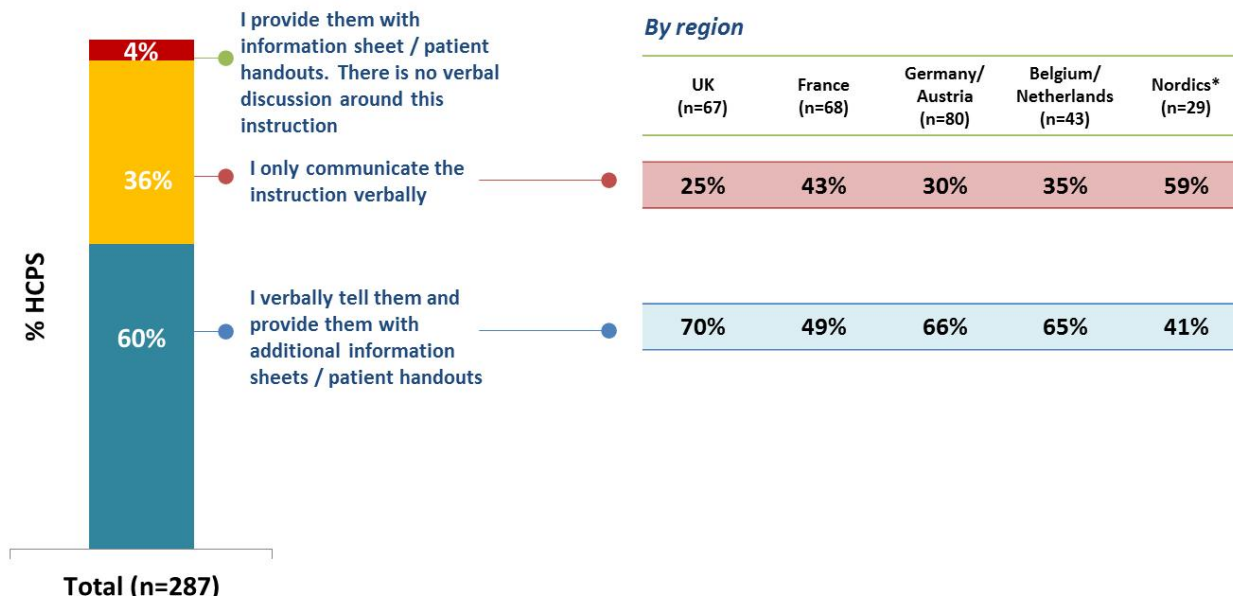
Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT must be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 202-204)

**Figure 10: Mean proportion of HCPs by method for providing instruction that EVIPLERA must be taken with food / with a meal (Q8), overall and by region**

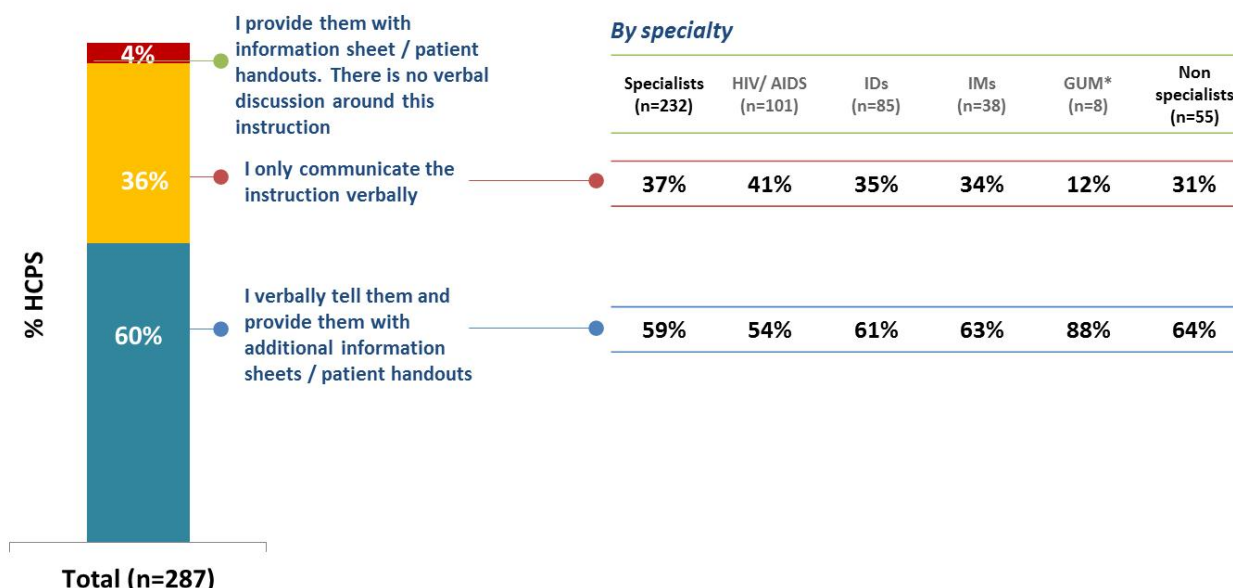


\* Small base

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA must be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 210-212)

**Figure 11: Mean proportion of HCPs by method for providing instruction that EVIPLERA must be taken with food / with a meal (Q8), overall and by specialty**



\* Small base

Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists

n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA must be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 210-212)

### 10.4.3. Sense of importance of the prescribing instructions by the respondents

#### 10.4.3.1. Question 5 and Question 6

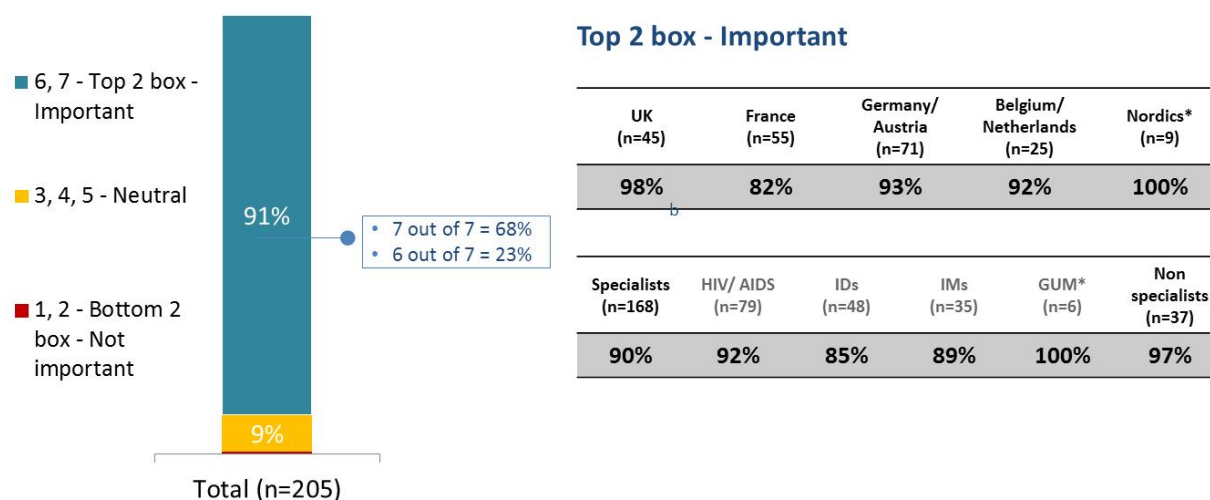
The sense of importance of the prescribing instructions by the respondents was determined based on responses to the following questions:

*Q5. On a scale of 1 to 7, where 1=not at all important and 7=extremely important, how important do you believe it is to communicate the instructions for taking Eviplera/Edurant with food/with a meal?*

*Q6. Why do you say that?*

The majority of the HCPs (205 for EDURANT, 287 for EVIPLERA, 91% for both) consider communicating to the patients that EDURANT/EVIPLERA must be taken with a meal/food important (ie, score 6 or 7 on a scale from 1-7) (see [Figure 12](#) and [Figure 13](#)). Of the 187 HCPs who were aware that EDURANT needs to be taken with a meal and considered this important to communicate to the patients, the drivers were the improved absorption (33%) and the efficacy gain (32%) (Q6, refer to statistical output in [ANNEX 1](#), output for EDURANT, pages 154-161). For EVIPLERA, the same drivers were mentioned by 37% and 28%, respectively, of the 262 HCPs who were aware that EVIPLERA needs to be taken with food/with a meal and considered this important to communicate to the patients (Q6, refer to statistical output in [ANNEX 1](#), output for EVIPLERA, pages 161-168).

**Figure 12: Mean proportion of HCPs by importance scale score for providing instruction that EDURANT must be taken with a meal (Q5), overall and by region and specialty**



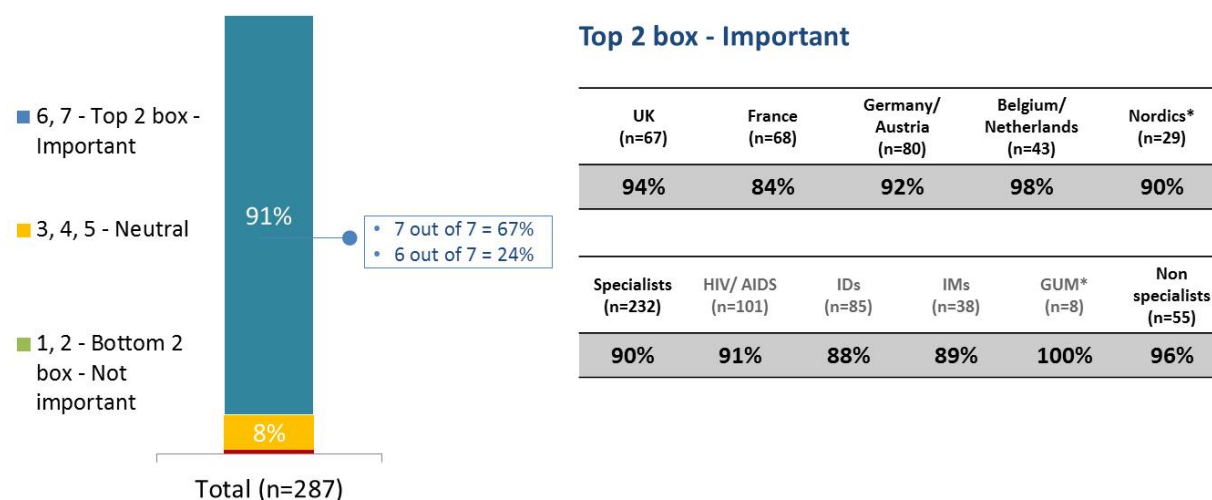
\* Small base

Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialists, IDs: infectious disease specialists, IMs: internal medicine specialists  
n = number of HCPs who prescribed EDURANT in the last 3 months and were aware that EDURANT must be taken with a meal

Source: Statistical output in [ANNEX 1](#) (EDURANT, pages 149-151)



**Figure 13: Mean proportion of HCPs by importance scale score for providing instruction that EVIPLERA must be taken with food / with a meal (Q5), overall and by region and specialty**

\* Small base

Non-specialists include general practitioners/primary care physicians, nurses and pharmacists

GUMs: genitourinary medicine specialist, IDs: infectious disease specialists, IMs: internal medicine specialists  
n = number of HCPs who prescribed EVIPLERA in the last 3 months and were aware that EVIPLERA must be taken with food/with a meal

Source: Statistical output in [ANNEX 1](#) (EVIPLERA, pages 155-157)

## 10.5. Other Analyses

Answers to Question 4a provided insight as to why the respondents did not communicate the EDURANT/EVIPLERA instructions regarding intake with a meal/food to all their patients (see Section 10.4.2.1). Upon questioning 27 EDURANT and 27 EVIPLERA HCPs (including 15 HCPs who did not communicate the correct instruction to all their patients for both EDURANT and EVIPLERA; data on file) who answered (Q3a) they do not always communicate to all their patients that EDURANT and EVIPLERA must be taken with a meal/with food when they prescribed the treatment for the first time, it appeared that for 9 HCPs who prescribed EDURANT and 7 HCPs who prescribed EVIPLERA, these instructions were actually always provided to the patients (refer to statistical output in [ANNEX 1](#), output for EDURANT from page 119 onwards and output for EVIPLERA from page 124 onwards). Therefore, their response to Q3a was set to 100% and the proportions were recalculated of patients who received the instruction that EDURANT/EVIPLERA must be taken with a meal/with food when prescribed for the first time; the recalculated proportions were 97% for EDURANT (refer to statistical output in [ANNEX 1](#), output for EDURANT, pages 107-109) and 98% for EVIPLERA (refer to statistical output in [ANNEX 1](#), output for EVIPLERA, pages 112-114).

Furthermore, as an additional analysis, for Question 3a the average proportion of patients receiving the correct instruction were also calculated taking into account all HCPs who prescribed EDURANT/EVIPLERA in the last 3 months regardless of their response to Question 2 (see Section 10.4.2.1). With this analysis, the percentages for Question 3a were also

above the prespecified >80% threshold (ie, 84% for EDURANT and 87% for EVIPLERA; refer to statistical output in [ANNEX 1](#), output for EDURANT: page 220; output for EVIPLERA: page 227).

## **10.6. Adverse Events/Adverse Reactions**

Adverse events were not part of the data collection in the survey. No adverse events were spontaneously reported.

## **11. DISCUSSION**

### **11.1. Key Results**

As explained in Section [9.4.1](#), the key results are those obtained from Question 2 (see Section [10.4.1.2](#)) and Question 3a (see Section [10.4.2.1](#)). The SmPCs of EDURANT and EVIPLERA provide instructions on taking the treatments with a meal/with food. For the prescribing conditions of EDURANT/EVIPLERA to be considered effective to minimize the risk of potentially decreased exposure and lack of therapeutic effect associated with taking RPV-containing regimens without a meal/food, potentially leading to development of resistance (ie, a safety concern in the RMP), at least 80% of the HCPs needed to correctly identify the instructions (Question 2) and communicate them to at least 80% of patients, on average of those HCPs who correctly identified the food intake instruction (Question 2), when prescribing the treatment for the first time (Question 3a).

These criteria were met: for EDURANT, 89% of the 230 HCPs correctly identified the meal instruction; for EVIPLERA, 91% of the 317 HCPs correctly identified the food/meal instruction (Question 2, Section [10.4.1.2](#)). In addition, 94%, on average, of the patients of the 205 HCPs who were aware that EDURANT needs to be taken with a meal, received the instruction that EDURANT must be taken with a meal when prescribed for the first time; and 96%, on average, of the patients of the 287 HCPs who were aware that EVIPLERA needs to be taken with food/with a meal, received the instruction that EVIPLERA must be taken with food/with a meal, when prescribed for the first time (Question 3a, Section [10.4.2.1](#)).

### **11.2. Limitations**

A limitation of the online quantitative survey approach is that it only provided feedback on HCP behavior with regard to providing the correct instructions. It did not provide an assessment of whether patients actually are compliant with the SmPC instructions. Also, the online quantitative approach did not allow for in-depth probing of respondent answers in order to gain deep understanding of HCP behavior as the answers to the closed questions in the survey were pre-defined.

### **11.3. Interpretation**

Results discussed in Sections [10.4.1](#), [10.4.2](#), [10.4.3](#) show that the majority ( $\geq 89\%$ ) of HCPs were aware of the prescribing instructions with regard to intake of the treatment with a meal/food for EDURANT/EVIPLERA and communicate them to the majority of their patients the first time they prescribe the treatment and during follow-up appointments. Instructions are communicated



verbally and through patient information sheets. Providing the instructions to the patients is considered important, because of improved absorption and efficacy, related to correct food intake, which is also communicated to the patients.

The results of the survey show that the current prescribing information for EDURANT and EVIPLERA is effective (> 80%) with regard to the instructions provided for the intake of the treatment with a meal/food (see Section 11.1 for the results of the 2 key questions: Question 2: 89% for EDURANT and 91% for EVIPLERA; Question 3a: 94% for EDURANT and 96% for EVIPLERA). Therefore, the current prescribing information for both EDURANT and EVIPLERA remains adequate to minimize the risk of potentially decreased exposure and lack of therapeutic effect associated with taking RPV-containing regimens without a meal/food, potentially leading to development of resistance, and there is no need for additional risk minimization measures. Furthermore, the results of this survey have no impact on the overall favorable benefit/risk ratio of both EDURANT and EVIPLERA.

#### **11.4. Generalizability**

Because of the well-chosen sample size (see Section 9.7) and well-designed survey (see Section 9.5) the results can be applied to the general HIV treating HCP population in Europe.

### **12. OTHER INFORMATION**

Not applicable.

### **13. CONCLUSION**

The results of the HCP survey indicate that the prescribing conditions for EDURANT/EVIPLERA are effective in minimizing the risk associated with taking the products without a meal/food. Based on the results of this survey, no additional risk minimization measures are warranted. The benefit/risk ratios of both EDURANT and EVIPLERA remain favorable.

### **14. REFERENCES**

None.

## ANNEX 1: STAND-ALONE DOCUMENTS

**The following appendices are either included with the report or are available on request.**

- 1 **Protocol (ie, HCP survey proposal)** and Amendments (Not applicable)
- 2 **EDURANT and EVIPLERA HCP Survey**
- 3 Sample Case Report Form(s) (Not applicable)
- 4 List of IECs or IRBs and Sample Consent Forms (Not applicable)
- 5 List and Description of Investigators and Sites (Not applicable)
- 6 Signature of Sponsor's Responsible Medical Officer (located at the end of this document)  
Signature of Principal or Coordinating Investigator(s) (Not applicable)
- 7 Listing of Patients Receiving Test Drug(s) from Specified Batch (Not Applicable)
- 8 Randomization Scheme (Not Applicable)
- 9 Audit Certificates (Not applicable)
- 10 Documentation of Statistical Methods and Interim Analysis Plans (Not applicable; described in HCP survey proposal; see also [ANNEX 2](#))
- 11 Documentation of Interlaboratory Standardization Methods and Quality Assurance Procedures if Used (Not Applicable)
- 12 Publications Based on the Study (Not Applicable)
- 13 Important Publications Referenced in the Report (Not Applicable)
- 14 Statistical Output (**document for EDURANT** and **document for EVIPLERA**)

## ANNEX 2: ADDITIONAL/SUPPORTING INFORMATION

### Planned analysis as outlined in Appendix 1 of the HCP survey proposal

| Question Number                                    | Table Title  | Crossed with  | Base reference   | Notes   |
|--|--|---|--|---|
| S1   | Country of practice (individual and groupings eg, Germany + Austria, Sweden + Norway + Denmark etc)                    | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists)   | All HCPs   |   |
| S2   | Specialty (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists)                    | S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc)   | All HCPs   |   |
| S3   | Level/ Grade   | S2 - Current role / job title   | All specialists  |   |
| S4   | Number of HIV patients seen in an average month  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists)   | All HCPs   | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| S5   | Most involved person in providing instruction to patients regarding their HIV medication                               | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs   |   |
| S6   | To approximately how many patients in the last 3 months have you prescribed / dispensed / instructed to take Eviplera? | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs   |   |
| S6   | To approximately how many patients in the last 3 months have you prescribed / dispensed / instructed to take Edurant?  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs   |   |
| Main Questionnaire - for both Eviplera and Edurant |  |   |  |   |
| Q1   | Prescription of Eviplera and Edurant - instructions to be communicated to the patients about taking this medication    | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months | Verbatim responses will be coded into appropriate groupings   |
| Q1   | Prescription of Eviplera - instructions to be communicated to the patients about taking this medication                | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera in the last 3 months             | Verbatim responses will be coded into appropriate groupings   |

| Question Number | Table Title   | Crossed with  | Base reference   | Notes   |
|-----------------|---|---|--|---|
| Q1              | Prescription of Edurant - instructions to be communicated to the patients about taking this medication              | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Edurant in the last 3 months              | Verbatim responses will be coded into appropriate groupings |
| Q1              | Prescription of Eviplera - instructions to be communicated to the patients about taking this medication             | S6 - Number of Eviplera prescriptions in last 3 months - grouped into low, medium, high depending on data   | All HCPs who have prescribed Eviplera in the last 3 months             | Verbatim responses will be coded into appropriate groupings |
| Q1              | Prescription of Edurant - instructions to be communicated to the patients about taking this medication              | S6 - Number of Edurant prescriptions in last 3 months - grouped into low, medium, high depending on data  | All HCPs who have prescribed Edurant in the last 3 months              | Verbatim responses will be coded into appropriate groupings |
| Q1              | Prescription of Eviplera and Edurant - instructions to be communicated to the patients about taking this medication | Q2  | All HCPs who have prescribed Eviplera and Edurant in the last 3 months | Verbatim responses will be coded into appropriate groupings |
| Q1              | Prescription of Eviplera - instructions to be communicated to the patients about taking this medication             | Q2  | All HCPs who have prescribed Eviplera in the last 3 months             | Verbatim responses will be coded into appropriate groupings |
| Q1              | Prescription of Edurant - instructions to be communicated to the patients about taking this medication              | Q2  | All HCPs who have prescribed Edurant in the last 3 months              | Verbatim responses will be coded into appropriate groupings |
| Q2              | Which of the following instructions applies to Eviplera and Edurant   | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months |   |
| Q2              | Which of the following instructions applies to Eviplera   | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera in the last 3 months             |   |
| Q2              | Which of the following instructions applies to Edurant  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Edurant in the last 3 months              |   |

| Question Number | Table Title  | Crossed with  | Base reference   | Notes   |
|-----------------|--|---|--|---|
| Q2              | Which of the following instructions applies to Eviplera  | S6 - Number of Eviplera prescriptions in last 3 months - grouped into low, medium, high depending on data   | All HCPs who have prescribed Eviplera in the last 3 months             |   |
| Q2              | Which of the following instructions applies to Edurant   | S6 - Number of Edurant prescriptions in last 3 months - grouped into low, medium, high depending on data  | All HCPs who have prescribed Edurant in the last 3 months              |   |
| Q3              | Proportion of patients who are instructed that Eviplera must be taken with food/ with a meal / Edurant must be taken with a meal - for patients receiving the treatment for the first time | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q3              | Proportion of patients who are instructed that Eviplera must be taken with food/ with a meal / Edurant must be taken with a meal - during subsequent follow-up appointments                | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q3              | Proportion of patients who are instructed that Eviplera must be taken with food/ with a meal - for patients receiving the treatment for the first time                                     | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera in the last 3 months             | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q3              | Proportion of patients who are instructed that Edurant must be taken with a meal - for patients receiving the treatment for the first time   | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Edurant in the last 3 months              | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q3              | Proportion of patients who are instructed that Eviplera must be taken with food/ with a meal during subsequent follow-up appointments  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera in the last 3 months             | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |

| Question Number | Table Title   | Crossed with  | Base reference  | Notes   |
|-----------------|---|---|---|---|
| Q3              | Proportion of patients who are instructed that Edurant must be taken with food/ with a meal during subsequent follow-up appointments  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Edurant in the last 3 months   | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q3              | Proportion of patients who are instructed that Eviplera must be taken with food/ with a meal - for patients receiving the treatment for the first time                                  | S6 - Number of Eviplera prescriptions in last 3 months - grouped into low, medium, high depending on data   | All HCPs who have prescribed Eviplera in the last 3 months  | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q3              | Proportion of patients who are instructed that Edurant must be taken with a meal - for patients receiving the treatment for the first time  | S6 - Number of Edurant prescriptions in last 3 months - grouped into low, medium, high depending on data  | All HCPs who have prescribed Edurant in the last 3 months   | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q3              | Proportion of patients who are instructed that Eviplera must be taken with food/ with a meal during subsequent follow-up appointments   | S6 - Number of Eviplera prescriptions in last 3 months - grouped into low, medium, high depending on data   | All HCPs who have prescribed Eviplera in the last 3 months  | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q3              | Proportion of patients who are instructed that Edurant must be taken with food/ with a meal during subsequent follow-up appointments  | S6 - Number of Edurant prescriptions in last 3 months - grouped into low, medium, high depending on data  | All HCPs who have prescribed Edurant in the last 3 months   | Responses will be grouped into sensible bands eg, 0%, 1-10%, 11-20% etc and a mean score will also be shown |
| Q4a             | Reasons for not communicating the instructions that patients must take Eviplera with food/ with a meal / Edurant with a meal - for patients receiving this treatment for the first time | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months                                      | Verbatim responses will be coded into appropriate groupings   |
| Q4a             | Reasons for not communicating the instructions that patients must take Eviplera with food/ with a meal - for patients receiving this treatment for the first time                       | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who do not always communicate the food / meal instructions when giving Eviplera for the first time | Verbatim responses will be coded into appropriate groupings   |

| Question Number | Table Title  | Crossed with  | Base reference   | Notes   |
|-----------------|--|---|--|---|
| Q4a             | Reasons for not communicating the instructions that patients must take Edurant with a meal - for patients receiving this treatment for the first time                  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who do not always communicate the meal instructions when giving Edurant for the first time                    | Verbatim responses will be coded into appropriate groupings |
| Q4b             | Reasons for not communicating the instructions that patients must take Eviplera with food/ with a meal / Edurant with a meal - during subsequent follow-up appointment | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months   | Verbatim responses will be coded into appropriate groupings |
| Q4b             | Reasons for not communicating the instructions that patients must take Eviplera with food/ with a meal - during subsequent follow-up appointment                       | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who do not always communicate the food / meal instructions when giving Eviplera during follow-up appointments | Verbatim responses will be coded into appropriate groupings |
| Q4b             | Reasons for not communicating the instructions that patients must take Edurant with a meal - during subsequent follow-up appointment                                   | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who do not always communicate the meal instructions when giving Edurant during follow-up appointments         | Verbatim responses will be coded into appropriate groupings |
| Q5              | Importance of communicating the instructions for taking Eviplera with food/ with a meal / Edurant with a meal  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months   |   |
| Q5              | Importance of communicating the instructions for taking Eviplera with food/ with a meal  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera in the last 3 months   |   |
| Q5              | Importance of communicating the instructions for taking Edurant with a meal  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Edurant in the last 3 months  |   |

| Question Number | Table Title   | Crossed with  | Base reference   | Notes   |
|-----------------|---|---|--|---|
| Q5              | Importance of communicating the instructions for taking Eviplera with food/ with a meal                                 | Q3 - Bands will be created based on responses given eg, 0%, 1-10%, 11-20% etc   | All HCPs who have prescribed Eviplera in the last 3 months                                       |   |
| Q5              | Importance of communicating the instructions for taking Edurant with a meal   | Q3 - Bands will be created based on responses given eg, 0%, 1-10%, 11-20% etc   | All HCPs who have prescribed Edurant in the last 3 months  |   |
| Q6              | Reasons why communicating the instructions regarding Eviplera/Edurant is important                                      | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who believe giving the food / meal instructions with Eviplera/ Edurant is important     | Verbatim responses will be coded into appropriate groupings |
| Q6              | Reasons why communicating the instructions regarding Eviplera is important  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who believe giving the food / meal instructions with Eviplera is important              | Verbatim responses will be coded into appropriate groupings |
| Q6              | Reasons why communicating the instructions regarding Edurant is important   | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who believe giving the meal instructions with Edurant is important                      | Verbatim responses will be coded into appropriate groupings |
| Q6              | Reasons why communicating the instructions regarding Eviplera/Edurant is not important                                  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who believe giving the food / meal instructions with Eviplera/ Edurant is not important | Verbatim responses will be coded into appropriate groupings |
| Q6              | Reasons why communicating the instructions regarding Eviplera is not important  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who believe giving the food / meal instructions with Eviplera is not important          | Verbatim responses will be coded into appropriate groupings |
| Q6              | Reasons why communicating the instructions regarding Edurant is not important   | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who believe giving the meal instructions with Edurant is not important                  | Verbatim responses will be coded into appropriate groupings |
| Q7              | Way of explaining the instructions that Eviplera/Edurant must be taken with food/ with a meal (spontaneous, open ended) | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months                           | Verbatim responses will be coded into appropriate groupings |



| Question Number | Table Title   | Crossed with  | Base reference   | Notes   |
|-----------------|---|---|--|---|
| Q7              | Way of explaining the instructions that Eviplera must be taken with food/ with a meal (spontaneous, open ended)   | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera in the last 3 months             | Verbatim responses will be coded into appropriate groupings |
| Q7              | Way of explaining that Edurant must be taken with a meal (spontaneous, open ended)  | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Edurant in the last 3 months              | Verbatim responses will be coded into appropriate groupings |
| Q7              | Way of explaining the instructions that Eviplera must be taken with food/ with a meal (spontaneous, open ended)   | Q5 - 1-2 Not important, 3-5 Neutral, 6-7 Important  | All HCPs who have prescribed Eviplera in the last 3 months             |   |
| Q7              | Way of explaining that Edurant must be taken with a meal (spontaneous, open ended)  | Q5 - 1-2 Not important, 3-5 Neutral, 6-7 Important  | All HCPs who have prescribed Edurant in the last 3 months              |   |
| Q8              | Way of communicating the instructions to the patients that Eviplera must be taken with food/ with a meal / Edurant with a meal (pre-coded, closed question) | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months |   |
| Q8              | Way of communicating the instructions to the patients that Eviplera must be taken with food/ with a meal (pre-coded, closed question)                       | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera in the last 3 months             |   |
| Q8              | Way of communicating the instructions to the patients that Edurant must be taken with a meal (pre-coded, closed question)                                   | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Edurant in the last 3 months              |   |
| Q8              | Way of communicating the instructions to the patients that Eviplera must be taken with food/ with a meal (pre-coded, closed question)                       | Q5 - 1-2 Not important, 3-5 Neutral, 6-7 Important  | All HCPs who have prescribed Eviplera in the last 3 months             |   |
| Q8              | Way of communicating the instructions to the patients that Edurant must be taken with a meal (pre-coded, closed question)                                   | Q5 - 1-2 Not important, 3-5 Neutral, 6-7 Important  | All HCPs who have prescribed Edurant in the last 3 months              |   |

| Question Number | Table Title  | Crossed with  | Base reference  | Notes |
|-----------------|--|---|---|-------|
| Q9              | Additional information sheets/ patients handouts for Eviplera/Edurant provided to their patients | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera and Edurant in the last 3 months and provide additional information sheets / patient handouts |       |
| Q9              | Additional information sheets/ patients handouts for Eviplera provided to their patients         | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Eviplera in the last 3 months and provide additional information sheets / patient handouts             |       |
| Q9              | Additional information sheets/ patients handouts for Edurant provided to their patients          | S2 - Current role / job title (Specialists grouped together and shown individually, GPs / PCPs, Nurses and Pharmacists) / S1 - Country groupings (eg, Germany + Austria, Sweden + Norway + Denmark etc) | All HCPs who have prescribed Edurant in the last 3 months and provide additional information sheets / patient handouts              |       |

**SIGNATURE OF SPONSOR'S RESPONSIBLE MEDICAL OFFICER**

STUDY TITLE: EDURANT/EVIPLERA Health Care Professional Survey

REPORT CONTRIBUTORS: Dominique Devogel, MSc, Carla Truysers, PhD, Marita Stevens, MD

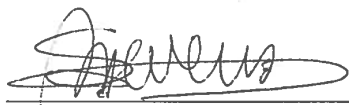
**SPONSOR'S RESPONSIBLE MEDICAL OFFICER**

NAME: Marita Stevens

TITLE: MD

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

SIGNATURE:



DATE:

16 Oct 2014