PASS Information

Title	**Drug Utilization Study on the Prescribing Indications for CPA/EE[1] in 5 European Countries**
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Date of last version of the final study report	23th May 2016
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Medicinal product	Diane-35 and its generics: coated tablets 0.035 mg ethinylestradiol, 2.0 mg cyproterone acetate (CPA/EE)
Product reference	n/a
Procedure number	EMEA/H/A-107i/1357
Marketing authorization holder(s)	Bayer HealthCare Pharmaceuticals Müllerstraße 178 13353 Berlin Germany On behalf of a group of MAHs
Joint PASS	Yes
Research question and objectives	This drug utilization study is designed to compile the reasons and specific indications for the prescription of CPA/EE. The primary objective of the study is to characterize the prescribing behaviors for CPA/EE in 5 European countries including: • prescription indications for CPA/EE • use of CPA/EE in accordance with the updated label • concomitant use of CPA/EE and CHCs • second-line treatment with CPA/EE for the indication acne
Country(-ies) of study	Austria, Czech Republic, France, The Netherlands, and Spain
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[1] Cyproterone acetate and ethinylestradiol

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1. Abstract

Title

Drug Utilization Study on the Prescribing Indications for CPA/EE[2] in 5 European Countries

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Rationale and background

Cyproterone acetate (CPA) 2mg, in combination with ethinylestradiol (EE) 35mcg (CPA/EE), is a medicinal product currently indicated for the treatment of moderate to severe acne and/or hirsutism in women of reproductive age. For the treatment of acne, CPA/EE should only be used when alternative treatments, such as topical therapy and systemic antibiotic treatment, have failed. Due to the mode of action, the dosing and the regimen, the preparation also acts as effective contraceptive.

In 2012 the French health authority conducted a national review of CPA/EE and highlighted a rare but serious risk of thromboembolic events and off-label use of these medicines as a contraceptive only. This triggered an Urgent Union Procedure at the beginning of 2013. The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) concluded that the benefits of CPA/EE combinations (cyproterone acetate 2mg / ethinylestradiol 35mcg) outweigh the risks, providing that several measures are taken to minimize the risk of thromboembolism. These medicines should be used solely for the treatment of moderate to severe acne related to androgen sensitivity and/or hirsutism in women of reproductive age. Since CPA/EE also acts as a hormonal contraceptive, women should not take these medicines in combination with other hormonal contraceptives. As one of the risk minimization measures, the Marketing Authorization Holders (MAHs) were required to conduct a number of studies including the drug utilization survey described in this final study report.

Research question and objectives

This drug utilization study was designed to compile the reasons and specific indications for the prescription of CPA/EE. The study used a cross-sectional design with a special focus on the clinical decision-making process. The primary objective of the study was to characterize the prescribing

[2] Cyproterone acetate and ethinylestradiol

behaviors for CPA/EE in 5 European countries (Austria, Czech Republic, France, The Netherlands and Spain), including:

- prescription indications for CPA/EE
- use of CPA/EE in accordance with the updated label
- concomitant use of CPA/EE and other combined hormonal contraceptives (CHCs)
- second-line treatment of CPA/EE for the indication acne

Study design

This was a multi-national, cross-sectional study. Physicians from the specialties gynecology and dermatology, as well as general practitioners (GPs) were recruited. Each patient who received a CPA/EE prescription during the study period was asked if she was willing to participate. The physicians were requested to provide information on the prescribed CPA/EE drug, the history of CPA/EE prescription for the individual patient, use of concomitant hormonal contraceptives, the patient's androgen-dependent condition(s) characteristics and treatments (including over-the-counter [OTC] medicines), and the reasons for prescribing CPA/EE.

Setting

Physicians were recruited from networks of gynecologists, dermatologists and general practitioners (GPs) in 5 European countries (Austria, Czech Republic, France, The Netherlands and Spain). Because of the very low rate of Dutch physicians willing to participate, additional contact was made in The Netherlands to physicians outside the existing network.

Subjects and Study size

All women that received a prescription of CPA/EE and consented to participate were eligible for this drug utilization study.

The study planned to recruit 1,000 patients per country from a network of 250 physicians (50 per country). Physicians would be a representative sample of those prescribing CPA/EE (i.e. a mix of gynecologists, dermatologists, and GPs). However, the number of physicians willing to participate in the study and the total number of patients receiving CPA/EE was found to be markedly lower than expected, despite various efforts to improve accrual and by prolonging the period of recruitment.

A total of 1,513 patients were recruited by 120 physicians.

Variables and data sources

Recruiting physicians completed a baseline physician questionnaire providing information on the prescriber, including age, gender, specialty, and years of experience. In addition, a baseline questionnaire was completed for each new patient receiving a CPA/EE prescription. Baseline questionnaires were filled in by recruiting physicians and provided details on the following items:

- the brand name and the date of the prescribed CPA/EE-containing drug
- first use, re-use after a break, or continuous use of CPA/EE
- information about androgen-dependent condition(s) (duration, previous and concomitant treatment including OTC medicines and information on treatment failure)
- reasons for prescribing CPA/EE
- concomitant hormonal contraceptive use

For reasons of data protection, date-of-birth was obtained from the patient's informed consent form.

Data capture was completed using paper questionnaires.

Results

A total of 314 physicians agreed to participate in the study, of which 120 physicians recruited at least one patient. The mean age of the participating physicians was 52.2 years, that of the non-participating physicians 53.1 years. The gender distribution was 57.6% male for participating physicians, vs. 44.9% for the non-participating physicians. The specialties were represented as follows: For those participating, 63.1% gynecologists, 20.1% GPs, 16.9% dermatologists. For the non-participating physicians 36.6% GPs, 31.9% dermatologists, 31.5% gynecologists. In both groups (participating and non-participating) the majority of physicians had 15 or more years of professional experience. Surprisingly, the willingness of physicians to take part in this study was generally very low, particularly in The Netherlands. In France the three-tiered approval process took eight months and was only completed as late as 24th November 2015. As the frequency of prescriptions was lower than anticipated, additional physicians were contacted in all participating countries. Furthermore, the recruitment period was extended in Austria, Czech Republic, The Netherlands and Spain, and continued up until study end in April 2016 instead of the planned date October 2015. Timelines associated with the agreed final report date prevented further recruitment in any of the countries. Due to the late start in France, the French arm of the study is ongoing. However, data that have been obtained in France until the 8th April 2016 were integrated into this report.

Overall, the intended number of patients (1,000 patients/county) was not achieved in any of the participating countries. 1,513 patients were recruited at study end.

The most frequent indication was acne with 65.6% of the prescriptions (n = 993) followed by. Contraception was mentioned as a reason in 66.7% of all participating patients however the percentage of prescriptions stating contraception only as reason was 16.3%. 2.9% (n = 44) of the enrolled patient used an additional HC.

The physicians were able to select multiple reasons for the prescription of CPA/EE. The main reasons for prescription of CPA/EE were contraception (66.7%, n = 1,009) and acne (65.6%, n = 993). The severity distribution of the patients with acne was 36.7% with mild acne, 54.7% with moderate and 8.7% with severe acne. Other androgen-dependent conditions included seborrhea (12.9%), hirsutism (12.6%), PCOS (11.4%) and androgenetic alopecia (5.0%). Overall, 83.3% (n = 1,261) of all prescriptions for androgen-dependent conditions. 16.3% of the prescriptions were made due to contraception only, predominantly by GPs and gynecologists.

Prescriptions in 522 patients (34.5% of the total study population) reflect an approximation to accordance with the updated label of CPA/EE in the study population of 1513 patients: 301 (19.9%) patients with a diagnosis of moderate to severe acne who had “previous topical and/or systemic antibiotic treatment” and those with hirsutism (14.6%, n = 221). Regarding the previous treatment in the category “moderate to severe acne without hirsutism” (37.3%, n = 564) with topical agents and/or systemic antibiotics (19.9%, n = 301), there seems to be a difference between dermatologists (73.5%) and GPs (77.7%) on the one side, whose patients seem to have been prescribed these modalities more often, and gynecologists (40.1%), whose patients tend to have been prescribed hormonal therapy in the form of CPA/EE more often without such preceding therapy.

The prescription of CPA/EE together with another hormonal contraceptive was 2.9% (n = 44). Of those 42 were oral contraceptives and 2 non-oral contraceptives. 35 of the additional HCs were stated by gynecologists.

Of 1,028 patients diagnosed with acne, 586 (57.0%) received previous treatment. In 428 (41.6%) the treatment was reported to have failed. 564 (54.9%) patients in the category “moderate to severe acne without hirsutism”. Of these, 301 (29.3%) received previous topical treatment and/or systemic antibiotics, which had failed in 249 (24.2%) cases.

Discussion

Most prescriptions of CPA/EE were indicated for the treatment of androgen-dependent conditions. Prominent among these conditions was acne, which was mentioned in two thirds of all prescriptions. When acne, seborrhea, hirsutism, polycystic ovaries and androgenetic alopecia are included, alone or in combination, 83.1 % of prescriptions were related to androgenic pathology. Prescriptions exclusively for indications not related to an androgen-dependent conditions (contraception only)

constitute 16.3% or approximately one sixth of all prescription events. The severity of acne is described as moderate to severe in almost two thirds (63.1%) of the prescriptions. The documentation of preceding treatments with other topical agents or systemic therapeutics is likely to be incomplete because of the more intense work needed to fill out the details, including preparations and dates of treatment. Additionally, patient initiated skin-care with OTC and cosmeceuticals is probably subject to recall bias. Therefore, this information may represent the prescribing behavior to a lesser extent than the documentation of acne itself. The prescription of CPA/EE together with another hormonal contraceptive is less than 3%. The study indicates a strong relationship between the prescription of CPA/EE and disorders with a pathophysiology associated with an androgen excess. For the 16.3% of cases where CPA/EE is prescribed as a contraceptive without documentation of any such disorder, the motives for the choice of this particular combination cannot be clarified by this study.

2. List of abbreviations

Abbreviation	*Definition*
ADB	Administrative Database
ADR	Adverse Drug Reaction
ANSM	Agence nationale de sécurité du médicament et des produits de santé
ATC	Anatomical Therapeutic Chemical Classification System
CCTIRS	Comité consultative sur le traitement de l'information en matière de recherche dans le domaine de la santé
CHC	Combined Hormonal Contraceptive
CMDh	Coordination Group for Mutual Recognition and Decentralized Procedures – Human
CNIL	Commission nationale de l'information et des libertés
CNOM	Conseil national de l'Ordre des médicins
CPA	Cyproterone Acetate
DUS	Drug Utilization Study
EE	Ethinylestradiol
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
FIGO	International Federation of Gynecology and Obstetrics
GEP	Good Epidemiological Practices
GP	General Practitioner
GPP	Good Pharmacoepidemiology Practices
GVP	Good Pharmacovigilance Practice
GXP	Good Practice Guidelines
ICMJE	International Committee on Medical Journal Editors
ISPE	International Society for Pharmacoepidemiology
MAH	Marketing Authorization Holder
OTC	Over-the-counter
PCOS	Polycystic Ovary Syndrome
PRAC	Pharmacovigilance Risk Assessment Committee
SAE	Serious Adverse Event
SDB	Study Database
SOP	Standard Operating Procedure

ZEG	Berlin Center for Epidemiology & Health Research (acronym for the German term 'Zentrum für Epidemiologie & Gesundheitsforschung Berlin')

3. Investigator

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5. Milestones

Task	Planned date	Actual date
Study protocol submission	June 2014	June 2014
Registration in the EU PAS register		January 2015
Start of physician recruitment (Austria)	February 2015	March 2015
First patient (Austria)	February 2015	March 2015
Start of physician recruitment (Czech Republic)	February 2015	March 2015
First patient (Czech Republic)	February 2015	April 2015
Start of physician recruitment (The Netherlands)	February 2015	March 2015
First patient (The Netherlands)	February 2015	April 2015
Start of physician recruitment (Spain)	February 2015	May 2015
First patient (Spain)	February 2015	May 2015
Start of physician recruitment (France)	February 2015	December 2015
First patient (France)	February 2015	January 2016
End of data collection (excluding France)	October 2015	April 2016
Final report of study results	May 2016	May 2016

6. Rationale and background

Cyproterone acetate (CPA) 2mg, in combination with ethinylestradiol (EE) 35mcg (CPA/EE), is a medicinal product currently indicated for the treatment of moderate to severe acne and/or hirsutism in women of reproductive age. In the context of this study, androgen-dependent conditions such as acne (1) , hirsutism (2), seborrhea (3) androgenetic alopecia and Polycystic Ovary Syndrome (PCOS), have been considered potential therapeutic targets for CPA/EE. Due to the mode of action and the dose and regimen, this preparation also acts as effective contraceptives (4). Market authorization was first granted in 1985.

A review of CPA/EE was triggered by the French medicines agency, the National Agency for the Safety of Medicine and Health Products (ANSM), which on the basis of a national review in France had decided in January 2013 to suspend use of CPA/EE within three months. The review highlighted a rare but serious risk of thromboembolic events and off-label use of these medicines as a contraceptive only (5). The Coordination Group for Mutual Recognition and Decentralized Procedures – Human (CMDh) endorsed the recommendation by the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC), which concluded that the benefits of CPA/EE (cyproterone acetate 2mg / ethinylestradiol 35mcg) outweigh the risks, provided that several measures are taken to minimize the risk of thromboembolism (6). These medicines should be used solely for the treatment of moderate to severe acne related to androgen sensitivity and/or hirsutism in women of reproductive age. Furthermore, CPA/EE should only be used for the treatment of acne when alternative treatments, such as topical therapy and antibiotics, have failed.

Since CPA/EE also acts as a hormonal contraceptive, women should not take this medicine in combination with another hormonal contraceptive. Concomitant use of CPA/EE with another hormonal contraceptive would expose women to a higher hormonal dose and therefore potentially increase the risk of thromboembolism.

During the referral procedure, the risk of thromboembolism with CPA/EE use was assessed as low and well known. However, to minimize this risk, the respective MAHs were required to take further measures in addition to updating the product information (e.g. educational materials for prescribers and patients). The MAHs were also required to conduct three studies including the drug utilization study (DUS) that is described in this final study report. Following discussions with the authorities, Bayer agreed to take the lead in a joint approach to conducting the required studies.

7. Research question and objectives

This drug utilization study was designed to compile the reasons and specific indications for the prescription of CPA/EE. The study used a cross-sectional design with a special focus on the clinical decision-making process in order to assess prescribing practices for CPA/EE during typical clinical conditions for representative groups of prescribers. Questionnaires are an established tool for data collection on drug utilization and are widely used for this purpose. They are able to capture information on over-the-counter (OTC) medicines as well as on prescription medicines, which is of importance to this study.

The primary objective of the study was to characterize the prescribing behaviors for CPA/EE in 5 European countries (Austria, Czech Republic, France, The Netherlands and Spain), including:

- prescription indications for CPA/EE
- use of CPA/EE in accordance with the updated label
- concomitant use of CPA/EE and other combined hormonal contraceptives (CHCs)
- second-line treatment of CPA/EE for the indication acne

8. Amendments, updates and procedural changes

In view of the unexpectedly low rate of prescriptions, the number of physicians contacted/recruited was increased in all participating countries. Furthermore, the period of recruitment was prolonged as far as possible in order to increase the yield.

As the approval of CNIL was given on 24th November 2015, there was very limited time between the start of recruitment and the previously agreed study end date in France. It was decided to continue patient recruitment in France in order to compensate for the delayed start. All data collected up to 8th April 2016 was included in this report. Therefore, recruitment is currently continuing in France in order to increase numbers for France. These data will be reported separately in an amended study report.

A procedural variant was used in The Netherlands due to difficulties encountered in recruiting prescribing physicians via telephone. Whereas telephone contact to physicians could be achieved in all other countries, email contact was employed in The Netherlands, as well an additional invitation through postal mail.

As recruitment numbers – both for participating physicians and patients - in The Netherlands remained very low, specific measures to address these problems were initiated:

- A letter with an open invitation to 496 GPs sent by post (4 interested, none participated)
- A direct visit by a qualified recruiter to approximately 60 dermatologists (3 interested, 1 participated)
- An online-survey addressing 303 gynecologists (41 responded, 2 interested, none participated)
- An online-survey to find out more about the CPA/EE prescription behavior as well as asking for participation in the study (see Annex)

9. Research methods

9.1 Study design

The DUS CPA/EE was a multi-national, cross-sectional study that characterizes the reasons for prescribing CPA/EE in 5 European countries: Austria, Czech Republic, France, The Netherlands and Spain. Information was collected via paper questionnaires that the physicians filled out.

For this purpose, the physicians asked each patient who received a CPA/EE prescription during the study period if she was willing to participate in the study. The physicians explained the nature of the study, its purpose, and the extent of data collection prior to her study entry. Each potential participating patient had ample opportunity to ask questions and was informed about her right to withdraw from the study at any time without disadvantage and without having to provide reasons for her decision. This information was provided in an informed consent and data privacy form, which had to be signed by the patient and sent back to the field organization. The study documents were approved by the relevant local ethics committees and data privacy office, where applicable.

The physicians were asked to provide information on the prescribed CPA/EE drug, use of concomitant hormonal contraceptives, the patient's androgen-sensitive disease characteristics and treatments (including OTC medicines), and the reasons for prescribing CPA/EE. Data was collected in paper form and forwarded to local field institutes, where it was entered into a database. From the perspective of the individual patients, this was a one-time survey with no follow-up.

9.2 Setting

The study was performed by the Berlin Center for Epidemiology and Health Research (ZEG) in 5 European countries (Austria, Czech Republic, France, The Netherlands and Spain). Each country was expected to recruit 1,000 patients over a 5-month period. The countries selected show a high level of diversity with regard to their size (both small and large) and their geographical distribution within

Europe. Selection also took into account the fact that an accompanying database study will be performed on CPA/EE prescription data, and therefore this study also included countries where no information from such databases was available.

The participating HCPs in Austria, Czech Republic, France, The Netherlands and Spain were recruited from existing networks of contraceptive-prescribing health care professionals (gynecologists, dermatologists and GPs) who had participated in similar cohort studies in the past. Because of the very low rate of participation in The Netherlands, recruitment of physicians outside the existing network was initiated as well. The planned distribution of contacted physicians by specialty was based on the estimated CPA/EE prescribing patterns in each country:

- Austria: 75% gynecologists, 25% dermatologists
- Czech Republic: 75% gynecologists, 25% dermatologists
- France: 40% gynecologists, 40% GPs, 20% dermatologists
- The Netherlands: 75% GPs, 25% dermatologists
- Spain: 50% GPs, 25% gynecologists, 25% dermatologists

Physicians from the above-mentioned specialties were contacted by local field organizations in the respective countries. The primary method of contacting the HCPs was via telephone in Austria, Czech Republic, France and Spain.

Due to previously experienced difficulties with telephone contact to Dutch physicians, email contact was selected as the primary contact approach in The Netherlands.

During the first call, the study background was explained, and the interviewer verified that the physician prescribed CPA/EE. Following confirmation, a short physician interview questionnaire was administered. This questionnaire included questions on:

- Age
- Gender
- Specialty of the physician
- Level of experience (defined as number of years work experience).

The above-mentioned background characteristics were requested from both participating and non-participating physicians in order to determine whether the two groups differed in any way. This

information was not available for the majority of Dutch physicians, because of the differing contact approach, i.e. via email.

In The Netherlands initial contact and recruitment of the physicians was via email. The first email included a short and general description of the study as well as an inquiry as to whether the physician was interested in participating. To those physicians who showed interest in general, more detailed information was provided, including all information and study requirements that were provided via telephone to physicians recruited from other countries. The follow-up email also asked physicians for their age, level of experience and an estimated number of prescriptions of CPA/EE per month. If the physicians subsequently agreed to participate in the study, they were provided with the same documents as the physicians in the other countries.

In all 5 countries, physicians interested in study participation were provided the following documents:

- Drug utilization questionnaire
- Physician information
- Informed consent
- Patient information
- Information on data protection
- Help sheet for the physician

A signed *physician information* form needed to be sent back to the field organization prior to the start of recruitment.

All patients who received a CPA/EE prescription from a participating physician were invited to participate in the study. There were no specific inclusion or exclusion criteria. However, only after the decision to prescribe CPA/EE was made, could the physicians ask the patient about study participation. This sequence was important to ensure the non-interventional character of the study was maintained. The physicians explained the nature of the study, its purpose and associated procedures before study entry. Each patient was given ample opportunity to ask questions about the study and the associated use of her medical and personal data. She was informed about her right to withdraw from the study at any time without disadvantage and without having to provide reasons for her decision. If potential participating patients needed time to consider whether to participate,

they could leave the physician's office with their prescriptions and take an appropriate period to make their decision.

Personal information about the patient was needed to perform source data verification audits at the physician's office to compare documented study data with medical record data (see Section 9.11). This information was provided on the data privacy and informed consent form, which had to be signed by all patients, and sent back to the field organization (in Spain the informed consent stayed in the physician's office as this is a local ethics committee requirement).

The informed consent form included permission for study data to be collected and analyzed and for source data to be verified at the physician's office. Confidentiality was maintained throughout the study and no personal information was shared with any party outside the study team. The funder did not have access to names or addresses of the recruited patients and all individual subject data remained anonymous. Personal and medical information were recorded in separate documents. ZEG ensured that access to personal information was restricted in accordance with data privacy rules.

The study had no age restriction, however as adolescents are a specifically protected group, local laws were applied regarding requirements for parent's or guardian's signature, which was then also provided on the informed consent form. If requested by local law or ethical committees, a patient information and informed consent form that was easy to understand and adapted for adolescents was provided. All documents were approved by the relevant local ethics committees and data privacy office, if applicable.

9.3 Participants

Patients eligible for the study were all women who:

- received a prescription for a medication containing the combination of cyproterone acetate and ethinylestradiol during the study period and;
- agreed to participate in the study.

The physician discussed the study and asked the patient for participation only after the decision on treatment had been made.

There were no further criteria for eligibility in this drug utilization study.

9.4 Variables

During the first call, all contacted physicians were asked, in a short interview questionnaire, for the following data about themselves:

- Age
- Gender
- Specialty of the physician
- Level of experience (defined as number of years work experience).

(This information was obtained via email from the physicians in The Netherlands.)

Each participating physician was provided with prescription questionnaires for collecting drug utilization data on CPA/EE. Information about the patient and the prescription were taken from the prescription questionnaire (and from the informed consent form for the date of birth).

The prescription questionnaires included the following:

- name and date of the prescribed CPA/EE-containing drug
- first use, re-use after a break, or continuous use of CPA/EE
- information about androgen-sensitive diseases (duration, previous and concomitant treatment including OTC medicines and information on treatment failure)
- reasons for prescribing CPA/EE
- concomitant hormonal contraceptive use

9.5 Data sources

Data on the physicians, including age, gender, specialty and level of experience, were obtained and recorded in a short interview by the field organization during the first phone call (via email in The Netherlands). The questionnaires on prescribing behavior were filled out by participating physicians based on the patient's statements and medical records. Questionnaires documented use of hormonal contraceptives, reason for the prescription, concomitant use of another hormonal contraceptives, and status of androgen-sensitive diseases. The 'date of birth' information was taken from the informed consent form.

In line with data privacy regulations, personal data was documented on a separate sheet. During the study conduct and evaluation, these sheets and the electronic representations of their content were stored separately from the study questionnaires and their respective electronic representation. This also applied to the archiving of documents and databases at study end.

Questionnaires were collected by the local ZEG field organization in each participating country, and were reviewed for completeness and plausibility/consistency of the responses. Missing and

inconsistent information was clarified directly with the physicians. The completed questionnaires were then forwarded to ZEG. At ZEG all incoming data were subject to comprehensive quality control including electronic and manual plausibility checks. Unclear or inconsistent information was described in detailed queries which were forwarded to the local field organizations, who clarified these with the physicians. ZEG monitored and endorsed the timely processing of these queries.

9.6 Bias

Potential biases inherent in the study design are discussed in detail in Section 11.

9.7 Study size

Initial sample size calculations were based on an estimate that at least 50 participating physicians in Austria, Czech Republic, France, the Netherlands and Spain would write at least four CPA/EE prescriptions per month. This would result in a total of 1,000 prescriptions per country during the estimated 5 months of data collection (total sample size of 5,000 patients). The effective sample size was calculated as ESS = (m*k) / (1+p*(m-1)), where m = number of subjects in a cluster, k = number of clusters, mk = total number of subjects and ρ = intra-cluster correlation coefficient. With given assumptions the effective sample size would have been reduced to ESS≈730.

Table 1 shows the 95% confidence intervals for four different scenarios of contraceptive off-label use based on 1,000 CPA/EE users at a country level and an intra-cluster coefficient of 0.02 to adjust for potential cluster effects on the physician level. The level of ICC was derived from Adams et al., 2004 (7) and Murray et al., 2003 (8) who estimated patterns of intra-cluster coefficients based on different studies.

Table 1 - Expected precision of the point estimates for off-label use per country

	1%	5%	10%	20%
CPA/EE	0.4 – 2.0	3.5 – 6.8	8.0 – 12.5	17.2 – 23.1

The confidence limits were estimated using a conservative exact method proposed by Clopper and Pearson (Clopper & Pearson, 1934 (9); Agresti & Coull, 1983 (10). Calculations based on the effective sample size are corrected for variance inflation due to clustering. These results show that information on 1,000 representative prescriptions would be sufficient to estimate the extent of off-label use in each participating country with high precision.

9.8 Quantitative variables

Continuous variables were summarized using descriptive statistics (number of patients with an observation [N], mean, standard deviation [SD], median, 25th [Q1] and 75th [Q3] percentiles, minimum [Min] and maximum [Max]). Unless otherwise specified, the mean and median for a continuous variable was listed to 1 more decimal place than the original (raw) values and the SD was listed to 2 more decimal places than the original values. The minimum and maximum were listed to the same number of decimal places as the original values.

There were 3 different categories of quantitative variables:

Age of physicians

The age of physicians was obtained as an integral number in the physician initial interview questionnaire, which was administered in the physician recruitment process. It was then categorized in 5 age groups: <30 years, 30-39 years, 40-49 years, 50-59 years, >=60 years.

Age of patients

The age of patients was calculated as the time difference between the date of the current CPA/EE prescription given on the DUS CPA/EE questionnaire and the date given by the patient on the signed informed consent form. The patients age were categorized in 5 age groups: <18 years, 18-24 years, 25-34 years, 35 – 49 years, >=50 years.

Duration of treatment

The duration of treatment was calculated as the time difference between the date of the current CPA/EE prescription given on the DUS CPA/EE questionnaire and the documented date of first diagnosis given by the physician on the DUS CPA/EE questionnaire. It was categorized in the following 4 groups: <1 month, 1 - <6 months, 6 - <12 months, >=12 months.

9.9 Statistical methods

The purpose of the study was to assess utilization patterns for CPA/EE. Reasons for prescribing CPA/EE have been investigated with respect to concomitant hormonal contraceptive use and androgen-sensitive diseases, as well as second-line treatment of acne and co-medication to CPA/EE directed at acne. Data analysis was stratified by country and by physician specialization. Analysis of this cross-sectional study was limited to descriptive data. Categorical and continuous variables are summarized using frequencies/percentages and summary statistics (mean, standard deviation, median, minimum and maximum), respectively. No formal hypothesis testing has been performed. For the primary outcome proportions and exact confidence intervals are provided, which are

calculated in accordance with Clopper and Pearson, 1934 (9). Variance inflation due to intra-cluster (physician level) correlation was considered in terms of effective sample size by the modified Clopper-Pearson confidence limits described by Korn and Graubard, 1998 (11). Statistical evaluation was performed with the software package SAS®, release version 9.4, 2013 (12).

9.10 Data management

9.10.1 Databases

Two different databases were used for data collection: the administrative database (ADB) and the study database (SDB).

The ADB was provided by ZEG to national field organizations. Physician details including the data from the HCP interview, as well as contact details of patients, were entered and maintained in this database.

The SDB was validated according to GXP rules and contained the questionnaire data on prescription behavior. ZEG performed cross-checks and verification checks on the data and any inconsistencies or answers outside the anticipated framework were sent to the field organizations for further clarification.

Coding was performed in study specific categories predefined by ZEG.

9.10.2 Dataflow

Signed informed consent forms and corresponding study questionnaires were sent to national field organizations by participating physicians. Documents were cross-checked for legibility, completeness and plausibility and date-stamped. Where possible, relevant missing and/or inconsistent data were corrected by trained field organization staff prior to entry into the study database. If needed, questions were clarified with the prescribing physician. All corrections were completed in a manner that facilitated the clear and transparent documentation of data flow. All original entries remained legible. Any changes were initialed by the person correcting the data with accompanying date stamp.

Data was entered via formatted entry screens designed to reflect the appearance of the questionnaire. All corrections were dated and initialed by the data manager who received the information (e.g., via direct contact or a copy of medical reports/documents). Incorrect entries were crossed out but remained legible, with correct entries placed beside them. Reasons for any correction of medical data on the questionnaires had to be documented.

Quality control of entered data was supported by SAS plausibility programs which included range, coding, missing and date checks as well as cross-reference (consistency) checks between variables.

9.10.3 Database freeze/lock

For the (final) analysis the database was frozen at 11th May 2016. The database was 'cleaned' within 4 weeks of the database freeze. After freezing, no additional incoming data was entered in the database – this database represents the final data source for the analyses. Safety copies were made of the database.

9.10.4 Missing and inconsistent data

Missing data are a common occurrence and can have a significant effect, e.g. in studies where exposure-outcome relations are measured. In this study, missing and inconsistent data for specific questions, e.g. missing prescription date, missing questionnaire completion date etc., triggered contact with the physician to collect the information. If the data was still missing at the time of analysis, they were excluded from the analysis of those specific variables and listed in the tables under the category "missing".

Incoming questionnaires were checked for plausibility. Any relevant inconsistent data led to either logical corrections (where applicable and possible) or to contact with the physician for clarification. Any corrections on the questionnaires were made with indelible pens, and all original entries from the physicians remained legible. The initials of the person correcting the data and the date were added to each change of the data.

9.11 Quality control

ZEG established quality assurance procedures for all day-to-day work for both ZEG Berlin staff and national field organizations. Internal audits confirm that ZEG fully complies with GPP (Guidelines for Good Pharmacoepidemiology Practices issued by the International Society for Pharmacoepidemiology in 2007), GEP (Good Epidemiological Practice issued by the European Epidemiology Federation in 2007), GVP (Good Pharmacovigilance Practices issued by the European Medicines Agency (EMA) in 2012/2013), the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance's (ENCePP) Code of Conduct, the Nuremberg Code and the Declaration of Helsinki. Additionally, ZEG has been audited three times by large pharmaceutical companies, with no major issues identified. For this study, site audits at the local field organizations were conducted by ZEG. This included both standard operating procedures and source data verification.

ZEG's internal manual of standard operating procedures (SOPs) specifies standardized procedures to ensure high quality and compliance with all applicable guidelines. The SOPs are reviewed on an

annual basis and updated where necessary to ensure that all processes are in line with legal compliance and data integrity.

ZEG ensured that the study was conducted in compliance with the protocol and any applicable regulatory requirements. All processes that were relevant to legal compliance or data integrity were subject to quality control measures. These included: 1) development of the study protocol, questionnaire, databases and data entry screens; 2) data entry; 3) plausibility checks; 4) data analysis; 5) report writing; 6) publication of results; and 7) archiving of study materials (i.e. questionnaires, other study documents and electronic files). All quality control measures were based on the four-eye principle (i.e., the same person may not do quality control on his/her own work).

Source data verification was conducted for a subset of the recruited patients (10% of participating physicians per country with 100% of their recruited patients). The purpose was to review the documented data for completeness and plausibility, adherence to the study protocol, and verification with source documents. The verification was performed by professional monitors who had access to the relevant medical records on site. Overall, the quality of the data reflected in the questionnaires and compared to the source material was good, with minor findings (e.g., date of signature missing; birth date incorrect, but verified later; family name in wrong field in the informed consent). In addition, one case in Austria was entered twice, leading to the exclusion of the duplicate. One Spanish physician could not present the informed consent for any of the twenty enrolled patients. She claimed to have destroyed these forms after receiving payment, because she thought that the documents would not be of any further relevance. All these patients were excluded from the analysis.

9.12 Adverse events

There were no self-reported or physician reported adverse events.

9.13 Other aspects

None.

10. Results

This study was conducted in five European countries (Austria, the Czech Republic, France, The Netherlands and Spain). During the course of the study it became apparent that the envisaged targets for recruitment could not be reached within the given time frame. Despite numerous efforts to solve these problems, the achieved accrual of information on prescriptions remained below target

and varied considerably between the participating countries. Therefore, the total recruitment period was extended as far as possible. In Austria, the Czech Republic, The Netherlands, France and Spain the closing date for inclusion of the last patient in this analysis was moved from the end of October to the 8th April 2016, and the physicians had time to submit the last questionnaires until 14th April 2016.

In summary, a total of 1,574 patients were recruited by 120 physicians. A total of 61 (3.9%) of the recruited patients were found to be ineligible and excluded from enrollment. The main reasons for ineligibility were prescriptions that did not include a combination of CPA and EE (n = 20) and missing informed consent forms (n = 22). The remaining 1,513 quality-controlled computerized data sets were analyzed.

10.1 Physician recruitment

A total of 2,630 physicians were contacted of whom 11.9% (n = 314) agreed to participate and 4.6% (n = 120) recruited at least one patient.

The recruitment rate of physicians varied markedly between countries, but all countries showed lower than expected numbers. The proportion of contacted physicians that recruited at least one patient was similar in Austria (3.1%), the Czech Republic (4.6%), and France (2.9%); Spain had a much higher rate of active physicians (36.7%), whilst the active participation of physicians in The Netherlands was the lowest (0.9%).

The two main reasons for non-participation were no CPA/EE prescriptions (19.1%; n = 503) and a too low number of prescriptions (19.1%; n = 502).

The above data are summarized in Table A1 (see Annex)

10.1.1 Physician recruitment per country

Austria:

The distribution of physician specialties in Austria was originally planned to be 75% gynecologists and 25% dermatologists. Due to slow recruitment, more physicians than expected were contacted and the final distribution of specialties of contacted deviated from initial estimates. In sum, 718 physicians were contacted in Austria, 495 gynecologists and 223 dermatologists. Of these, 115 gynecologists and 4 dermatologists agreed to participate in the study. None of these 4 dermatologists, and only 22 of the gynecologists recruited at least one patient.

The main reasons for non-participation were the low number of prescriptions (n = 243), no prescriptions of CPA/EE-containing drugs at all (n = 92), no interest in the study (n = 119) and lack of time/too time-consuming (n = 68). Furthermore, 16 physicians had retired, 3 gave no reason and 58 had other reasons, not specified.

Czech Republic:

The distribution of physician specialties in the Czech Republic was planned to be 75% gynecologists, 25% dermatologists. Due to slow recruitment, more physicians than expected were contacted and the final distribution of specialties of contacted physicians deviated from initial estimates. In sum, 695 physicians were contacted in the Czech Republic, 276 gynecologists and 419 dermatologists. Of these, 33 gynecologists and 11 dermatologists agreed to participate in the study. 26 gynecologists and 6 dermatologists finally contributed at least one prescription.

The main reasons for non-participation of physicians were: no prescriptions of CPA/EE-containing drugs at all (n = 346), low number of prescriptions (n = 179), due to low incentives (n = 81) and no interest in the study (n = 30).

France:

The distribution of physician specialties in France was planned to be 40% gynecologists, 40% GPs, 20% dermatologists. Per protocol, a total of 50 doctors was envisaged for France; as of this report physician recruitment is ongoing, 37 physicians were recruited by the 8th April 2016.

Initiation of recruitment in France was considerably delayed due to a prolonged approval process. Non-interventional trials are governed by three regulatory bodies (CCTIRS, CNOM and CNIL) which only approve consecutively. All studies need approval from all three bodies prior to start of any study-related activities, e.g. recruitment of physicians.

CCTIRS deals with the research methodology from the perspective of current relevant legislation as well as issues concerning personal data, especially concerning the necessity of obtaining named patient data.

CNIL is the French data protection committee. The final CNIL approval can only be granted after CCTIRS has granted its approval.

CNOM is the professional organization of medical doctors. As the field organization is compliant with the CNOM's regulations further formal approval was not needed by CNOM.

Study documents were sent to CCTIRS on 17th March 2015. Approval was delayed for four months despite multiple efforts from both ZEG and the national field organization to expedite proceedings. Approval was awarded on 23rd July 2015. CNIL received the application – including the approval decision from CCTRIS – on 23rd July. 2015. Again there was a four-month delay in the approval process; CCTRIS approval was awarded on 24th November 2015.

Recruitment of physicians commenced in France in the end of 2015. The first patient was enrolled in January 2016.

Thus far, a total of 276 physicians have been contacted in France, 106 gynecologists, 54 dermatologists and 116 GPs. Of these, 22 gynecologists, 8 dermatologists and 7 GPs agreed to participate. Four gynecologists, 2 dermatologists and 2 GPs contributed at least one patient to the study as of data freeze.

The main reasons for non-participation were low number of prescriptions (n = 58), lack of time (n = 23), no interest in the study (n = 11), no reason provided (n = 9) and no prescriptions of CPA/EE-containing drugs (n = 8).

The Netherlands:

The distribution of physician specialties in The Netherlands was planned to be 75% GPs and 25% dermatologists. Due to slow recruitment, more physicians than expected were contacted and the final distribution of specialties of contacted physicians deviated from initial estimates.

A total of 802 physicians were contacted in The Netherlands, 748 GPs, 53 dermatologists and 1 gynecologist. Of these, 16 GPs, 2 dermatologists and 1 gynecologist agreed to participate in the study; at study end 6 GPs and 1 dermatologist had contributed at least one prescription. 62 physicians declined to participate and 721 did not respond to the initial emails.

The main reasons for non-participation were: no prescriptions of CPA/EE-containing drugs (n = 34), lack of time/too time-consuming (n = 10) and a low number of prescriptions (n = 8). Several physicians did not participate because of the possibility of an audit in the office (n = 3), without giving a reason (n = 1), due to the scope of the survey (n = 1) or other (n = 3).

There were two major country-specific conditions in The Netherlands that led to an unexpectedly low recruitment rate:

- repeat prescriptions filled by pharmacists resulting in limited patient-physician-contact
- difficult access to doctors via telephone.

Due to the above-mentioned issues a broad invitation was sent to 496 GPs by letter in order to recruit more physicians in May 2015. Of those, only 4 GPs showed interest in study participation and in the end none agreed to participate.

Subsequently a freelance recruiter was employed to target dermatological practices. Approximately 60 dermatologists were contacted of whom three were initially interested and one finally agreed to study participation.

In June 2015 a short online survey was conducted to elucidate whether gynecologists prescribe CPA/EE in The Netherlands and if they did, if they were willing to participate in the study. 303 gynecologists were contacted of whom 41 responded, 2 gynecologists showed initial interest in the study but none agreed to participate.

In August and September 2015 a widely distributed online survey was conducted to better understand prescription behavior in The Netherlands. Those who prescribed CPA/EE were asked if they were interested in participating in a DUS for CPA/EE. The following results were yielded:

Participation:

- 600 gynecologists (73 responded, 7 interested, 1 participated)
- 349 dermatologists (55 responded, 2 interested, 1 participated)
- 1,099 GPs (110 responded, 2 interested, 2 participated)

Prescribing behavior:

Between 25% and 33% of the physicians that responded to this survey prescribed CPA/EE less frequently than once a month, 6-13% prescribed CPA/EE between 1 and 5 times a month, 1% (n = 1) of the gynecologists and 1% (n = 1) of the GPs prescribed CPA/EE 6-20 times a month and 1% (n = 1) of the gynecologists prescribed CPA/EE more than 20 times a month.

Spain:

The distribution of physician specialties in Spain was planned to be 50% GPs, 25% gynecologists and 25% dermatologists. Due to slow recruitment, more physicians than expected were contacted and the final distribution of specialties of contacted physicians deviated from initial estimates

Physician recruitment began in May 2015. By the end of the study a total of 139 physicians had been contacted; 47 GPs, 50 gynecologists and 42 dermatologists. Of these, 40 GPs, 27 gynecologists and 28 dermatologists agreed to participate in the study. A total of 32 GPs, 11 gynecologists and 8 dermatologists contributed at least one patient.

The main reasons for non-participation were: no prescriptions of CPA/EE-containing drugs (n = 23), low number of prescriptions (n = 14), other reasons (N=7).

Table 2 provides an overview of the physician recruitment categorized by country.

Table 2 - Physician recruitment by country

	AT	CZ	FR	NL	ES	**Total**
Number (%) of contacted physicians	718 (100%)	695 (100%)	276 (100%)	802 (100%)	139 (100%)	**2630 (100%)**
Participating	119 (16.6%)	44 (6.3%)	37 (13.4%)	19 (2.4%)	95 (68.3%)	**314 (11.9%)**
Active	22 (3.1%)	32 (4.6%)	8 (2.9%)	7 (0.9%)	51 (36.7%)	**120 (4.6%)**
Non-participating	599 (83.4%)	651 (93.7%)	239 (86.6%)	783 (97.6%)	44 (31.7%)	**2316 (88.1%)**
Physician has been screened out (no CPA/EE prescriptions)	92 (12.8%)	346 (49.8%)	8 (2.9%)	34 (4.2%)	23 (16.5%)	**503 (19.1%)**
Physician has been screened out (too low number of CPA/EE prescriptions)	243 (33.8%)	179 (25.8%)	58 (21.0%)	8 (1.0%)	14 (10.1%)	**502 (19.1%)**
Physician declined (generally/without giving a reason)	3 (0.4%)	3 (0.4%)	9 (3.3%)	1 (0.1%)	0 (0.0%)	**16 (0.6%)**
Physician declined (due to scope of survey)	0 (0.0%)	4 (0.6%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	**5 (0.2%)**
Physician declined (due to possibility of validation in doctor's office)	0 (0.0%)	2 (0.3%)	4 (1.4%)	3 (0.4%)	0 (0.0%)	**9 (0.3%)**
Physician declined (due to payment)	0 (0.0%)	81 (11.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**81 (3.1%)**
Physician declined (due to no interest in studies)	119 (16.6%)	30 (4.3%)	11 (4.0%)	0 (0.0%)	0 (0.0%)	**160 (6.1%)**
Physician declined (due to lack of time/too time-consuming)	68 (9.5%)	4 (0.6%)	23 (8.3%)	10 (1.2%)	0 (0.0%)	**105 (4.0%)**
Physician declined (due to retirement/close of practice)	16 (2.2%)	2 (0.3%)	2 (0.7%)	0 (0.0%)	0 (0.0%)	**20 (0.8%)**
Other reason	58 (8.1%)	0 (0.0%)	0 (0.0%)	3 (0.4%)	7 (5.0%)	**68 (2.6%)**
Missing	0 (0.0%)	0 (0.0%)	124 (44.9%)	723 (90.1%)	0 (0.0%)	**847 (32.2%)**

Participating physicians are defined as those that agreed to participate (irrespective of returned questionnaires).
Active physicians are defined as those that returned at least one analyzable questionnaire (including a corresponding informed consent from the woman).
Date of analysis: 11MAY2016

The above data are summarized in Table A1-A1.3 (see Annex)

10.1.2 Physician age

226 of 314 participating physicians and 370 of 2,316 non-participating physicians gave information about their age.

Combined analysis of all participating countries showed the average age of the participating physicians was 52.2 years, while it was 53.1 years for the non-participating physicians. The age range of the physicians was 29 to 70 in participating physicians and 27 to 78 in non-participating physicians.

The average ages per country among the participating physicians ranged from 48.6 years in The Netherlands to 55.6 years in France. There were minor differences only in the average age between participating and non-participating physicians when stratified by country.

The above data are summarized in Table A2-A2.5 (see Annex)

10.1.3 Physician gender

181 (57.6%) of the 314 participating physicians were male, while 133 (42.4%) were female, whereas 1,041 (44.9%) of the 2,316 non-participating physicians were male and 1,222 (52.8%) female. Information on gender was missing in 53 of the non-participating physicians.

The Czech Republic and France showed a distribution of just above 50% female, whereas in Austria, Spain and The Netherlands around 60% male and 40% female physicians participated.

The above data are summarized in Table A3-A3.5 (see Annex)

10.1.4 Physician specialties

Of the 314 participating physicians 198 were gynecologists, 63 GPs and 53 dermatologists. Of the 2,316 non-participating physicians, 848 were GPs 738 dermatologists and 730 were gynecologists. Gynecologists were the most likely to participate in the study when contacted.

The above data are summarized in Table A4-A4.5 (see Annex)

10.1.5 Physician level of experience

71.0% of the participating physicians had 15 or more years of working experience.

81.6% of the non-participating physicians did not give information about their level of experience, but the ones who did showed the same trend as the participating physicians. There was no large difference between the participating and the non-participating physicians in terms of level of experience. Furthermore, the general trend for participating and non-participating physicians was in the same order of magnitude in all 5 countries,.

The above data are summarized in Table A5-A5.5 (see Annex)

10.2 Patient recruitment and eligibility

Due to low physician participation rates and lower than expected numbers of CPA/EE prescriptions, the planned recruitment of 1,000 patient/prescription events per participating country was not reached. However, in total, meaningful results could be obtained. On a country level this holds also true for Austria, Czech Republic and Spain. The low overall study recruitment is reflected in the results below.

10.2.1 Patient recruitment per country

The first patient was recruited in Austria on 6th March 2015. By 8th April 2016, 292 patients had been recruited of whom 282 were eligible. All patients were recruited by gynecologists.

In the Czech Republic the first patient was recruited on 8th April 2015. Exactly one year later, by 8th April 2016, 581 patients have been recruited of whom 563 were eligible. 526 eligible patients were recruited by gynecologists and 37 by dermatologists.

In France the first patient was recruited on 15th January 2016. By 8th April 2016, 24 patients had been recruited of whom all were eligible. 12 patients were recruited by dermatologists, 7 by gynecologists and 5 by GPs.

In The Netherlands the first patient was recruited on 13th April 2015. By 8th April 2016, 45 patients had been recruited, of whom 32 were eligible. 24 eligible patients were recruited by GPs and 8 by dermatologists.

In Spain the first patient was recruited on 11th May 2015. By 8th April 2016, 632 patients had been recruited of whom 612 were eligible. 381 patients were recruited by GPs, 121 by gynecologists and 110 by dermatologists. Table 3 provides data on the patient recruitment by country and specialty.

Table 3 - Patient recruitment by country

	AT	CZ	FR	NL	ES	**Total**
Number (%) of recruited patients	292 (100%)	581 (100%)	24 (100%)	45 (100%)	632 (100%)	**1574 (100%)**
Eligible	282 (96.6%)	563 (96.9%)	24 (100%)	32 (71.1%)	612 (96.8%)	**1513 (96.1%)**
Specialty:						
Gynecology	*282 (100%)*	*526 (93.4%)*	*7 (29.2%)*	*0 (0.0%)*	*121 (19.8%)*	***936 (61.9%)***
Dermatology	*0 (0.0%)*	*37 (6.6%)*	*12 (50.0%)*	*8 (25.0%)*	*110 (18.0%)*	***167 (11.0%)***
General Practitioner (GP)	*0 (0.0%)*	*0 (0.0%)*	*5 (20.8%)*	*24 (75.0%)*	*381 (62.3%)*	***410 (27.1%)***
Ineligible	10 (3.4%)	18 (3.1%)	0 (0.0%)	13 (28.9%)	20 (3.2%)	**61 (3.9%)**
Duplicate	0 (0.0%)	5 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**5 (0.3%)**
No complete informed consent available	1 (0.3%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	20 (3.2%)	**22 (1.4%)**
No Baseline questionnaire available	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.4%)	0 (0.0%)	**2 (0.1%)**
Recruited after study recruitment closure	1 (0.3%)	11 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**12 (0.8%)**
No CPA/EE prescription	8 (2.7%)	2 (0.3%)	0 (0.0%)	10 (22.2%)	0 (0.0%)	**20 (1.3%)**

Date of analysis: 11MAY2016

Note: For specialties (in italics) the percentages relate to the number of eligible patients. All other percentages relate to "Number (%) of recruited patients".

10.2.2 Age distribution of eligible patients

The mean age of recruited patients prescribed CPA/EE for the combined cohort (n = 1,513) was 26.0 years with a range of 13 to 60 years. The age range from 18 to 34 years accounted for 73.7% of the users. 13.1% were younger than 18 years, and 12.3% in the age range 35 to 49 years. 14 patients (0.9%) fell into the age of 50 or more years.

Stratification of data by individual country (Tables B1.1 to B1.5) shows similar trends, with the majority of prescriptions made in the age range of 18 to 34 years. However, the percentage of prescriptions below the age of 18 years is higher in Austria (19.1%) and the Czech Republic (17.9%) than in Spain (5.9%). The total mean age in the different countries ranged from 24.5 years in Austria to 27.9 years in The Netherlands.

The above data are summarized in Table B1-B1.5 (see Annex)

10.2.3 Age distribution of eligible patients by specialty

The overall age distribution of patients recruited by physician specialty was similar with the exception of a higher percentage of patients under the age of 18 years prescribed CPA/EE by gynecologists (17.4%), versus 7.2% for dermatologists and 5.6% for GPs.

The average age of eligible patients recruited by gynecologists was 25.9 years, by dermatologists 28.3 years and by GPs 25.9 years.

The above data are summarized in Table B1.6- B1.8 (see Annex)

10.3 CPA/EE prescriptions

10.3.1 Prescription status

Combined analysis revealed 42.0% (n = 635) of the prescriptions were starters, 42.6% (n = 645) were continuous users and 14.7% (n = 223) of patients were re-starters[3]. The distribution pattern in Spain mirrored the combined cohort. In Austria, the percentage of continuous users was higher than average (57.8%), and in the Czech Republic there were more starters (48.7%). Numbers in France and The Netherlands were too small to detect any meaningful trends.

Analysis by physician specialty showed that prescriptions by gynecologists (n = 936) were most frequently performed for starters (45.8%), followed by 38.8% of prescriptions for continuous users, and 14.4% for re-starters. Prescriptions by dermatologists were more evenly distributed with 40.7% for starters, 35.3% for continuous users, and 24.0% for re-starters. Prescriptions by GPs had the lowest percentage of starters (33.7%), the highest percentage of continuous users (54.4%), and the lowest percentage of prescriptions for re-starters (11.7%).

The above data are summarized in Table B2 – B2.8 (see Annex)

10.3.2 Prescribing reasons

In the context of this study, the following androgen-dependent conditions were predefined in the questionnaire: acne, hirsutism, seborrhea, androgenetic alopecia and Polycystic Ovary Syndrome (PCOS). In addition, the physician was asked to document whether CPA/EE was prescribed for contraception and whether the patient was using a hormonal contraceptive at the time of

[3] Starters are patients that have never been prescribed CPA/EE before; continuous users are patients that had no break or a break of less than 4 weeks since their last CPA/EE prescription; re-starters are patients that were prescribed CPA/EE after a break of more than 4 weeks.

prescription. The questionnaire allowed for a prescription to be made for multiple indications for one patient.

Overall, the main reasons for CPA/EE prescription were acne (65.6%, n = 993) and contraception (66.7%, n = 1,009) followed by seborrhea (12.9%), hirsutism (12.6%) and PCOS (11.4%). Androgenetic alopecia and "other reasons" were the least mentioned with 5.0% and 3.7%, respectively. In 16.3% (n = 246) contraception was the only listed reason for the prescription. The proportions for "PCOS only" were 3.1% (n = 47) and 1.4% (n = 21) for androgenetic alopecia. Table 4 shows the reasons for the prescription of CPA/EE.

The above data are summarized in Table B3 (see Annex)

Table 4 - Prescribing reasons for CPA/EE

	CPA/EE	95%-CI
Number (%) of eligible patients	1513 (100%)	
Reason		
Acne	993 (65.6%)	[57.2%;73.4%]
Seborrhea	195 (12.9%)	[9.3%;17.3%]
Hirsutism	191 (12.6%)	[9.8%;15.9%]
Androgenetic alopecia	75 (5.0%)	[3.2%;7.2%]
PCOS	173 (11.4%)	[7.9%;15.8%]
Contraception	1009 (66.7%)	[58.8%;74.0%]
Other reason	56 (3.7%)	[1.9%;6.5%]
Contraception only (no other reasons)	246 (16.3%)	[9.1%;25.9%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998
Date of analysis: 10MAY2016

10.3.3 Prescribing reasons per country

Stratified analysis by country showed marked differences in prescribing patterns. Spanish prescribers listed acne the least frequently as a reason for CPA/EE prescription (50.3%), whereas in the Czech Republic 80.1% of the prescriptions listed acne as an indication for today's script. Similarly, in the Czech Republic 86.5% of the patients were prescribed CPA/EE for contraception as one of the reasons for prescriptions, whereas only 49.7% of Spanish prescribers used it for this purpose. The percentage of prescriptions indicated for contraception only by country ranged from 8.3% in France to 22.0% in Austria. The Czech Republic (13.5%), The Netherlands (15.6%) and Spain (16.5%) fell within this range. Spain showed significantly higher numbers of seborrhea (20.9%; n = 128), PCOS (21.4%; n = 131) and hirsutism (23.1%; n = 142) based prescriptions.

The above data are summarized in Table B3.1-B3.5 (see Annex)

Table 5 - Prescribing reasons for CPA/EE by country

	AT	CZ	FR	NL	ES
Number (%) of eligible patients	282 (100%)	563 (100%)	24 (100%)	32 (100%)	612 (100%)
Reason					
Acne	189 (67.0%)	451 (80.1%)	21 (87.5%)	24 (75.0%)	308 (50.3%)
Seborrhea	13 (4.6%)	52 (9.2%)	1 (4.2%)	1 (3.1%)	128 (20.9%)
Hirsutism	12 (4.3%)	35 (6.2%)	1 (4.2%)	1 (3.1%)	142 (23.2%)
Androgenetic alopecia	2 (0.7%)	21 (3.7%)	0 (0.0%)	2 (6.3%)	50 (8.2%)
PCOS	19 (6.7%)	23 (4.1%)	0 (0.0%)	0 (0.0%)	131 (21.4%)
Contraception	186 (66.0%)	487 (86.5%)	10 (41.7%)	22 (68.8%)	304 (49.7%)
Other reason	19 (6.7%)	22 (3.9%)	1 (4.2%)	0 (0.0%)	14 (2.3%)
Contraception only (no other reasons)	62 (22.0%)	76 (13.5%)	2 (8.3%)	5 (15.6%)	101 (16.5%)

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998
Date of analysis: 10MAY2016

10.3.4 Prescribing reasons per specialty

Gynecologists stated acne as a reason for prescribing CPA/EE in 72.5 % of cases, contraception in 78.4%, seborrhea in 9.7%, hirsutism in 8.1%, PCOS in 7.9%, and androgenetic alopecia in 3.2%. 4.9% of CPA/EE prescriptions were made for other reasons and 16.2% of the prescriptions by gynecologists were for contraception only.

Dermatologists also prescribed CPA/EE frequently for acne (71.3% of all prescriptions); however, the percentage of contraception linked prescriptions was only 28.1%, markedly lower than other specialties. Seborrhea (28.1%) and androgenetic alopecia (21.0%) were also proportionally more frequently indicated as a reason for today's prescription compared to other specialties. Only 1.2% of the CPA/EE prescriptions made by dermatologists were exclusively for contraceptive reasons.

In contrast, GPs prescribed CPA/EE 47.6% of the time for acne. Contraception was stated as a reason in 57.8%, seborrhea in 13.9%, hirsutism in 20.7%, PCOS in 21.2% and androgenetic alopecia in 2.4%. Contraception as the only reason was stated in 23.0% of the prescriptions by GPs. Reasons for prescription by specialty are listed in Table 6.

The above data are summarized in Table B3.6- B3.8 (see Annex)

Table 6 - Prescribing reasons for CPA/EE by specialty

	GYN	DERM	GP
Number (%) of eligible patients	936 (100%)	167 (100%)	410 (100%)
Reason			
Acne	679 (72.5%)	119 (71.3%)	195 (47.6%)
Seborrhea	91 (9.7%)	47 (28.1%)	57 (13.9%)
Hirsutism	76 (8.1%)	30 (18.0%)	85 (20.7%)
Androgenetic alopecia	30 (3.2%)	35 (21.0%)	10 (2.4%)
PCOS	74 (7.9%)	12 (7.2%)	87 (21.2%)
Contraception	734 (78.4%)	38 (22.8%)	237 (57.8%)
Other reason	46 (4.9%)	0 (0.0%)	10 (2.4%)
Contraception only (no other reason)	152 (16.2%)	2 (1.2%)	92 (22.4%)

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998
Date of analysis: 10MAY2016

10.4 Previous and concomitant treatment of androgen-dependent conditions

10.4.1 Previous treatment of acne

Of the 1,028 patients who had an acne diagnosis, 377 had mild acne, 562 moderate acne and 89 severe acne. 57.0% (n = 586) of the patients who had an acne diagnosis had received previous treatment. There was a marked difference in the number of patients who had previously been treated for acne according to the diagnostic severity of disease; previous treatment was stated in 42.7% of the patients with mild acne, 63.2% with moderate acne and 78.7% of the severely affected patients. 82.7% of all patients with acne have had their acne diagnosis for more than 12 months and 41.6% (n = 428) of the previous treatments were documented as failed or insufficient. For moderate to severe acne (i.e. without mild acne) previous treatment failure was 51.8% (see Table 7).

For patients with mild acne the three most frequently mentioned previous treatments were ”various topical therapies/keratolytics”, of which OTC medications and washing lotions (n = 46, 12.2%), topical antibiotics without combinations (n = 39, 10.3%) and CPA/EE (n = 32, 8.5%). In 24.1% of the cases, the previous treatment was documented as failed or insufficient.

For patients with moderate acne the most common previous treatments were topical antibiotics without combinations (n = 100, 17.8%), antibiotics combined with benzoyl peroxide (n = 77, 13.7%), systemic antibiotics (n = 68, 12.1%), various topical therapies/keratolytics (n = 55, 9.8%) and CPA/EE (n = 44, 7.8%).

In patients with moderate acne the proportion of failed or insufficient previous treatments was 49.6%.

For patients with severe acne the most frequently mentioned previous treatments were systemic antibiotics (n = 19, 21.3%), topical antibiotics (n = 14, 15.7%), and antibiotics combined with benzoyl peroxide (n = 10, 11.2%). Patients with severe acne had the highest proportion of failed or insufficient treatments (65.2%).

Stratification by country showed differences in the frequency of previous treatment for acne in patients who received CPA/EE. In France 95.7%, of patients had previous treatment, in Spain 73.2%, in the Czech Republic 55.4%, in The Netherlands 54.2%, and in Austria 29.8%.

Stratification by professional specialties showed differences between gynecologists, dermatologists, and GPs with regard to previous treatment of acne. This may be due to either differing therapeutic or prescribing preferences or on differing patient populations, e.g. patients with other hormonal problems, e.g. bleeding disorders, seeking the care of gynecologists rather than dermatologists. Of the 695 patients recruited by gynecologists and affected by acne who received a CPA/EE prescription, 53.2 % had received no previous treatment for their condition. For dermatologists the frequency of patients without previous treatment was 15.4%, i.e. 84.6% had received other treatments for acne prior to the index CPA/EE prescription. The GPs were in between these frequencies, with 27.6% of patients having received no previous treatment for acne and 72.4% having had preceding acne therapy.

The above data are summarized in Table B4-1-B4-1.8 (see Annex)

Table 7 – Previous acne treatment by severity

	Mild	Moderate	Severe	**Total**
Number (%) of patients with acne	377 (100%)	562 (100%)	89 (100%)	**1028 (100%)**
Previous treatment				
No	216 (57.3%)	207 (36.8%)	19 (21.3%)	**442 (43.0%)**
Yes	161 (42.7%)	355 (63.2%)	70 (78.7%)	**586 (57.0%)**
Anti-androgenic therapy	2 (0.5%)	5 (0.9%)	2 (2.2%)	**9 (0.9%)**
Antibiotic combined with benzoyl peroxide (topical)	9 (2.4%)	77 (13.7%)	10 (11.2%)	**96 (9.3%)**
Antibiotic combined with retinoid (topical)	2 (0.5%)	5 (0.9%)	3 (3.4%)	**10 (1.0%)**
Antibiotics (form of application not specified/unclear)	14 (3.7%)	27 (4.8%)	9 (10.1%)	**50 (4.9%)**
Antimycotics	12 (3.2%)	8 (1.4%)	0 (0.0%)	**20 (1.9%)**
Azelaic-acid	9 (2.4%)	28 (5.0%)	8 (9.0%)	**45 (4.4%)**
CPA/EE	32 (8.5%)	44 (7.8%)	7 (7.9%)	**83 (8.1%)**
Isotretinoin (form of application not specified/unclear)	1 (0.3%)	3 (0.5%)	7 (7.9%)	**11 (1.1%)**
Isotretinoin systemic	6 (1.6%)	27 (4.8%)	7 (7.9%)	**40 (3.9%)**
Monoclonal antibody	1 (0.3%)	0 (0.0%)	0 (0.0%)	**1 (0.1%)**
Oral Contraceptives (not including CPA/EE)	14 (3.7%)	23 (4.1%)	1 (1.1%)	**38 (3.7%)**
Physical therapy	1 (0.3%)	1 (0.2%)	0 (0.0%)	**2 (0.2%)**
Retinoids combined with benzoyl peroxide (topical)	1 (0.3%)	14 (2.5%)	1 (1.1%)	**16 (1.6%)**
Systemic antibiotics	8 (2.1%)	68 (12.1%)	19 (21.3%)	**95 (9.2%)**
Topical antibiotics	39 (10.3%)	100 (17.8%)	14 (15.7%)	**153 (14.9%)**
Topical corticosteroids	3 (0.8%)	3 (0.5%)	0 (0.0%)	**6 (0.6%)**
Topical retinoids	6 (1.6%)	39 (6.9%)	8 (9.0%)	**53 (5.2%)**
Topical treatment with benzoyl peroxide	6 (1.6%)	31 (5.5%)	7 (7.9%)	**44 (4.3%)**
Various topical therapies/ keratolytics	46 (12.2%)	55 (9.8%)	8 (9.0%)	**109 (10.6%)**
Zinc powder	0 (0.0%)	8 (1.4%)	2 (2.2%)	**10 (1.0%)**
Zinc tablets/various oral therapies	1 (0.3%)	5 (0.9%)	0 (0.0%)	**6 (0.6%)**
Missing	1 (0.3%)	2 (0.4%)	0 (0.0%)	**3 (0.3%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**

Note: Patient may have more than one entry for previous and concomitant treatment.

Date of analysis: 11MAY2016

10.4.2 Concomitant treatment of acne

Overall 31.2% (n = 321) of the patients with an acne diagnosis received treatment in addition to CPA/EE. There was a marked difference in concomitant treatment percentage between the three groups of severity; 16.4% (n = 62) of the patients with mild acne received concomitant treatment, whereas 37.9% (n = 213) with moderate acne, and 51.7% (n = 46) of the patients severely affected by acne received concomitant treatment (see Table 8).

Of the 16.4% of patients (n = 62) with mild acne receiving concomitant therapy, the most frequently mentioned concomitant treatments were various topical therapies/keratolytics (n = 24, 6.4%) and topical antibiotics (n = 12, 3.2%).

For patients with moderate acne receiving concomitant treatment (n = 187) the most frequently mentioned concomitant treatments were topical antibiotics (n = 46, 8.2%), various topical therapies / keratolytics (n = 45, 8.0%), antibiotics combined with benzoyl peroxide (n = 33, 5.9%), and systemic antibiotics (n = 24, 4.3%)

For patients with severe acne, those receiving concomitant treatment (n = 40) the most frequently mentioned treatments were systemic isotretinoin (n = 9, 10.1%), various topical treatments / keratolytics (n = 8, 9.0%) and topical antibiotics (n = 8, 9.0%).

The percentage of concomitant treatment of acne also varied between countries; in France, 65.2% of the patients who received a CPA/EE prescription also used concomitant treatment. The respective proportion was lower in the other countries; 43.9% in Spain, 32.1% in Czech Republic, 16.7% in The Netherlands, and 6.1% in Austria.

Differences in concomitant therapy use were also observed between specialties; 68.3% of the patients prescribed CPA/EE for the management of acne by dermatologists received concomitant treatment. This proportion was lower for patients treated by GPs (37.4%) and Gynecologists (22.8%).

The above data are summarized in Table B4-1-B4-1.8 (see Annex)

Table 8 – Concomitant acne treatment by severity

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	377 (100%)	562 (100%)	89 (100%)	**1028 (100%)**
Concomitant treatment				
No	301 (79.8%)	322 (57.3%)	40 (44.9%)	**663 (64.5%)**
Yes	62 (16.4%)	213 (37.9%)	46 (51.7%)	**321 (31.2%)**
Anti-androgenic therapy	0 (0.0%)	1 (0.2%)	2 (2.2%)	**3 (0.3%)**
Antibiotic combined with benzoyl peroxide (topical)	3 (0.8%)	33 (5.9%)	4 (4.5%)	**40 (3.9%)**
Antibiotic combined with retinoid (topical)	0 (0.0%)	1 (0.2%)	1 (1.1%)	**2 (0.2%)**
Antibiotics (form of application not specified/unclear)	1 (0.3%)	6 (1.1%)	2 (2.2%)	**9 (0.9%)**
Antimycotics	7 (1.9%)	4 (0.7%)	2 (2.2%)	**13 (1.3%)**
Azelaic-acid	2 (0.5%)	8 (1.4%)	2 (2.2%)	**12 (1.2%)**
Isotretinoin (form of application not specified/unclear)	1 (0.3%)	5 (0.9%)	6 (6.7%)	**12 (1.2%)**
Isotretinoin systemic	0 (0.0%)	11 (2.0%)	9 (10.1%)	**20 (1.9%)**
Retinoids combined with benzoyl peroxide (topical)	3 (0.8%)	15 (2.7%)	0 (0.0%)	**18 (1.8%)**
Systemic antibiotics	3 (0.8%)	24 (4.3%)	4 (4.5%)	**31 (3.0%)**
Topical antibiotics	12 (3.2%)	46 (8.2%)	8 (9.0%)	**66 (6.4%)**
Topical corticosteroids	0 (0.0%)	2 (0.4%)	0 (0.0%)	**2 (0.2%)**
Topical retinoids	5 (1.3%)	19 (3.4%)	1 (1.1%)	**25 (2.4%)**
Topical treatment with benzoyl peroxide	6 (1.6%)	18 (3.2%)	3 (3.4%)	**27 (2.6%)**
Various topical therapies/ keratolytics	24 (6.4%)	45 (8.0%)	8 (9.0%)	**77 (7.5%)**
Zinc powder	0 (0.0%)	1 (0.2%)	0 (0.0%)	**1 (0.1%)**
Zinc tablets/various oral therapies	0 (0.0%)	1 (0.2%)	1 (1.1%)	**2 (0.2%)**
Missing	1 (0.3%)	2 (0.4%)	0 (0.0%)	**3 (0.3%)**
Missing	14 (3.7%)	27 (4.8%)	3 (3.4%)	**44 (4.3%)**

Note: Patient may have more than one entry for previous and concomitant treatment.

Date of analysis: 11MAY2016

10.4.3 Previous treatment of seborrhea

In total, 267 patients had a diagnosis of seborrhea, of which 39.0% (n = 104) had received previous treatment. The most frequently stated treatment was local/topical keratolysis/therapy (11.2%, n = 30), antimycotics (4.9%, n = 13), CPA/EE (4.1%, n = 11) and topical treatment with benzoyl peroxide (4.1%, n = 11).

Differences were observed between countries although no meaningful comparison across (sub)-cohorts could be performed due to low sub-cohort numbers.

Differences were also observed between specialty groups; 57.4% (n = 31) of patients treated by a dermatologist and 52.2% (n = 47) of patients treated by a GP had received previous treatment in comparison to 21.1% (n = 26) of patients treated by a gynecologist.

The above data are summarized in Table B4-2-B4-2.8 (see Annex)

10.4.4 Concomitant treatment of seborrhea

52 of the 267 (19.5%) patients with a seborrhea diagnosis were taking concomitant treatment. Local/topical keratolysis/therapy accounted for the highest percentage of the concomitant treatment with (n = 26) followed by topical antibiotics with (n = 10).

Differences were again observed between countries. In Austria and The Netherlands no patients with seborrhea received concomitant treatment, while in Spain 28.5% (n = 47) of patients used additional treatments to manage their seborrhea. The Czech Republic had a proportion of 6.8% (n = 4) and France 20.0% (n= 1).

A breakdown of the use of concomitant treatment by specialty group ranged from 7.3 % (n = 9) in gynecologists to 25.6% (n = 23) in GPs to 37.0% (n = 20) in dermatologists.

Dermatologists and gynecologists prescribed local/topical keratolysis/therapy most frequently, whereas GPs prescribed topical antibiotics more often than local/topical keratolysis/therapy as concomitant treatment for the indication seborrhea.

10.4.5 Previous treatment of hirsutism

A total of 221 patients were affected by hirsutism. Of these, 42 (19.0%) stated they had received previous treatment, 162 (73.3%) have not been previously treated for their disorder. Information was missing for 17 (7.7%) of patients.

The most frequently used previous treatments in this (sub)-cohort was CPA/EE (5.0%, n = 11), anti-androgenic therapy (3.6%, n = 8), oral contraceptives not including CPA/EE (2.3%, n = 5), Eflornithine (2.3%, n = 5) and laser diode hair removal (1.8%, n = 4).

Across countries the Czech Republic showed a rate of previous treatment of hirsutism of 21.1% (n = 8). Treatment with CPA/EE accounted for six of these cases. In Spain, who had the highest total number of patients with hirsutism (n = 160), 19.4% (n = 31) had received previous treatment. 2 patients (10%) in Austria had received previous treatment.

Regarding the specialties, the highest proportion of patients with hirsutism who had received previous treatment was reported by dermatologists (25.8%; n = 8), followed by the gynecologists (21.1%; n = 19) and GPs (15.0%; n = 15). Specific treatments differed across specialty; CPA/EE (n = 9) and anti-androgenic therapy (n = 5) were the most frequently reported treatments for hirsutism amongst gynecologists, whereas Eflornithine (n = 5) was the most common treatment among dermatologists. For GPs no preferences are obvious.

The above data are summarized in Table B4-3-B4-3.8 (see Annex)

10.4.6 Concomitant treatment of hirsutism

Of 221 patients affected by hirsutism, 16 (7.2%) received concomitant treatment. Laser diode hair removal (n = 5) and anti-androgenic therapy (n = 3) were reported most frequently as concomitant treatments.

The Czech Republic and Spain were the only countries where concomitant therapy was reported. Consequently, no meaningful comparison across (sub)-cohorts could be performed.

No trends could be seen in concomitant therapy prescribing patterns across specialty group. A breakdown of the figures by specialty group showed 5 concomitant treatments of hirsutism from gynecologists (5.6% of the eligible patients recruited by gynecologists), 4 from dermatologists (12.9%) and 7 from GPs (7.0%)

The above data are summarized in Table B4-3-B4-3.8 (see Annex)

10.4.7 Previous treatment of androgenetic alopecia

89 patients had a diagnosis of androgenetic alopecia, of which 37 (41.6%) had been previously treated. Of the previous treatments Minoxidil was the leading prescription with 21 (23.6%).

Previous treatment of androgenetic alopecia varied across countries; in Spain 44.8% (n = 27) and in the Czech Republic 32.0% (n = 8) of the patients had been previously treated. Two patients from The Netherlands, 1 patient from France and no patients from Austria had previously been treated for androgenetic alopecia prior to the CPA/EE prescription.

When stratified by specialty, the highest proportion of previous treatments for androgenetic alopecia was reported by the dermatologists with 66.7% (n = 24), gynecologists 24.3% (n = 9), GPs 25.0% (n = 4). The most common treatment prescribed by dermatologists was Minoxidil.

The above data are summarized in Table B4-4-B4-4.8 (see Annex)

10.4.8 Concomitant treatment of androgenetic alopecia

17 (19.1%) of the patients with androgenetic alopecia received concomitant treatment and 9 (10.1%) of these were prescribed Minoxidil as concomitant treatment.

Spain had the highest rate of concomitant treatment (n = 12; 20.7%). Two patients from the Czech Republic, two from The Netherlands and one from France were further receiving concomitant treatment.

Dermatologists also reported the highest proportion of concomitant treatment (36.1%; n = 13).

The above data are summarized in Table B4-4-B4-4.8 (see Annex)

10.4.9 Previous treatment of PCOS

192 patients with a diagnosis of PCOS were recruited into the study, of which 22.4% (n = 43) had received previous treatment. Oral contraceptives (not including CPA/EE) stood out as being the most frequent previous treatment mentioned (13%; n = 25), followed by folic acid plus inositol and anti-androgenic therapy (both 2.6%; n = 5).

Data observed across countries are limited due to the fact of no patients in France or The Netherlands having previously been treated for PCOS. Of the remaining three countries, patients previously treated for PCOS came from Austria (n = 1), the Czech Republic (n = 2) and Spain (n = 40).

The highest proportion of previous treatment for PCOS amongst specialists was observed in dermatologists (50.0%, n = 8), followed by GPs (20.9%; n = 19) and gynecologists (18.8%; n = 16). Oral contraceptives were the most frequently prescribed treatment with GPs and the gynecologists, whereas the dermatologists showed more evenly distributed previous treatments of PCOS.

The above data are summarized in Table B4-5-B4-5.8 (see Annex)

10.4.10 Concomitant treatment of PCOS

Relatively few patients received concomitant treatment for PCOS, consequently meaningful comparison across countries and specialty groups is limited. The Czech Republic had two patients (8.7%) and Spain had 11 patients (7.6%) reporting concomitant treatment.

The distribution of the concomitant treatment of PCOS with regard to specialties ranged from 5.5% (n = 5) concomitant treatment by GPs to 12.5% (n = 2) by dermatologists. For gynecologists 7.1% (n =6) for concomitant treatment of PCOS were reported.

The above data are summarized in Table B4-5-B4-5.8 (see Annex)

10.5 Concomitant use of other hormonal contraceptives and CPA/EE

Of the total number of 1,513 CPA/EE users, the vast majority (97.1%, N=1,469) did not report use of additional hormonal contraception at the time CPA/EE prescription. However, 44 (2.9%) patients stated that they used additional hormonal contraception, of whom 42 (2.8% of the total) used oral contraceptives and 2 (0.1% of the total) non-oral contraceptives. It is important to consider that these patients are reported to use other hormonal contraceptives at the time of issuance of CPA/EE prescription. It cannot be assumed that all of them would be using other hormonal contraceptives along with CPA/EE. They might stop using other hormonal contraceptive once CPA/EE is started.

Prescription of additional hormonal contraception was similar in the Czech Republic (3.7%, n = 21) and Spain (3.4%, n = 21). Austria and The Netherlands reported no prescriptions of additional hormonal contraceptives and in France 8.3% (n = 2) of a total of 24 patients were prescribed additional hormonal contraceptives. The numbers for France and The Netherlands are too small to be reasonably interpreted.

Additional hormonal contraceptive use was observed in 35 out of a total of 936 CPA/EE prescriptions made by gynecologists (3.7%). In contrast, 3 out of 167 CPA/EE prescriptions by dermatologists (1.8%) and 6 out of 410 CPA/EE prescriptions by GPs (1.5%) were concomitant to additional hormonal contraceptives.

The above data are summarized in Table B5-B5.8 (see Annex)

10.6 Utilization of CPA/EE for the indication of acne and hirsutism

According to the updated label CPA/EE is indicated for the treatment of moderate to severe acne when topical therapy or systemic antibiotic treatments have failed, and for hirsutism in women of reproductive age.

Of overall 1513 patients (100%) the proportion of patients with moderate or severe acne without hirsutism was 37.3% (n = 564). 13.2% of the total study population (n = 199) had received “previous topical treatment only” and 2.2% (n = 34) “previous systemic antibiotic treatment only”. Of the 301 patients (19.9%) who had received “previous topical and/or systemic antibiotic treatment”, failed or insufficient treatment was reported for 249 cases (16.5%).

Analyzing for acne separately: Of 1028 patients diagnosed with acne, 586 (57.0%) received previous treatment. In 428 (41.6%) the treatment was reported to have failed. 564 (54.9%) patients in the category “moderate to severe acne without hirsutism”. Of these, 301 (29.3%) received previous topical treatment and/or systemic antibiotics, which had failed in 249 (24.2%) cases.

A total of 221 (14.6%) patients had a diagnosis of hirsutism.

522 patients (34.5% of the total study population) reflect an approximation of the strict in-label use of CPA/EE in the study population of 1513 patients: 301 patients with a diagnosis of moderate to severe acne who had “previous topical and/or systemic antibiotic treatment” and those with hirsutism (n = 221). (Tables B6 to B6.8 (see Annex)).

Table 9 shows the treatment for the indication of acne and hirsutism in users of CPA/EE.

It should be considered that the above analysis does not completely reflect CPA/EE use according to the updated indication wording, since the proportion of cases where previous treatment for acne had failed could not be reliably established. Restricting analysis within this report to cases where previous “failed treatment” is explicitly stated would ignore cases where unsatisfactory treatment results triggered the new treatment with CPA/EE.

The above data are summarized in Table B6-B6.8 (see Annex)

Table 9 – CPA/EE use and treatment for the indication of acne and hirsutism

	CPA/EE	95%-CI
Number (%) of eligible patients with	1513 (100%)	
Moderate or severe acne (without hirsutism)	564 (37.3%)	[29.8%;45.3%]
Previous topical treatment only	199 (13.2%)	[6.5%;22.8%]
Previous systemic antibiotic treatment only	34 (2.2%)	[1.2%;3.8%]
Previous topical and/or systemic antibiotic treatment	301 (19.9%)	[12.8%;28.7%]
No previous topical and systemic antibiotic treatment	263 (17.4%)	[12.5%;23.2%]
Other previous treatment only	60 (4.0%)	[2.6%;5.7%]
Missing	1 (0.1%)	[0.0%;0.4%]
Acne with hirsutism	118 (7.8%)	[5.7%;10.4%]
Previous topical treatment only	43 (2.8%)	[1.6%;4.6%]
Previous systemic antibiotic treatment only	6 (0.4%)	[0.1%;1.0%]
Previous topical and/or systemic antibiotic treatment	64 (4.2%)	[2.6%;6.5%]
No previous topical and systemic antibiotic treatment	54 (3.6%)	[2.3%;5.3%]
Other previous treatment only	13 (0.9%)	[0.4%;1.6%]
Missing	1 (0.1%)	[0.0%;0.4%]
Hirsutism (without acne)	103 (6.8%)	[4.8%;9.4%]
Neither moderate or severe acne nor hirsutism	728 (48.1%)	[39.4%;56.9%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 10MAY2016

"Previous topical treatment only" means that the patients received topical treatment (no systemic antibiotics) and may have received other treatments additionally excluding systemic antibiotics.

"Previous systemic antibiotic treatment only" means that the patients were prescribed a systemic antibiotic (no topical treatment) and may have received other treatments additionally excluding topical treatment.

"Previous topical and/or systemic antibiotic treatment" means that the patients received topical treatment and/or systemic antibiotic treatment and may have received other treatments additionally.

"No previous topical and systemic antibiotic treatment" means that the patients did not receive topical treatment and/or systemic antibiotic treatment but may have been treated with other treatments.

"Other previous treatments only" means that the patients did not receive topical treatment and/or systemic antibiotic treatment but do have been treated with other treatments.

10.6.1 Utilization of CPA/EE for the indication of acne and hirsutism by country

France had the highest proportion of patients with moderate to severe acne without hirsutism (58.3%; n = 14) and Spain the lowest (30.4%; n = 186). Austria had 33.0% (n = 93), Czech Republic 45.1% (n = 254) and The Netherlands 53.1% (n = 17). The proportion of "previous topical and/or systemic antibiotic treatment" ranged from 33.3% (n = 8) as the highest in France to 5.7% (n = 16) as the lowest value in Austria. Figures for the Czech Republic (24.9%; N=140), The Netherlands (18.8%; n = 6) and Spain 21.4% (n = 131) fell between France and Austria.

Acne with hirsutism and hirsutism without acne were most frequently stated in Spain with 12.1% and 14.1%, respectively.

10.6.2 Utilization of CPA/EE for the indication of acne and hirsutism by specialty

Diagnosis of moderate or severe acne without hirsutism varied across specialty groups; these accounted for 58.7% (n = 98) of the patients recruited by dermatologists, 37.8% (n = 354) recruited by gynecologists and 27.3% (n = 112) recruited by GPs. The proportion of "previous topical and/or systemic antibiotic treatment" was the highest for the dermatologists (43.1%; n = 72) and lowest for gynecologists (15.2%; n = 142). GPs reported previous antibiotic treatment in 21.2% of cases (n = 87).

Acne with hirsutism has been diagnosed most often amongst GPs (12.0%; n = 49). Dermatologists and gynecologists both had proportions between 6% and 7%.

Hirsutism without acne accounted for around 12% of the patients recruited by GPs and dermatologists and 3.4% of patients recruited by gynecologists.

10.7 CPA/EE use and androgen-sensitive diseases

In total, for 83.3% of all patients included in this study the prescribing physician either reported an underlying androgenic disease (acne, seborrhea, hirsutism, androgenetic alopecia or PCOS) or named at least one of these disease entities as a reason for today's CPA/EE prescription(Austria 76.6%, all other countries showed a proportion above 83%) (Table 10).

Stratified by physician specialty 99.4% of the CPA/EE prescriptions by dermatologists were prescribed to patients with an underlying androgenic disease. This number was slightly lower for gynecologists (83.0%) and GPs (77.6%).

Table 10 – CPA/EE use and androgen-sensitive diseases by country

	CPA/EE	95%-CI
Number (%) of eligible patients with at least one of the 5 androgen-sensitive diseases		
Austria	216 (76.6%)	[47.0%;94.4%]
Czech Republic	484 (86.0%)	[63.3%;97.2%]
France	23 (95.8%)	[73.9%;100.0%]
Spain	511 (83.5%)	[71.9%;91.7%]
The Netherlands	27 (84.4%)	[24.2%;100.0%]
Total	1261 (83.3%)	[73.8%;90.5%]

Date of analysis: 11MAY2016

11. Discussion

The reason for conducting this study was the request by the EMA to investigate the implementation of the revised label following the Article 107i referral in 2013: CPA/EE should only be used for the treatment of moderate to severe acne related to androgen-sensitivity (with or without seborrhea) or hirsutism in women of reproductive age.

For the treatment of acne, these medicines should only be used after topical therapy or systemic antibiotic treatment had failed.

Since CPA/EE acts also as a hormonal contraceptive it should not be used in combination with other hormonal contraceptives.

In order to assess the degree to which these recommendations are being followed, the current practice of gynecologists, dermatologists, and GPs prescribing CPA/EE has been recorded and the reasons for prescription have been explicitly collected in this survey drug utilization study.

The original goal for the number of CPA/EE prescriptions, i.e. 1,000 per participating country, could not be met in this study (Austria 282; Czech Republic 563; France 24; The Netherlands 32; Spain 612). This was mainly driven by a lack of interest on the side of the physicians when they were invited to take part in this DUS. The specific investigation into this phenomenon in The Netherlands, where recruitment of physicians was particularly difficult, showed an extremely low level of interest in the study (see Section 10.1.1). It is of note also that the expected prescribing frequency per participating physician (4 per patients per month) did not match with the prescribing behavior in routine clinical practice in any of the countries. Extensive additional efforts (e.g. to the extent of contacting all

gynecologists and dermatologists in Austria and the Czech Republic) were made to deal with this trend, with very little success.

In France, the formal approval process was only completed when the data collection of this study was coming to an end. As a consequence of these obstacles the data collection period of the DUS CPA/EE was prolonged to the maximum extent that would still allow compliance with the date for the final report.

Overall, the total of over 1,500 sets of prescription data collected is sufficient for general conclusions on an aggregate European level. As foreseen in the statistical analysis plan, analyses per country have also been done, but data on the individual country level allowing meaningful interpretation are limited. Only Spain and the Czech Republic, and to some degree Austria provide samples that allow meaningful country-specific interpretation of the data outside the pooled data. Additionally, comparisons between countries are also compromised because the varying distribution of specialties between the participating countries.

The overall analysis across all participating countries and medical specialties shows that in the majority of cases (n = 1,261; 83.3%) the diagnosis and/or the reason for prescription were related to androgen-dependent conditions.

The 221 cases suffering from hirsutism are prescribed strictly within the current label, since hirsutism is an indication that requires neither quantification nor previous treatment.

In the case of the 1,028 cases of acne, the situation is more complex because of the two additional conditions that required fulfilment: 1. the acne has to be classified as moderate or severe, in order to qualify for treatment with CPA/EE, 2. previous treatment with topical therapy or with systemic antibiotics must have failed. The actual distribution was as follows:

Of the 1,513 recruited patients 1,028 (67.9%) had either been diagnosed with acne and/or acne was given as the reason for the prescription. 564 of these patients without hirsutism were classified into the categories moderate and severe. Since the questionnaire did not state which point in time the severity referred to, i.e. at the time of the prescription of CPA/EE or an earlier status of the disease that has been addressed only insufficiently by the previous treatment scheme some ambiguity remains with the data captured. Furthermore, the categorization of acne in mild, moderate or severe may be subjective depending on individual physicians. Qualified previous treatment (topical treatment or systemic antibiotics) for moderate to severe acne was documented in 301 cases.

The data reflect different treatment patterns between specialties. GPs started CPA/EE in moderate to severe acne after preceding topical therapy or systemic antibiotic treatment in 77.7% of the cases.

Dermatologists tend to start with topical treatment or systemic antibiotic (73.5%) before turning to CPA/EE. Prescriptions of CPA/EE by gynecologists are less frequently (40.1%) preceded by topical treatment or systemic antibiotics. This contrast might be exaggerated because of two potential modulating factors. Firstly, the documentation of previous treatments, especially with OTCs and with cosmeceuticals might be less complete when done by gynecologists (who are less familiar with these treatment modalities), than by dermatologists (who work with topical treatments on a daily basis).

Secondly, it is not unlikely that the patients seeking the help of gynecologists differ from those that consult dermatologists. Gynecological symptoms pointing to more pronounced hormonal problems, e.g. those associated with PCOS, would channel patients in the direction of gynecologists. The focus on endocrine pathophysiology might, therefore, be more prominent for gynecologists than in everyday dermatological practice.

Overall, previous treatment failure was documented for 73.0% of the 586 cases of acne treatment. Whether the 27.0% had really been completely successful or whether the patients regarded them as sufficient/satisfactory remains unclear, especially as the questionnaire was completed by the physician and the patient's perspective was not directly targeted. The term treatment failure covers a broad range of constellations and cannot capture the clinical situation comprehensively. Failure could either mean total lack of efficacy or unsatisfactory efficacy or unpleasant side effects (e.g. burning sensation with topical treatments; diarrhea or other gastrointestinal symptoms with systemic antibiotics). However, the fact that a new treatment modality is being initiated gives some indication that the preceding measures might have not been adequate for the given patient.

Altogether, on an aggregate level, the study is informative with regard to the clinical scenario when prescribing CPA/EE by gynecologists, dermatologists, and GPs. Most prescriptions are directed at one of the diseases with a pathophysiology associated with androgenic action.

11.1 Key results

1,513 patients with CPA/EE prescriptions were recruited.

<u>Prescription indications for CPA/EE:</u>

Overall, 83.3% (n = 1,261) of all prescriptions were directed at patients with at least one condition with a pathophysiology associated with androgenicity. The main reason for prescription of CPA/EE was acne (65.6%, n = 993). Other androgen-dependent conditions ranged from 12.9% (n = 195) for seborrhea to 5.0% (n = 75) for androgenetic alopecia. Contraception was reported as one of the

reasons for the prescriptions in 66.7% (n = 1,009). In 16.3% of cases the prescriptions were made due to contraception only, predominantly by GPs and gynecologists.

Use of CPA/EE in accordance with the updated label:

Of 522 patients (34.5% of the total study population of 1,513 patients) 301 (19.9%) patients had a diagnosis of moderate to severe acne with "previous topical and/or systemic antibiotic treatment" and 221 (14.6%) had hirsutism.

In the category "moderate to severe acne without hirsutism" (37.3%n = 564) previous treatment with topical agents and/or systemic antibiotics was prescribed to19.9% (n = 301). With respect to these 564 patients dermatologists (73.5%) and GPs (77.7%) prescribed CPA/EE for acne according to the label more often than gynecologists (40.1%), whose patients are more likely to have been prescribed hormonal therapy in the form of CPA/EE without such preceding therapy.

Concomitant use of CPA/EE and other combined hormonal contraceptives:

The prescription of CPA/EE together with another hormonal contraceptive was 2.9% (n = 44). Of those 42 were oral contraceptives and 2 non-oral contraceptives. Most of the concomitant prescriptions (n=35) were reported by gynecologists.

Second-line treatment of CPA/EE for the indication acne:

Of the 1,028 patients diagnosed with acne, 586 (57.0%) received previous treatment and in 428 (41.6%) the treatment was reported to have failed. There were 564 (54.9%) patients in the category "moderate to severe acne without hirsutism". Of these, 301 (29.3%) received previous topical treatment and/or systemic antibiotics, which had failed in 249 (24.2%) cases.

11.2 Limitations of the research methods

This survey is based on the willingness of physicians to provide information about their reasons for prescribing CPA/EE. The data cannot indicate whether there is a difference in prescribing habits between participating and non-participating physicians, so that a degree of bias cannot be excluded. Selection of patients can be reduced by sequential request for participation of patients. The information about previous treatments of acne is likely to be incomplete because of recall bias, especially for OTC treatments, cosmeceuticals and special therapies like light-therapies (e.g. UV-radiation).

Since the study did not reach the original goal of 1,000 prescriptions per country, the sample sizes are not representative for all the individual countries. Nevertheless, because the information

acquisition was directly based on the prescribers themselves, the achieved 1,513 prescriptions can provide some insight into the prescribing habits of European physicians.

The generalizability of such patient data collected in existing physicians networks has been questioned in the past, but the comparison of a large women's health study conducted by ZEG and pooled information from National Health Surveys (which were found to be representative for the general population) showed good agreement, indicating an acceptable level of generalizability of cross-sectional results for the general population (13).

There were two levels of non-participation in this study. The first was at the level of physician recruitment. The second was at the level of patient recruitment by the participating physician. The factors determining physicians' participation in the study and their diligence regarding documentation are critical in this study: Firstly, the interest of physicians to participate in this study was very low, as expressed by the low rate of actual participation. Secondly, the ongoing discussions regarding restrictions of indication have led to a degree of scepticism on the part of the prescribing physicians. The feedback from many physicians approached indicated that they do not prescribe CPA/EE at all or very rarely. The informed consent requirement added an additional burden to both, patient and physician, further limiting recruitment.

If the recruitment guidelines are not strictly observed, there is a risk that the selection of cases could lead to a skewed sample and thereby undermine representativeness. Therefore, in order to avoid any pre-selection of participants, the physicians were instructed to ensure that all eligible patients (i.e., all those receiving a prescription for CPA/EE) were asked whether they were willing to take part in the study.

Despite the limitations the study provided an overall picture of the CPA/EE use by the prescribing physicians.

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13. Appendix DUS CPA/EE - Tables (SAP)

Section A - Administrative data

Table A1 - Physician recruitment by country

	Austria	Czech Republic	France	The Netherlands	Spain	**Total**
Number (%) of contacted physicians	718 (100%)	695 (100%)	276 (100%)	802 (100%)	139 (100%)	**2630 (100%)**
Participating	119 (16.6%)	44 (6.3%)	37 (13.4%)	19 (2.4%)	95 (68.3%)	**314 (11.9%)**
Active	22 (3.1%)	32 (4.6%)	8 (2.9%)	7 (0.9%)	51 (36.7%)	**120 (4.6%)**
Non-participating	599 (83.4%)	651 (93.7%)	239 (86.6%)	783 (97.6%)	44 (31.7%)	**2316 (88.1%)**
Physician has been screened out (no CPA/EE prescriptions)	92 (12.8%)	346 (49.8%)	8 (2.9%)	34 (4.2%)	23 (16.5%)	**503 (19.1%)**
Physician has been screened out (too low number of CPA/EE prescriptions)	243 (33.8%)	179 (25.8%)	58 (21.0%)	8 (1.0%)	14 (10.1%)	**502 (19.1%)**
Physician declined (generally/without giving a reason)	3 (0.4%)	3 (0.4%)	9 (3.3%)	1 (0.1%)	0 (0.0%)	**16 (0.6%)**
Physician declined (due to scope of survey)	0 (0.0%)	4 (0.6%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	**5 (0.2%)**
Physician declined (due to possibility of validation in doctor's office)	0 (0.0%)	2 (0.3%)	4 (1.4%)	3 (0.4%)	0 (0.0%)	**9 (0.3%)**
Physician declined (due to payment)	0 (0.0%)	81 (11.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**81 (3.1%)**
Physician declined (due to no interest in studies)	119 (16.6%)	30 (4.3%)	11 (4.0%)	0 (0.0%)	0 (0.0%)	**160 (6.1%)**
Physician declined (due to lack of time/too time-consuming)	68 (9.5%)	4 (0.6%)	23 (8.3%)	10 (1.2%)	0 (0.0%)	**105 (4.0%)**
Physician declined (due to retirement/close of practice)	16 (2.2%)	2 (0.3%)	2 (0.7%)	0 (0.0%)	0 (0.0%)	**20 (0.8%)**
Other reason	58 (8.1%)	0 (0.0%)	0 (0.0%)	3 (0.4%)	7 (5.0%)	**68 (2.6%)**
Missing	0 (0.0%)	0 (0.0%)	124 (44.9%)	723 (90.1%)	0 (0.0%)	**847 (32.2%)**

Participating physicians are defined as those that agreed to participate (irrespective of returned questionnaires).
Active physicians are defined as those that returned at least one analyzable questionnaire (including a corresponding informed consent from the woman).
Non-participating physicians are defined as those who had not signed the physician information and therefore, declined participation.
Date of analysis: 12MAY2016

Table A1.1 Physician recruitment by country - gynecology

	Austria	Czech Republic	France	The Netherlands	Spain	**Total**
Number (%) of contacted physicians	495 (100%)	276 (100%)	106 (100%)	1 (100%)	50 (100%)	**928 (100%)**
Participating	115 (23.2%)	33 (12.0%)	22 (20.8%)	1 (100%)	27 (54.0%)	**198 (21.3%)**
Active	22 (4.4%)	26 (9.4%)	4 (3.8%)	0 (0.0%)	11 (22.0%)	**63 (6.8%)**
Non-participating	380 (76.8%)	243 (88.0%)	84 (79.2%)	0 (0.0%)	23 (46.0%)	**730 (78.7%)**
Physician has been screened out (no CPA/EE prescriptions)	14 (2.8%)	104 (37.7%)	3 (2.8%)	0 (0.0%)	15 (30.0%)	**136 (14.7%)**
Physician has been screened out (too low number of CPA/EE prescriptions)	207 (41.8%)	85 (30.8%)	20 (18.9%)	0 (0.0%)	4 (8.0%)	**316 (34.1%)**
Physician declined (generally/without giving a reason)	3 (0.6%)	2 (0.7%)	3 (2.8%)	0 (0.0%)	0 (0.0%)	**8 (0.9%)**
Physician declined (due to scope of survey)	0 (0.0%)	4 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**4 (0.4%)**
Physician declined (due to possibility of validation in doctor's office)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	**1 (0.1%)**
Physician declined (due to payment)	0 (0.0%)	23 (8.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**23 (2.5%)**
Physician declined (due to no interest in studies)	62 (12.5%)	19 (6.9%)	3 (2.8%)	0 (0.0%)	0 (0.0%)	**84 (9.1%)**
Physician declined (due to lack of time/too time-consuming)	64 (12.9%)	4 (1.4%)	7 (6.6%)	0 (0.0%)	0 (0.0%)	**75 (8.1%)**
Physician declined (due to retirement/close of practice)	13 (2.6%)	2 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**15 (1.6%)**
Other reason	17 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (8.0%)	**21 (2.3%)**
Missing	0 (0.0%)	0 (0.0%)	47 (44.3%)	0 (0.0%)	0 (0.0%)	**47 (5.1%)**

Participating physicians are defined as those that agreed to participate (irrespective of returned questionnaires).
Active physicians are defined as those that returned at least one analyzable questionnaire (including a corresponding informed consent from the woman).
Non-participating physicians are defined as those who had not signed the physician information and therefore, declined participation.
Date of analysis: 12MAY2016

Table A1.2 Physician recruitment by country - dermatology

	Austria	Czech Republic	France	The Netherlands	Spain	**Total**
Number (%) of contacted physicians	223 (100%)	419 (100%)	54 (100%)	53 (100%)	42 (100%)	**791 (100%)**
Participating	4 (1.8%)	11 (2.6%)	8 (14.8%)	2 (3.8%)	28 (66.7%)	**53 (6.7%)**
Active	0 (0.0%)	6 (1.4%)	2 (3.7%)	1 (1.9%)	8 (19.0%)	**17 (2.1%)**
Non-participating	219 (98.2%)	408 (97.4%)	46 (85.2%)	51 (96.2%)	14 (33.3%)	**738 (93.3%)**
Physician has been screened out (no CPA/EE prescriptions)	78 (35.0%)	242 (57.8%)	2 (3.7%)	14 (26.4%)	5 (11.9%)	**341 (43.1%)**
Physician has been screened out (too low number of CPA/EE prescriptions)	36 (16.1%)	94 (22.4%)	11 (20.4%)	2 (3.8%)	8 (19.0%)	**151 (19.1%)**
Physician declined (generally/without giving a reason)	0 (0.0%)	1 (0.2%)	3 (5.6%)	0 (0.0%)	0 (0.0%)	**4 (0.5%)**
Physician declined (due to scope of survey)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Physician declined (due to possibility of validation in doctor's office)	0 (0.0%)	2 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**2 (0.3%)**
Physician declined (due to payment)	0 (0.0%)	58 (13.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**58 (7.3%)**
Physician declined (due to no interest in studies)	57 (25.6%)	11 (2.6%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	**69 (8.7%)**
Physician declined (due to lack of time/too time-consuming)	4 (1.8%)	0 (0.0%)	4 (7.4%)	0 (0.0%)	0 (0.0%)	**8 (1.0%)**
Physician declined (due to retirement/close of practice)	3 (1.3%)	0 (0.0%)	1 (1.9%)	0 (0.0%)	0 (0.0%)	**4 (0.5%)**
Other reason	41 (18.4%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	1 (2.4%)	**43 (5.4%)**
Missing	0 (0.0%)	0 (0.0%)	24 (44.4%)	34 (64.2%)	0 (0.0%)	**58 (7.3%)**

Participating physicians are defined as those that agreed to participate (irrespective of returned questionnaires).
Active physicians are defined as those that returned at least one analyzable questionnaire (including a corresponding informed consent from the woman).
Non-participating physicians are defined as those who had not signed the physician information and therefore, declined participation.
Date of analysis: 12MAY2016

Table A1.3 Physician recruitment by country - general practitioner (GP)

	Austria	Czech Republic	France	The Netherlands	Spain	**Total**
Number (%) of contacted physicians	0 (0.0%)	0 (0.0%)	116 (100%)	748 (100%)	47 (100%)	**911 (100%)**
Participating	0 (0.0%)	0 (0.0%)	7 (6.0%)	16 (2.1%)	40 (85.1%)	**63 (6.9%)**
Active	0 (0.0%)	0 (0.0%)	2 (1.7%)	6 (0.8%)	32 (68.1%)	**40 (4.4%)**
Non-participating	0 (0.0%)	0 (0.0%)	109 (94.0%)	732 (97.9%)	7 (14.9%)	**848 (93.1%)**
Physician has been screened out (no CPA/EE prescriptions)	0 (0.0%)	0 (0.0%)	3 (2.6%)	20 (2.7%)	3 (6.4%)	**26 (2.9%)**
Physician has been screened out (too low number of CPA/EE prescriptions)	0 (0.0%)	0 (0.0%)	27 (23.3%)	6 (0.8%)	2 (4.3%)	**35 (3.8%)**
Physician declined (generally/without giving a reason)	0 (0.0%)	0 (0.0%)	3 (2.6%)	1 (0.1%)	0 (0.0%)	**4 (0.4%)**
Physician declined (due to scope of survey)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	**1 (0.1%)**
Physician declined (due to possibility of validation in doctor's office)	0 (0.0%)	0 (0.0%)	3 (2.6%)	3 (0.4%)	0 (0.0%)	**6 (0.7%)**
Physician declined (due to payment)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Physician declined (due to no interest in studies)	0 (0.0%)	0 (0.0%)	7 (6.0%)	0 (0.0%)	0 (0.0%)	**7 (0.8%)**
Physician declined (due to lack of time/too time-consuming)	0 (0.0%)	0 (0.0%)	12 (10.3%)	10 (1.3%)	0 (0.0%)	**22 (2.4%)**
Physician declined (due to retirement/close of practice)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	**1 (0.1%)**
Other reason	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.3%)	2 (4.3%)	**4 (0.4%)**
Missing	0 (0.0%)	0 (0.0%)	53 (45.7%)	689 (92.1%)	0 (0.0%)	**742 (81.4%)**

Participating physicians are defined as those that agreed to participate (irrespective of returned questionnaires).
Active physicians are defined as those that returned at least one analyzable questionnaire (including a corresponding informed consent from the woman).
Non-participating physicians are defined as those who had not signed the physician information and therefore, declined participation.
Date of analysis: 12MAY2016

Table A2 - Physician age by participation

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	314 (100%)	2316 (100%)	**2630 (100%)**
Age (years)			
n	226 (72.0%)	370 (16.0%)	**596 (22.7%)**
Missing	88 (28.0%)	1946 (84.0%)	**2034 (77.3%)**
Mean	52.2	53.1	**52.8**
SD	8.52	9.59	**9.20**
Min	27	29	**27**
Q1	46.0	47.0	**46.0**
Median	53.0	54.0	**54.0**
Q3	59.0	60.0	**60.0**
Max	70	78	**78**
Age groups (years)			
<30	1 (0.3%)	1 (0.0%)	**2 (0.1%)**
30 - 39	14 (4.5%)	35 (1.5%)	**49 (1.9%)**
40 - 49	71 (22.6%)	76 (3.3%)	**147 (5.6%)**
50 - 59	89 (28.3%)	151 (6.5%)	**240 (9.1%)**
>= 60	51 (16.2%)	107 (4.6%)	**158 (6.0%)**
Missing	88 (28.0%)	1946 (84.0%)	**2034 (77.3%)**

Date of analysis: 12MAY2016

Table A2.1 Physician age by participation - Austria

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	119 (100%)	599 (100%)	**718 (100%)**
Age (years)			
n	80 (67.2%)	112 (18.7%)	**192 (26.7%)**
Missing	39 (32.8%)	487 (81.3%)	**526 (73.3%)**
Mean	52.5	53.8	**53.2**
SD	7.87	8.44	**8.21**
Min	34	36	**34**
Q1	48.0	50.0	**48.5**
Median	51.5	52.5	**52.0**
Q3	58.0	58.0	**58.0**
Max	69	77	**77**
Age groups (years)			
<30	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
30 - 39	3 (2.5%)	3 (0.5%)	**6 (0.8%)**
40 - 49	30 (25.2%)	24 (4.0%)	**54 (7.5%)**
50 - 59	31 (26.1%)	62 (10.4%)	**93 (13.0%)**
>= 60	16 (13.4%)	23 (3.8%)	**39 (5.4%)**
Missing	39 (32.8%)	487 (81.3%)	**526 (73.3%)**

Date of analysis: 12MAY2016

Table A2.2 Physician age by participation - Czech Republic

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	44 (100%)	651 (100%)	**695 (100%)**
Age (years)			
n	37 (84.1%)	56 (8.6%)	**93 (13.4%)**
Missing	7 (15.9%)	595 (91.4%)	**602 (86.6%)**
Mean	52.1	52.9	**52.6**
SD	9.38	10.28	**9.89**
Min	27	33	**27**
Q1	46.0	45.0	**45.0**
Median	51.0	52.0	**52.0**
Q3	58.0	60.0	**60.0**
Max	67	78	**78**
Age groups (years)			
<30	1 (2.3%)	0 (0.0%)	**1 (0.1%)**
30 - 39	1 (2.3%)	3 (0.5%)	**4 (0.6%)**
40 - 49	10 (22.7%)	17 (2.6%)	**27 (3.9%)**
50 - 59	16 (36.4%)	21 (3.2%)	**37 (5.3%)**
>= 60	9 (20.5%)	15 (2.3%)	**24 (3.5%)**
Missing	7 (15.9%)	595 (91.4%)	**602 (86.6%)**

Date of analysis: 12MAY2016

Table A2.3 Physician age by participation - France

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	37 (100%)	239 (100%)	**276 (100%)**
Age (years)			
n	37 (100%)	133 (55.6%)	**170 (61.6%)**
Missing	0 (0.0%)	106 (44.4%)	**106 (38.4%)**
Mean	57.0	55.2	**55.6**
SD	7.53	9.76	**9.33**
Min	35	29	**29**
Q1	54.0	50.0	**50.0**
Median	60.0	59.0	**59.0**
Q3	61.0	62.0	**62.0**
Max	67	68	**68**
Age groups (years)			
<30	0 (0.0%)	1 (0.4%)	**1 (0.4%)**
30 - 39	2 (5.4%)	15 (6.3%)	**17 (6.2%)**
40 - 49	2 (5.4%)	13 (5.4%)	**15 (5.4%)**
50 - 59	14 (37.8%)	41 (17.2%)	**55 (19.9%)**
>= 60	19 (51.4%)	63 (26.4%)	**82 (29.7%)**
Missing	0 (0.0%)	106 (44.4%)	**106 (38.4%)**

Date of analysis: 12MAY2016

Table A2.4 Physician age by participation - The Netherlands

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	19 (100%)	783 (100%)	**802 (100%)**
Age (years)			
n	12 (63.2%)	34 (4.3%)	**46 (5.7%)**
Missing	7 (36.8%)	749 (95.7%)	**756 (94.3%)**
Mean	50.5	47.9	**48.6**
SD	12.64	9.00	**9.99**
Min	31	30	**30**
Q1	39.5	41.0	**41.0**
Median	53.0	47.5	**49.5**
Q3	59.5	56.0	**56.0**
Max	70	64	**70**
Age groups (years)			
<30	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
30 - 39	3 (15.8%)	5 (0.6%)	**8 (1.0%)**
40 - 49	2 (10.5%)	13 (1.7%)	**15 (1.9%)**
50 - 59	4 (21.1%)	13 (1.7%)	**17 (2.1%)**
>= 60	3 (15.8%)	3 (0.4%)	**6 (0.7%)**
Missing	7 (36.8%)	749 (95.7%)	**756 (94.3%)**

Date of analysis: 12MAY2016

Table A2.5 Physician age by participation - Spain

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	95 (100%)	44 (100%)	**139 (100%)**
Age (years)			
n	60 (63.2%)	35 (79.5%)	**95 (68.3%)**
Missing	35 (36.8%)	9 (20.5%)	**44 (31.7%)**
Mean	49.4	48.4	**49.1**
SD	7.28	8.80	**7.84**
Min	35	32	**32**
Q1	44.0	39.0	**43.0**
Median	49.0	49.0	**49.0**
Q3	55.5	56.0	**56.0**
Max	64	65	**65**
Age groups (years)			
<30	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
30 - 39	5 (5.3%)	9 (20.5%)	**14 (10.1%)**
40 - 49	27 (28.4%)	9 (20.5%)	**36 (25.9%)**
50 - 59	24 (25.3%)	14 (31.8%)	**38 (27.3%)**
>= 60	4 (4.2%)	3 (6.8%)	**7 (5.0%)**
Missing	35 (36.8%)	9 (20.5%)	**44 (31.7%)**

Date of analysis: 12MAY2016

Table A3 - Physician gender by participation

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	314 (100%)	2316 (100%)	**2630 (100%)**
Gender			
Male	181 (57.6%)	1041 (44.9%)	**1222 (46.5%)**
Female	133 (42.4%)	1222 (52.8%)	**1355 (51.5%)**
Missing	0 (0.0%)	53 (2.3%)	**53 (2.0%)**

Date of analysis: 12MAY2016

Table A3.1 Physician gender by participation - Austria

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	119 (100%)	599 (100%)	**718 (100%)**
Gender			
Male	71 (59.7%)	373 (62.3%)	**444 (61.8%)**
Female	48 (40.3%)	226 (37.7%)	**274 (38.2%)**
Missing	0 (0.0%)	0 (0.0%)	**0 (0.0%)**

Date of analysis: 12MAY2016

Table A3.2 Physician gender by participation - Czech Republic

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	44 (100%)	651 (100%)	**695 (100%)**
Gender			
Male	21 (47.7%)	195 (30.0%)	**216 (31.1%)**
Female	23 (52.3%)	404 (62.1%)	**427 (61.4%)**
Missing	0 (0.0%)	52 (8.0%)	**52 (7.5%)**

Date of analysis: 12MAY2016

Table A3.3 Physician gender by participation - France

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	37 (100%)	239 (100%)	**276 (100%)**
Gender			
Male	17 (45.9%)	125 (52.3%)	**142 (51.4%)**
Female	20 (54.1%)	113 (47.3%)	**133 (48.2%)**
Missing	0 (0.0%)	1 (0.4%)	**1 (0.4%)**

Date of analysis: 12MAY2016

Table A3.4 Physician gender by participation - The Netherlands

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	19 (100%)	783 (100%)	**802 (100%)**
Gender			
Male	12 (63.2%)	328 (41.9%)	**340 (42.4%)**
Female	7 (36.8%)	455 (58.1%)	**462 (57.6%)**
Missing	0 (0.0%)	0 (0.0%)	**0 (0.0%)**

Date of analysis: 12MAY2016

Table A3.5 Physician gender by participation - Spain

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	95 (100%)	44 (100%)	**139 (100%)**
Gender			
Male	60 (63.2%)	20 (45.5%)	**80 (57.6%)**
Female	35 (36.8%)	24 (54.5%)	**59 (42.4%)**
Missing	0 (0.0%)	0 (0.0%)	**0 (0.0%)**

Date of analysis: 12MAY2016

Table A4 - Physician specialty by participation

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	314 (100%)	2316 (100%)	**2630 (100%)**
Specialty			
Gynecology	198 (63.1%)	730 (31.5%)	**928 (35.3%)**
Dermatology	53 (16.9%)	738 (31.9%)	**791 (30.1%)**
General Practitioner (GP)	63 (20.1%)	848 (36.6%)	**911 (34.6%)**

Date of analysis: 12MAY2016

Table A4.1 Physician specialty by participation - Austria

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	119 (100%)	599 (100%)	**718 (100%)**
Specialty			
Gynecology	115 (96.6%)	380 (63.4%)	**495 (68.9%)**
Dermatology	4 (3.4%)	219 (36.6%)	**223 (31.1%)**
General Practitioner (GP)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**

Date of analysis: 12MAY2016

Table A4.2 Physician specialty by participation - Czech Republic

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	44 (100%)	651 (100%)	**695 (100%)**
Specialty			
Gynecology	33 (75.0%)	243 (37.3%)	**276 (39.7%)**
Dermatology	11 (25.0%)	408 (62.7%)	**419 (60.3%)**
General Practitioner (GP)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**

Date of analysis: 12MAY2016

Table A4.3 Physician specialty by participation - France

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	37 (100%)	239 (100%)	**276 (100%)**
Specialty			
Gynecology	22 (59.5%)	84 (35.1%)	**106 (38.4%)**
Dermatology	8 (21.6%)	46 (19.2%)	**54 (19.6%)**
General Practitioner (GP)	7 (18.9%)	109 (45.6%)	**116 (42.0%)**

Date of analysis: 12MAY2016

Table A4.4 Physician specialty by participation - The Netherlands

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	19 (100%)	783 (100%)	**802 (100%)**
Specialty			
Gynecology	1 (5.3%)	0 (0.0%)	**1 (0.1%)**
Dermatology	2 (10.5%)	51 (6.5%)	**53 (6.6%)**
General Practitioner (GP)	16 (84.2%)	732 (93.5%)	**748 (93.3%)**

Date of analysis: 12MAY2016

Table A4.5 Physician specialty by participation - Spain

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	95 (100%)	44 (100%)	**139 (100%)**
Specialty			
Gynecology	27 (28.4%)	23 (52.3%)	**50 (36.0%)**
Dermatology	28 (29.5%)	14 (31.8%)	**42 (30.2%)**
General Practitioner (GP)	40 (42.1%)	7 (15.9%)	**47 (33.8%)**

Date of analysis: 12MAY2016

Table A5 - Physician level of experience by participation

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	314 (100%)	2316 (100%)	**2630 (100%)**
Level of experience (years in medical professional life)			
< 1	0 (0.0%)	1 (0.0%)	**1 (0.0%)**
1 - 4	4 (1.3%)	13 (0.6%)	**17 (0.6%)**
5 - 9	17 (5.4%)	21 (0.9%)	**38 (1.4%)**
10 - 14	29 (9.2%)	48 (2.1%)	**77 (2.9%)**
>= 15	223 (71.0%)	342 (14.8%)	**565 (21.5%)**
Missing	41 (13.1%)	1891 (81.6%)	**1932 (73.5%)**

Date of analysis: 12MAY2016

Table A5.1 Physician level of experience by participation - Austria

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	119 (100%)	599 (100%)	**718 (100%)**
Level of experience (years in medical professional life)			
< 1	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
1 - 4	0 (0.0%)	1 (0.2%)	**1 (0.1%)**
5 - 9	1 (0.8%)	3 (0.5%)	**4 (0.6%)**
10 - 14	8 (6.7%)	9 (1.5%)	**17 (2.4%)**
>= 15	82 (68.9%)	124 (20.7%)	**206 (28.7%)**
Missing	28 (23.5%)	462 (77.1%)	**490 (68.2%)**

Date of analysis: 12MAY2016

Table A5.2 Physician level of experience by participation - Czech Republic

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	44 (100%)	651 (100%)	**695 (100%)**
Level of experience (years in medical professional life)			
< 1	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
1 - 4	1 (2.3%)	0 (0.0%)	**1 (0.1%)**
5 - 9	0 (0.0%)	2 (0.3%)	**2 (0.3%)**
10 - 14	3 (6.8%)	8 (1.2%)	**11 (1.6%)**
>= 15	34 (77.3%)	67 (10.3%)	**101 (14.5%)**
Missing	6 (13.6%)	574 (88.2%)	**580 (83.5%)**

Date of analysis: 12MAY2016

Table A5.3 Physician level of experience by participation - France

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	37 (100%)	239 (100%)	**276 (100%)**
Level of experience (years in medical professional life)			
< 1	0 (0.0%)	1 (0.4%)	**1 (0.4%)**
1 - 4	0 (0.0%)	6 (2.5%)	**6 (2.2%)**
5 - 9	2 (5.4%)	7 (2.9%)	**9 (3.3%)**
10 - 14	1 (2.7%)	9 (3.8%)	**10 (3.6%)**
>= 15	34 (91.9%)	109 (45.6%)	**143 (51.8%)**
Missing	0 (0.0%)	107 (44.8%)	**107 (38.8%)**

Date of analysis: 12MAY2016

Table A5.4 Physician level of experience by participation - The Netherlands

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	19 (100%)	783 (100%)	**802 (100%)**
Level of experience (years in medical professional life)			
< 1	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
1 - 4	1 (5.3%)	3 (0.4%)	**4 (0.5%)**
5 - 9	2 (10.5%)	3 (0.4%)	**5 (0.6%)**
10 - 14	1 (5.3%)	11 (1.4%)	**12 (1.5%)**
>= 15	8 (42.1%)	18 (2.3%)	**26 (3.2%)**
Missing	7 (36.8%)	748 (95.5%)	**755 (94.1%)**

Date of analysis: 12MAY2016

Table A5.5 Physician level of experience by participation - Spain

	Participating physicians	Non-participating physicians	**Total**
Number (%) of contacted physicians	95 (100%)	44 (100%)	**139 (100%)**
Level of experience (years in medical professional life)			
< 1	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
1 - 4	2 (2.1%)	3 (6.8%)	**5 (3.6%)**
5 - 9	12 (12.6%)	6 (13.6%)	**18 (12.9%)**
10 - 14	16 (16.8%)	11 (25.0%)	**27 (19.4%)**
>= 15	65 (68.4%)	24 (54.5%)	**89 (64.0%)**
Missing	0 (0.0%)	0 (0.0%)	**0 (0.0%)**

Date of analysis: 12MAY2016

Table A6 - Patient recruitment by country

	Austria	Czech Republic	France	The Netherlands	Spain	**Total**
Number (%) of recruited patients	292 (100%)	581 (100%)	24 (100%)	45 (100%)	632 (100%)	**1574 (100%)**
Eligible	282 (96.6%)	563 (96.9%)	24 (100%)	32 (71.1%)	612 (96.8%)	**1513 (96.1%)**
Ineligible	10 (3.4%)	18 (3.1%)	0 (0.0%)	13 (28.9%)	20 (3.2%)	**61 (3.9%)**
Duplicate	0 (0.0%)	5 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**5 (0.3%)**
No complete informed consent available	1 (0.3%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	20 (3.2%)	**22 (1.4%)**
No Baseline questionnaire available	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.4%)	0 (0.0%)	**2 (0.1%)**
Recruited after study recruitment closure	1 (0.3%)	11 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**12 (0.8%)**
No CPA/EE prescription	8 (2.7%)	2 (0.3%)	0 (0.0%)	10 (22.2%)	0 (0.0%)	**20 (1.3%)**

Date of analysis: 12MAY2016

Table A7 - Number of eligible patients by physician specialty and country

	Austria	Czech Republic	France	The Netherlands	Spain	**Total**
Number (%) of eligible patients	282 (100%)	563 (100%)	24 (100%)	32 (100%)	612 (100%)	**1513 (100%)**
Specialty						
Gynecology	282 (100%)	526 (93.4%)	7 (29.2%)	0 (0.0%)	121 (19.8%)	**936 (61.9%)**
Dermatology	0 (0.0%)	37 (6.6%)	12 (50.0%)	8 (25.0%)	110 (18.0%)	**167 (11.0%)**
General Practitioner (GP)	0 (0.0%)	0 (0.0%)	5 (20.8%)	24 (75.0%)	381 (62.3%)	**410 (27.1%)**

Date of analysis: 12MAY2016

Section B - Demographic and prescription data

Table B1 - Age distribution of eligible patients

	CPA/EE
Number (%) of eligible patients	1513 (100%)
Age (years)	
n	1513 (100%)
Missing	0 (0.0%)
Mean	26.0
SD	7.90
Min	13
Q1	20.1
Median	24.3
Q3	30.2
Max	60
Age groups (years)	
<18	198 (13.1%)
18 - 24	608 (40.2%)
25 - 34	507 (33.5%)
35 - 49	186 (12.3%)
>=50	14 (0.9%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B1.1 Age distribution of eligible patients - Austria

	CPA/EE
Number (%) of eligible patients	282 (100%)
Age (years)	
n	282 (100%)
Missing	0 (0.0%)
Mean	24.5
SD	7.42
Min	13
Q1	18.9
Median	22.9
Q3	28.0
Max	49
Age groups (years)	
<18	54 (19.1%)
18 - 24	113 (40.1%)
25 - 34	82 (29.1%)
35 - 49	33 (11.7%)
>=50	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B1.2 Age distribution of eligible patients - Czech Republic

	CPA/EE
Number (%) of eligible patients	563 (100%)
Age (years)	
n	563 (100%)
Missing	0 (0.0%)
Mean	25.9
SD	8.79
Min	14
Q1	18.9
Median	23.8
Q3	31.2
Max	60
Age groups (years)	
<18	101 (17.9%)
18 - 24	212 (37.7%)
25 - 34	163 (29.0%)
35 - 49	78 (13.9%)
>=50	9 (1.6%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B1.3 Age distribution of eligible patients - France

	CPA/EE
Number (%) of eligible patients	24 (100%)
Age (years)	
n	24 (100%)
Missing	0 (0.0%)
Mean	25.8
SD	8.23
Min	15
Q1	19.5
Median	24.9
Q3	29.9
Max	46
Age groups (years)	
<18	4 (16.7%)
18 - 24	9 (37.5%)
25 - 34	9 (37.5%)
35 - 49	2 (8.3%)
>=50	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B1.4 Age distribution of eligible patients - The Netherlands

	CPA/EE
Number (%) of eligible patients	32 (100%)
Age (years)	
n	32 (100%)
Missing	0 (0.0%)
Mean	27.9
SD	8.61
Min	15
Q1	22.0
Median	26.2
Q3	29.5
Max	47
Age groups (years)	
<18	3 (9.4%)
18 - 24	9 (28.1%)
25 - 34	15 (46.9%)
35 - 49	5 (15.6%)
>=50	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B1.5 Age distribution of eligible patients - Spain

	CPA/EE
Number (%) of eligible patients	612 (100%)
Age (years)	
n	612 (100%)
Missing	0 (0.0%)
Mean	26.6
SD	7.10
Min	14
Q1	21.2
Median	25.1
Q3	30.4
Max	57
Age groups (years)	
<18	36 (5.9%)
18 - 24	265 (43.3%)
25 - 34	238 (38.9%)
35 - 49	68 (11.1%)
>=50	5 (0.8%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B1.6 Age distribution of eligible patients - gynecology

	CPA/EE
Number (%) of eligible patients	936 (100%)
Age (years)	
n	936 (100%)
Missing	0 (0.0%)
Mean	25.6
SD	8.10
Min	13
Q1	19.1
Median	23.9
Q3	30.2
Max	55
Age groups (years)	
<18	163 (17.4%)
18 - 24	359 (38.4%)
25 - 34	285 (30.4%)
35 - 49	122 (13.0%)
>=50	7 (0.7%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B1.7 Age distribution of eligible patients - dermatology

	CPA/EE
Number (%) of eligible patients	167 (100%)
Age (years)	
n	167 (100%)
Missing	0 (0.0%)
Mean	28.3
SD	9.48
Min	15
Q1	21.5
Median	25.9
Q3	31.9
Max	60
Age groups (years)	
<18	12 (7.2%)
18 - 24	61 (36.5%)
25 - 34	59 (35.3%)
35 - 49	28 (16.8%)
>=50	7 (4.2%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B1.8 Age distribution of eligible patients - general practitioner (GP)

	CPA/EE
Number (%) of eligible patients	410 (100%)
Age (years)	
n	410 (100%)
Missing	0 (0.0%)
Mean	25.9
SD	6.46
Min	14
Q1	21.0
Median	24.8
Q3	29.8
Max	47
Age groups (years)	
<18	23 (5.6%)
18 - 24	188 (45.9%)
25 - 34	163 (39.8%)
35 - 49	36 (8.8%)
>=50	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B2 - Prescription status of CPA/EE users

	CPA/EE
Number (%) of eligible patients	1513 (100%)
Prescription status	
First-time user (starter)	635 (42.0%)
Continous user (no break or break of <4 weeks)	645 (42.6%)
Re-starter (break of 4 weeks or more)	223 (14.7%)
Missing	10 (0.7%)

Date of analysis: 12MAY2016

Table B2.1 Prescription status of CPA/EE users - Austria

	CPA/EE
Number (%) of eligible patients	282 (100%)
Prescription status	
First-time user (starter)	88 (31.2%)
Continous user (no break or break of <4 weeks)	163 (57.8%)
Re-starter (break of 4 weeks or more)	26 (9.2%)
Missing	5 (1.8%)

Date of analysis: 12MAY2016

Table B2.2 Prescription status of CPA/EE users - Czech Republic

	CPA/EE
Number (%) of eligible patients	563 (100%)
Prescription status	
First-time user (starter)	274 (48.7%)
Continous user (no break or break of <4 weeks)	197 (35.0%)
Re-starter (break of 4 weeks or more)	90 (16.0%)
Missing	2 (0.4%)

Date of analysis: 12MAY2016

Table B2.3 Prescription status of CPA/EE users - France

	CPA/EE
Number (%) of eligible patients	24 (100%)
Prescription status	
First-time user (starter)	6 (25.0%)
Continous user (no break or break of <4 weeks)	15 (62.5%)
Re-starter (break of 4 weeks or more)	3 (12.5%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B2.4 Prescription status of CPA/EE users - The Netherlands

	CPA/EE
Number (%) of eligible patients	32 (100%)
Prescription status	
First-time user (starter)	2 (6.3%)
Continous user (no break or break of <4 weeks)	25 (78.1%)
Re-starter (break of 4 weeks or more)	5 (15.6%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B2.5 Prescription status of CPA/EE users - Spain

	CPA/EE
Number (%) of eligible patients	612 (100%)
Prescription status	
First-time user (starter)	265 (43.3%)
Continous user (no break or break of <4 weeks)	245 (40.0%)
Re-starter (break of 4 weeks or more)	99 (16.2%)
Missing	3 (0.5%)

Date of analysis: 12MAY2016

Table B2.6 Prescription status of CPA/EE users - gynecology

	CPA/EE
Number (%) of eligible patients	936 (100%)
Prescription status	
First-time user (starter)	429 (45.8%)
Continous user (no break or break of <4 weeks)	363 (38.8%)
Re-starter (break of 4 weeks or more)	135 (14.4%)
Missing	9 (1.0%)

Date of analysis: 12MAY2016

Table B2.7 Prescription status of CPA/EE users - dermatology

	CPA/EE
Number (%) of eligible patients	167 (100%)
Prescription status	
First-time user (starter)	68 (40.7%)
Continous user (no break or break of <4 weeks)	59 (35.3%)
Re-starter (break of 4 weeks or more)	40 (24.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B2.8 Prescription status of CPA/EE users - general practitioner (GP)

	CPA/EE
Number (%) of eligible patients	410 (100%)
Prescription status	
First-time user (starter)	138 (33.7%)
Continous user (no break or break of <4 weeks)	223 (54.4%)
Re-starter (break of 4 weeks or more)	48 (11.7%)
Missing	1 (0.2%)

Date of analysis: 12MAY2016

Table B3 - Prescribing reasons for CPA/EE

	CPA/EE	95%-CI
Number (%) of eligible patients	1513 (100%)	
Reason		
Acne	993 (65.6%)	[57.2%;73.4%]
Seborrhea	195 (12.9%)	[9.3%;17.3%]
Hirsutism	191 (12.6%)	[9.8%;15.9%]
Androgenetic alopecia	75 (5.0%)	[3.2%;7.2%]
PCOS	173 (11.4%)	[7.9%;15.8%]
Contraception	1009 (66.7%)	[58.8%;74.0%]
Other reasons	56 (3.7%)	[1.9%;6.5%]
Bleeding problems	34 (2.2%)	[0.9%;4.5%]
Other skin problems	14 (0.9%)	[0.3%;2.0%]
Other hair problems	2 (0.1%)	[0.0%;0.5%]
Gynecologic problems	4 (0.3%)	[0.0%;1.1%]
Personal reasons	4 (0.3%)	[0.1%;0.7%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	246 (16.3%)	[9.1%;25.9%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B3.1 Prescribing reasons for CPA/EE - Austria

	CPA/EE	95%-CI
Number (%) of eligible patients	282 (100%)	
Reason		
Acne	189 (67.0%)	[42.9%;86.0%]
Seborrhea	13 (4.6%)	[1.2%;11.9%]
Hirsutism	12 (4.3%)	[1.2%;10.4%]
Androgenetic alopecia	2 (0.7%)	[0.0%;3.8%]
PCOS	19 (6.7%)	[2.5%;14.1%]
Contraception	186 (66.0%)	[51.2%;78.8%]
Other reasons	19 (6.7%)	[3.2%;12.3%]
Bleeding problems	6 (2.1%)	[0.6%;5.4%]
Other skin problems	9 (3.2%)	[1.1%;7.2%]
Other hair problems	1 (0.4%)	[0.0%;2.0%]
Gynecologic problems	1 (0.4%)	[0.0%;2.1%]
Personal reasons	3 (1.1%)	[0.2%;3.3%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	62 (22.0%)	[4.8%;51.8%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B3.2 Prescribing reasons for CPA/EE - Czech Republic

	CPA/EE	95%-CI
Number (%) of eligible patients	563 (100%)	
Reason		
Acne	451 (80.1%)	[60.5%;92.8%]
Seborrhea	52 (9.2%)	[5.3%;14.7%]
Hirsutism	35 (6.2%)	[3.4%;10.2%]
Androgenetic alopecia	21 (3.7%)	[1.7%;7.1%]
PCOS	23 (4.1%)	[1.7%;8.0%]
Contraception	487 (86.5%)	[80.2%;91.4%]
Other reasons	22 (3.9%)	[0.7%;11.6%]
Bleeding problems	17 (3.0%)	[0.6%;9.0%]
Other skin problems	4 (0.7%)	[0.0%;3.9%]
Other hair problems	1 (0.2%)	[0.0%;1.0%]
Gynecologic problems	0 (0.0%)	[0.0%;0.0%]
Personal reasons	1 (0.2%)	[0.0%;1.1%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	76 (13.5%)	[2.4%;36.6%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B3.3 Prescribing reasons for CPA/EE - France

	CPA/EE	95%-CI
Number (%) of eligible patients	24 (100%)	
Reason		
Acne	21 (87.5%)	[53.6%;99.3%]
Seborrhea	1 (4.2%)	[0.0%;27.5%]
Hirsutism	1 (4.2%)	[0.1%;21.1%]
Androgenetic alopecia	0 (0.0%)	[0.0%;0.0%]
PCOS	0 (0.0%)	[0.0%;0.0%]
Contraception	10 (41.7%)	[6.0%;86.2%]
Other reasons	1 (4.2%)	[0.0%;26.1%]
Bleeding problems	0 (0.0%)	[0.0%;0.0%]
Other skin problems	1 (4.2%)	[0.0%;26.1%]
Other hair problems	0 (0.0%)	[0.0%;0.0%]
Gynecologic problems	0 (0.0%)	[0.0%;0.0%]
Personal reasons	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	2 (8.3%)	[0.7%;29.9%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B3.4 Prescribing reasons for CPA/EE - The Netherlands

	CPA/EE	95%-CI
Number (%) of eligible patients	32 (100%)	
Reason		
Acne	24 (75.0%)	[22.0%;99.1%]
Seborrhea	1 (3.1%)	[0.0%;21.0%]
Hirsutism	1 (3.1%)	[0.0%;21.0%]
Androgenetic alopecia	2 (6.3%)	[0.0%;43.2%]
PCOS	0 (0.0%)	[0.0%;0.0%]
Contraception	22 (68.8%)	[9.2%;99.5%]
Other reasons	0 (0.0%)	[0.0%;0.0%]
Bleeding problems	0 (0.0%)	[0.0%;0.0%]
Other skin problems	0 (0.0%)	[0.0%;0.0%]
Other hair problems	0 (0.0%)	[0.0%;0.0%]
Gynecologic problems	0 (0.0%)	[0.0%;0.0%]
Personal reasons	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	5 (15.6%)	[0.0%;75.8%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B3.5 Prescribing reasons for CPA/EE - Spain

	CPA/EE	95%-CI
Number (%) of eligible patients	612 (100%)	
Reason		
Acne	308 (50.3%)	[41.7%;58.9%]
Seborrhea	128 (20.9%)	[13.9%;29.5%]
Hirsutism	142 (23.2%)	[17.9%;29.2%]
Androgenetic alopecia	50 (8.2%)	[4.8%;12.8%]
PCOS	131 (21.4%)	[14.1%;30.3%]
Contraception	304 (49.7%)	[35.9%;63.5%]
Other reasons	14 (2.3%)	[0.5%;6.2%]
Bleeding problems	11 (1.8%)	[0.4%;5.3%]
Other skin problems	0 (0.0%)	[0.0%;0.0%]
Other hair problems	0 (0.0%)	[0.0%;0.0%]
Gynecologic problems	3 (0.5%)	[0.0%;2.9%]
Personal reasons	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	101 (16.5%)	[8.2%;28.4%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B3.6 Prescribing reasons for CPA/EE - gynecology

	CPA/EE	95%-CI
Number (%) of eligible patients	936 (100%)	
Reason		
Acne	679 (72.5%)	[59.4%;83.3%]
Seborrhea	91 (9.7%)	[6.3%;14.2%]
Hirsutism	76 (8.1%)	[5.6%;11.3%]
Androgenetic alopecia	30 (3.2%)	[1.8%;5.3%]
PCOS	74 (7.9%)	[4.9%;11.9%]
Contraception	734 (78.4%)	[71.9%;84.0%]
Other reasons	46 (4.9%)	[2.3%;9.2%]
Bleeding problems	25 (2.7%)	[0.9%;5.9%]
Other skin problems	13 (1.4%)	[0.5%;3.1%]
Other hair problems	2 (0.2%)	[0.0%;0.8%]
Gynecologic problems	4 (0.4%)	[0.0%;1.8%]
Personal reasons	4 (0.4%)	[0.1%;1.1%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	152 (16.2%)	[6.4%;31.4%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B3.7 Prescribing reasons for CPA/EE - dermatology

	CPA/EE	95%-CI
Number (%) of eligible patients	167 (100%)	
Reason		
Acne	119 (71.3%)	[51.1%;86.7%]
Seborrhea	47 (28.1%)	[15.4%;44.1%]
Hirsutism	30 (18.0%)	[8.2%;32.1%]
Androgenetic alopecia	35 (21.0%)	[13.1%;30.8%]
PCOS	12 (7.2%)	[1.7%;18.5%]
Contraception	38 (22.8%)	[7.3%;46.8%]
Other reasons	0 (0.0%)	[0.0%;0.0%]
Bleeding problems	0 (0.0%)	[0.0%;0.0%]
Other skin problems	0 (0.0%)	[0.0%;0.0%]
Other hair problems	0 (0.0%)	[0.0%;0.0%]
Gynecologic problems	0 (0.0%)	[0.0%;0.0%]
Personal reasons	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	2 (1.2%)	[0.1%;4.8%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B3.8 Prescribing reasons for CPA/EE - general practitioner (GP)

	CPA/EE	95%-CI
Number (%) of eligible patients	410 (100%)	
Reason		
Acne	195 (47.6%)	[37.2%;58.1%]
Seborrhea	57 (13.9%)	[6.5%;25.0%]
Hirsutism	85 (20.7%)	[14.0%;28.9%]
Androgenetic alopecia	10 (2.4%)	[0.7%;5.9%]
PCOS	87 (21.2%)	[11.7%;33.8%]
Contraception	237 (57.8%)	[39.5%;74.7%]
Other reasons	10 (2.4%)	[0.4%;7.8%]
Bleeding problems	9 (2.2%)	[0.3%;7.8%]
Other skin problems	1 (0.2%)	[0.0%;1.4%]
Other hair problems	0 (0.0%)	[0.0%;0.0%]
Gynecologic problems	0 (0.0%)	[0.0%;0.0%]
Personal reasons	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Contraception only	92 (22.4%)	[11.2%;37.6%]

Note: Multiple prescribing indications per patient may be possible.
Note: Frequencies of reasons for prescription are displayed relatively to the number of patients.
Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B4 - Duration and treatment of androgen-sensitive diseases

Table B4-1 Duration and treatment of acne by severity

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	377 (100%)	562 (100%)	89 (100%)	**1028 (100%)**
Duration (in months)				
<1	2 (0.5%)	5 (0.9%)	3 (3.4%)	**10 (1.0%)**
1 - <6	20 (5.3%)	45 (8.0%)	2 (2.2%)	**67 (6.5%)**
6 - <12	34 (9.0%)	40 (7.1%)	7 (7.9%)	**81 (7.9%)**
>=12	312 (82.8%)	468 (83.3%)	75 (84.3%)	**855 (83.2%)**
Missing	9 (2.4%)	4 (0.7%)	2 (2.2%)	**15 (1.5%)**
Previous treatment				
No	216 (57.3%)	207 (36.8%)	19 (21.3%)	**442 (43.0%)**
Yes	161 (42.7%)	355 (63.2%)	70 (78.7%)	**586 (57.0%)**
Anti androgenic therapy	2 (0.5%)	5 (0.9%)	2 (2.2%)	**9 (0.9%)**
Antibiotic combined with benzoyl peroxide (topical)	9 (2.4%)	77 (13.7%)	10 (11.2%)	**96 (9.3%)**
Antibiotic combined with retinoid (topical)	2 (0.5%)	5 (0.9%)	3 (3.4%)	**10 (1.0%)**
Antibiotics (form of application not specified/unclear)	14 (3.7%)	27 (4.8%)	9 (10.1%)	**50 (4.9%)**
Antimycotics	12 (3.2%)	8 (1.4%)	0 (0.0%)	**20 (1.9%)**
Azelaic-acid	9 (2.4%)	28 (5.0%)	8 (9.0%)	**45 (4.4%)**
CPA/EE	32 (8.5%)	44 (7.8%)	7 (7.9%)	**83 (8.1%)**
Isotretinoin (form of application not specified/unclear)	1 (0.3%)	3 (0.5%)	7 (7.9%)	**11 (1.1%)**
Isotretinoin systemic	6 (1.6%)	27 (4.8%)	7 (7.9%)	**40 (3.9%)**
Monoclonal antibody	1 (0.3%)	0 (0.0%)	0 (0.0%)	**1 (0.1%)**
Oral Contraceptives (not including CPA/EE)	14 (3.7%)	23 (4.1%)	1 (1.1%)	**38 (3.7%)**
Physical therapy	1 (0.3%)	1 (0.2%)	0 (0.0%)	**2 (0.2%)**
Retinoids combined with benzoyl peroxide (topical)	1 (0.3%)	14 (2.5%)	1 (1.1%)	**16 (1.6%)**
Systemic antibiotics	8 (2.1%)	68 (12.1%)	19 (21.3%)	**95 (9.2%)**
Topical antibiotics	39 (10.3%)	100 (17.8%)	14 (15.7%)	**153 (14.9%)**
Topical corticosteroids	3 (0.8%)	3 (0.5%)	0 (0.0%)	**6 (0.6%)**
Topical retinoids	6 (1.6%)	39 (6.9%)	8 (9.0%)	**53 (5.2%)**
Topical treatment with benzoyl peroxide	6 (1.6%)	31 (5.5%)	7 (7.9%)	**44 (4.3%)**
Various topical therapies/ keratolytics	46 (12.2%)	55 (9.8%)	8 (9.0%)	**109 (10.6%)**
Zinc powder	0 (0.0%)	8 (1.4%)	2 (2.2%)	**10 (1.0%)**
Zinc tablets/various oral therapies	1 (0.3%)	5 (0.9%)	0 (0.0%)	**6 (0.6%)**
Missing	1 (0.3%)	2 (0.4%)	0 (0.0%)	**3 (0.3%)**
Treatment failed / insufficient				
Yes	91 (24.1%)	279 (49.6%)	58 (65.2%)	**428 (41.6%)**
No	62 (16.4%)	70 (12.5%)	12 (13.5%)	**144 (14.0%)**
Not applicable	8 (2.1%)	5 (0.9%)	0 (0.0%)	**13 (1.3%)**
Missing	0 (0.0%)	1 (0.2%)	0 (0.0%)	**1 (0.1%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	301 (79.8%)	322 (57.3%)	40 (44.9%)	**663 (64.5%)**

	Mild	Moderate	Severe	**Total**
Yes	62 (16.4%)	213 (37.9%)	46 (51.7%)	**321 (31.2%)**
Anti androgenic therapy	0 (0.0%)	1 (0.2%)	2 (2.2%)	**3 (0.3%)**
Antibiotic combined with benzoyl peroxide (topical)	3 (0.8%)	33 (5.9%)	4 (4.5%)	**40 (3.9%)**
Antibiotic combined with retinoid (topical)	0 (0.0%)	1 (0.2%)	1 (1.1%)	**2 (0.2%)**
Antibiotics (form of application not specified/unclear)	1 (0.3%)	6 (1.1%)	2 (2.2%)	**9 (0.9%)**
Antimycotics	7 (1.9%)	4 (0.7%)	2 (2.2%)	**13 (1.3%)**
Azelaic-acid	2 (0.5%)	8 (1.4%)	2 (2.2%)	**12 (1.2%)**
Isotretinoin (form of application not specified/unclear)	1 (0.3%)	5 (0.9%)	6 (6.7%)	**12 (1.2%)**
Isotretinoin systemic	0 (0.0%)	11 (2.0%)	9 (10.1%)	**20 (1.9%)**
Retinoids combined with benzoyl peroxide (topical)	3 (0.8%)	15 (2.7%)	0 (0.0%)	**18 (1.8%)**
Systemic antibiotics	3 (0.8%)	24 (4.3%)	4 (4.5%)	**31 (3.0%)**
Topical antibiotics	12 (3.2%)	46 (8.2%)	8 (9.0%)	**66 (6.4%)**
Topical corticosteroids	0 (0.0%)	2 (0.4%)	0 (0.0%)	**2 (0.2%)**
Topical retinoids	5 (1.3%)	19 (3.4%)	1 (1.1%)	**25 (2.4%)**
Topical treatment with benzoyl peroxide	6 (1.6%)	18 (3.2%)	3 (3.4%)	**27 (2.6%)**
Various topical therapies/ keratolytics	24 (6.4%)	45 (8.0%)	8 (9.0%)	**77 (7.5%)**
Zinc powder	0 (0.0%)	1 (0.2%)	0 (0.0%)	**1 (0.1%)**
Zinc tablets/various oral therapies	0 (0.0%)	1 (0.2%)	1 (1.1%)	**2 (0.2%)**
Missing	1 (0.3%)	2 (0.4%)	0 (0.0%)	**3 (0.3%)**
Missing	14 (3.7%)	27 (4.8%)	3 (3.4%)	**44 (4.3%)**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-1.1 Duration and treatment of acne by severity – Austria

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	98 (100%)	79 (100%)	21 (100%)	**198 (100%)**
Duration (in months)				
<1	1 (1.0%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
1 - <6	5 (5.1%)	3 (3.8%)	0 (0.0%)	**8 (4.0%)**
6 - <12	6 (6.1%)	11 (13.9%)	1 (4.8%)	**18 (9.1%)**
>=12	81 (82.7%)	62 (78.5%)	18 (85.7%)	**161 (81.3%)**
Missing	5 (5.1%)	3 (3.8%)	2 (9.5%)	**10 (5.1%)**
Previous treatment				
No	69 (70.4%)	59 (74.7%)	11 (52.4%)	**139 (70.2%)**
Yes	29 (29.6%)	20 (25.3%)	10 (47.6%)	**59 (29.8%)**
Antibiotics (form of application not specified/unclear)	4 (4.1%)	2 (2.5%)	3 (14.3%)	**9 (4.5%)**
Azelaic-acid	1 (1.0%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
CPA/EE	4 (4.1%)	3 (3.8%)	1 (4.8%)	**8 (4.0%)**
Isotretinoin systemic	3 (3.1%)	4 (5.1%)	1 (4.8%)	**8 (4.0%)**
Oral Contraceptives (not including CPA/EE)	2 (2.0%)	1 (1.3%)	0 (0.0%)	**3 (1.5%)**
Physical therapy	1 (1.0%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
Systemic antibiotics	0 (0.0%)	4 (5.1%)	1 (4.8%)	**5 (2.5%)**
Topical antibiotics	1 (1.0%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
Various topical therapies/ keratolytics	16 (16.3%)	8 (10.1%)	5 (23.8%)	**29 (14.6%)**
Zinc tablets/various oral therapies	1 (1.0%)	1 (1.3%)	0 (0.0%)	**2 (1.0%)**
Treatment failed / insufficient				
Yes	19 (19.4%)	15 (19.0%)	7 (33.3%)	**41 (20.7%)**
No	8 (8.2%)	4 (5.1%)	3 (14.3%)	**15 (7.6%)**
Not applicable	2 (2.0%)	1 (1.3%)	0 (0.0%)	**3 (1.5%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	86 (87.8%)	66 (83.5%)	17 (81.0%)	**169 (85.4%)**
Yes	4 (4.1%)	6 (7.6%)	2 (9.5%)	**12 (6.1%)**
Antibiotics (form of application not specified/unclear)	0 (0.0%)	1 (1.3%)	0 (0.0%)	**1 (0.5%)**
Systemic antibiotics	0 (0.0%)	1 (1.3%)	0 (0.0%)	**1 (0.5%)**
Topical antibiotics	1 (1.0%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
Topical retinoids	1 (1.0%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
Topical treatment with benzoyl peroxide	1 (1.0%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
Various topical therapies/ keratolytics	2 (2.0%)	3 (3.8%)	2 (9.5%)	**7 (3.5%)**
Missing	0 (0.0%)	1 (1.3%)	0 (0.0%)	**1 (0.5%)**
Missing	8 (8.2%)	7 (8.9%)	2 (9.5%)	**17 (8.6%)**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-1.2 Duration and treatment of acne by severity - Czech Republic

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	179 (100%)	253 (100%)	23 (100%)	**455 (100%)**
Duration (in months)				
<1	1 (0.6%)	2 (0.8%)	1 (4.3%)	**4 (0.9%)**
1 - <6	9 (5.0%)	29 (11.5%)	1 (4.3%)	**39 (8.6%)**
6 - <12	16 (8.9%)	18 (7.1%)	1 (4.3%)	**35 (7.7%)**
>=12	153 (85.5%)	203 (80.2%)	20 (87.0%)	**376 (82.6%)**
Missing	0 (0.0%)	1 (0.4%)	0 (0.0%)	**1 (0.2%)**
Previous treatment				
No	100 (55.9%)	101 (39.9%)	2 (8.7%)	**203 (44.6%)**
Yes	79 (44.1%)	152 (60.1%)	21 (91.3%)	**252 (55.4%)**
Anti androgenic therapy	1 (0.6%)	3 (1.2%)	1 (4.3%)	**5 (1.1%)**
Antibiotic combined with benzoyl peroxide (topical)	3 (1.7%)	51 (20.2%)	5 (21.7%)	**59 (13.0%)**
Antibiotic combined with retinoid (topical)	2 (1.1%)	5 (2.0%)	3 (13.0%)	**10 (2.2%)**
Antibiotics (form of application not specified/unclear)	6 (3.4%)	6 (2.4%)	1 (4.3%)	**13 (2.9%)**
Antimycotics	12 (6.7%)	8 (3.2%)	0 (0.0%)	**20 (4.4%)**
Azelaic-acid	8 (4.5%)	25 (9.9%)	8 (34.8%)	**41 (9.0%)**
CPA/EE	20 (11.2%)	34 (13.4%)	5 (21.7%)	**59 (13.0%)**
Isotretinoin systemic	0 (0.0%)	12 (4.7%)	2 (8.7%)	**14 (3.1%)**
Oral Contraceptives (not including CPA/EE)	9 (5.0%)	14 (5.5%)	0 (0.0%)	**23 (5.1%)**
Physical therapy	0 (0.0%)	1 (0.4%)	0 (0.0%)	**1 (0.2%)**
Systemic antibiotics	1 (0.6%)	6 (2.4%)	5 (21.7%)	**12 (2.6%)**
Topical antibiotics	22 (12.3%)	63 (24.9%)	11 (47.8%)	**96 (21.1%)**
Topical corticosteroids	3 (1.7%)	3 (1.2%)	0 (0.0%)	**6 (1.3%)**
Topical retinoids	4 (2.2%)	33 (13.0%)	6 (26.1%)	**43 (9.5%)**
Topical treatment with benzoyl peroxide	2 (1.1%)	2 (0.8%)	1 (4.3%)	**5 (1.1%)**
Various topical therapies/ keratolytics	25 (14.0%)	29 (11.5%)	2 (8.7%)	**56 (12.3%)**
Zinc powder	0 (0.0%)	8 (3.2%)	2 (8.7%)	**10 (2.2%)**
Zinc tablets/various oral therapies	0 (0.0%)	1 (0.4%)	0 (0.0%)	**1 (0.2%)**
Missing	1 (0.6%)	1 (0.4%)	0 (0.0%)	**2 (0.4%)**
Treatment failed / insufficient				
Yes	30 (16.8%)	102 (40.3%)	16 (69.6%)	**148 (32.5%)**
No	44 (24.6%)	46 (18.2%)	5 (21.7%)	**95 (20.9%)**
Not applicable	5 (2.8%)	4 (1.6%)	0 (0.0%)	**9 (2.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	142 (79.3%)	148 (58.5%)	6 (26.1%)	**296 (65.1%)**
Yes	35 (19.6%)	94 (37.2%)	17 (73.9%)	**146 (32.1%)**
Anti androgenic therapy	0 (0.0%)	1 (0.4%)	0 (0.0%)	**1 (0.2%)**
Antibiotic combined with benzoyl peroxide (topical)	0 (0.0%)	18 (7.1%)	4 (17.4%)	**22 (4.8%)**
Antibiotic combined with retinoid (topical)	0 (0.0%)	0 (0.0%)	1 (4.3%)	**1 (0.2%)**
Antimycotics	6 (3.4%)	4 (1.6%)	2 (8.7%)	**12 (2.6%)**
Azelaic-acid	2 (1.1%)	6 (2.4%)	2 (8.7%)	**10 (2.2%)**
Isotretinoin systemic	0 (0.0%)	3 (1.2%)	1 (4.3%)	**4 (0.9%)**

	Mild	Moderate	Severe	**Total**
Systemic antibiotics	2 (1.1%)	4 (1.6%)	2 (8.7%)	**8 (1.8%)**
Topical antibiotics	6 (3.4%)	29 (11.5%)	3 (13.0%)	**38 (8.4%)**
Topical retinoids	1 (0.6%)	8 (3.2%)	0 (0.0%)	**9 (2.0%)**
Topical treatment with benzoyl peroxide	1 (0.6%)	3 (1.2%)	1 (4.3%)	**5 (1.1%)**
Various topical therapies/ keratolytics	17 (9.5%)	21 (8.3%)	3 (13.0%)	**41 (9.0%)**
Zinc powder	0 (0.0%)	1 (0.4%)	0 (0.0%)	**1 (0.2%)**
Missing	2 (1.1%)	11 (4.3%)	0 (0.0%)	**13 (2.9%)**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-1.3 Duration and treatment of acne by severity - France

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	9 (100%)	10 (100%)	4 (100%)	**23 (100%)**
Duration (in months)				
<1	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
1 - <6	0 (0.0%)	1 (10.0%)	0 (0.0%)	**1 (4.3%)**
6 - <12	0 (0.0%)	0 (0.0%)	2 (50.0%)	**2 (8.7%)**
>=12	8 (88.9%)	9 (90.0%)	2 (50.0%)	**19 (82.6%)**
Missing	1 (11.1%)	0 (0.0%)	0 (0.0%)	**1 (4.3%)**
Previous treatment				
No	1 (11.1%)	0 (0.0%)	0 (0.0%)	**1 (4.3%)**
Yes	8 (88.9%)	10 (100%)	4 (100%)	**22 (95.7%)**
Anti androgenic therapy	1 (11.1%)	2 (20.0%)	0 (0.0%)	**3 (13.0%)**
Antibiotics (form of application not specified/unclear)	2 (22.2%)	3 (30.0%)	2 (50.0%)	**7 (30.4%)**
Isotretinoin (form of application not specified/unclear)	1 (11.1%)	0 (0.0%)	1 (25.0%)	**2 (8.7%)**
Isotretinoin systemic	1 (11.1%)	2 (20.0%)	2 (50.0%)	**5 (21.7%)**
Monoclonal antibody	1 (11.1%)	0 (0.0%)	0 (0.0%)	**1 (4.3%)**
Oral Contraceptives (not including CPA/EE)	1 (11.1%)	0 (0.0%)	0 (0.0%)	**1 (4.3%)**
Systemic antibiotics	1 (11.1%)	1 (10.0%)	0 (0.0%)	**2 (8.7%)**
Topical antibiotics	0 (0.0%)	0 (0.0%)	1 (25.0%)	**1 (4.3%)**
Topical retinoids	1 (11.1%)	2 (20.0%)	1 (25.0%)	**4 (17.4%)**
Topical treatment with benzoyl peroxide	0 (0.0%)	3 (30.0%)	1 (25.0%)	**4 (17.4%)**
Various topical therapies/ keratolytics	1 (11.1%)	2 (20.0%)	0 (0.0%)	**3 (13.0%)**
Zinc tablets/various oral therapies	0 (0.0%)	2 (20.0%)	0 (0.0%)	**2 (8.7%)**
Treatment failed / insufficient				
Yes	8 (88.9%)	10 (100%)	4 (100%)	**22 (95.7%)**
No	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Not applicable	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	4 (44.4%)	4 (40.0%)	0 (0.0%)	**8 (34.8%)**
Yes	5 (55.6%)	6 (60.0%)	4 (100%)	**15 (65.2%)**
Anti androgenic therapy	0 (0.0%)	0 (0.0%)	2 (50.0%)	**2 (8.7%)**
Antibiotics (form of application not specified/unclear)	0 (0.0%)	2 (20.0%)	2 (50.0%)	**4 (17.4%)**
Isotretinoin (form of application not specified/unclear)	0 (0.0%)	0 (0.0%)	1 (25.0%)	**1 (4.3%)**
Isotretinoin systemic	0 (0.0%)	0 (0.0%)	1 (25.0%)	**1 (4.3%)**
Retinoids combined with benzoyl peroxide (topical)	0 (0.0%)	1 (10.0%)	0 (0.0%)	**1 (4.3%)**
Systemic antibiotics	0 (0.0%)	3 (30.0%)	0 (0.0%)	**3 (13.0%)**
Topical retinoids	2 (22.2%)	4 (40.0%)	1 (25.0%)	**7 (30.4%)**
Topical treatment with benzoyl peroxide	2 (22.2%)	4 (40.0%)	1 (25.0%)	**7 (30.4%)**
Various topical therapies/ keratolytics	2 (22.2%)	0 (0.0%)	0 (0.0%)	**2 (8.7%)**
Zinc tablets/various oral therapies	0 (0.0%)	0 (0.0%)	1 (25.0%)	**1 (4.3%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**

	Mild	Moderate	Severe	**Total**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-1.4 Duration and treatment of acne by severity - The Netherlands

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	6 (100%)	16 (100%)	2 (100%)	**24 (100%)**
Duration (in months)				
<1	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
1 - <6	0 (0.0%)	2 (12.5%)	0 (0.0%)	**2 (8.3%)**
6 - <12	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
>=12	5 (83.3%)	14 (87.5%)	2 (100%)	**21 (87.5%)**
Missing	1 (16.7%)	0 (0.0%)	0 (0.0%)	**1 (4.2%)**
Previous treatment				
No	3 (50.0%)	6 (37.5%)	2 (100%)	**11 (45.8%)**
Yes	3 (50.0%)	10 (62.5%)	0 (0.0%)	**13 (54.2%)**
Antibiotics (form of application not specified/unclear)	0 (0.0%)	2 (12.5%)	0 (0.0%)	**2 (8.3%)**
CPA/EE	1 (16.7%)	3 (18.8%)	0 (0.0%)	**4 (16.7%)**
Isotretinoin systemic	0 (0.0%)	1 (6.3%)	0 (0.0%)	**1 (4.2%)**
Oral Contraceptives (not including CPA/EE)	0 (0.0%)	1 (6.3%)	0 (0.0%)	**1 (4.2%)**
Systemic antibiotics	0 (0.0%)	1 (6.3%)	0 (0.0%)	**1 (4.2%)**
Topical antibiotics	1 (16.7%)	2 (12.5%)	0 (0.0%)	**3 (12.5%)**
Topical retinoids	0 (0.0%)	1 (6.3%)	0 (0.0%)	**1 (4.2%)**
Topical treatment with benzoyl peroxide	0 (0.0%)	1 (6.3%)	0 (0.0%)	**1 (4.2%)**
Various topical therapies/ keratolytics	1 (16.7%)	2 (12.5%)	0 (0.0%)	**3 (12.5%)**
Treatment failed / insufficient				
Yes	2 (33.3%)	7 (43.8%)	0 (0.0%)	**9 (37.5%)**
No	0 (0.0%)	3 (18.8%)	0 (0.0%)	**3 (12.5%)**
Not applicable	1 (16.7%)	0 (0.0%)	0 (0.0%)	**1 (4.2%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	3 (50.0%)	10 (62.5%)	1 (50.0%)	**14 (58.3%)**
Yes	0 (0.0%)	3 (18.8%)	1 (50.0%)	**4 (16.7%)**
Antibiotics (form of application not specified/unclear)	0 (0.0%)	1 (6.3%)	0 (0.0%)	**1 (4.2%)**
Topical treatment with benzoyl peroxide	0 (0.0%)	1 (6.3%)	0 (0.0%)	**1 (4.2%)**
Various topical therapies/ keratolytics	0 (0.0%)	1 (6.3%)	1 (50.0%)	**2 (8.3%)**
Missing	0 (0.0%)	1 (6.3%)	0 (0.0%)	**1 (4.2%)**
Missing	3 (50.0%)	3 (18.8%)	0 (0.0%)	**6 (25.0%)**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-1.5 Duration and treatment of acne by severity - Spain

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	85 (100%)	204 (100%)	39 (100%)	**328 (100%)**
Duration (in months)				
<1	0 (0.0%)	3 (1.5%)	2 (5.1%)	**5 (1.5%)**
1 - <6	6 (7.1%)	10 (4.9%)	1 (2.6%)	**17 (5.2%)**
6 - <12	12 (14.1%)	11 (5.4%)	3 (7.7%)	**26 (7.9%)**
>=12	65 (76.5%)	180 (88.2%)	33 (84.6%)	**278 (84.8%)**
Missing	2 (2.4%)	0 (0.0%)	0 (0.0%)	**2 (0.6%)**
Previous treatment				
No	43 (50.6%)	41 (20.1%)	4 (10.3%)	**88 (26.8%)**
Yes	42 (49.4%)	163 (79.9%)	35 (89.7%)	**240 (73.2%)**
Anti androgenic therapy	0 (0.0%)	0 (0.0%)	1 (2.6%)	**1 (0.3%)**
Antibiotic combined with benzoyl peroxide (topical)	6 (7.1%)	26 (12.7%)	5 (12.8%)	**37 (11.3%)**
Antibiotics (form of application not specified/unclear)	2 (2.4%)	14 (6.9%)	3 (7.7%)	**19 (5.8%)**
Azelaic-acid	0 (0.0%)	3 (1.5%)	0 (0.0%)	**3 (0.9%)**
CPA/EE	7 (8.2%)	4 (2.0%)	1 (2.6%)	**12 (3.7%)**
Isotretinoin (form of application not specified/unclear)	0 (0.0%)	3 (1.5%)	6 (15.4%)	**9 (2.7%)**
Isotretinoin systemic	2 (2.4%)	8 (3.9%)	2 (5.1%)	**12 (3.7%)**
Oral Contraceptives (not including CPA/EE)	2 (2.4%)	7 (3.4%)	1 (2.6%)	**10 (3.0%)**
Retinoids combined with benzoyl peroxide (topical)	1 (1.2%)	14 (6.9%)	1 (2.6%)	**16 (4.9%)**
Systemic antibiotics	6 (7.1%)	56 (27.5%)	13 (33.3%)	**75 (22.9%)**
Topical antibiotics	15 (17.6%)	35 (17.2%)	2 (5.1%)	**52 (15.9%)**
Topical retinoids	1 (1.2%)	3 (1.5%)	1 (2.6%)	**5 (1.5%)**
Topical treatment with benzoyl peroxide	4 (4.7%)	25 (12.3%)	5 (12.8%)	**34 (10.4%)**
Various topical therapies/ keratolytics	3 (3.5%)	14 (6.9%)	1 (2.6%)	**18 (5.5%)**
Zinc tablets/various oral therapies	0 (0.0%)	1 (0.5%)	0 (0.0%)	**1 (0.3%)**
Missing	0 (0.0%)	1 (0.5%)	0 (0.0%)	**1 (0.3%)**
Treatment failed / insufficient				
Yes	32 (37.6%)	145 (71.1%)	31 (79.5%)	**208 (63.4%)**
No	10 (11.8%)	17 (8.3%)	4 (10.3%)	**31 (9.5%)**
Not applicable	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	1 (0.5%)	0 (0.0%)	**1 (0.3%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	66 (77.6%)	94 (46.1%)	16 (41.0%)	**176 (53.7%)**
Yes	18 (21.2%)	104 (51.0%)	22 (56.4%)	**144 (43.9%)**
Antibiotic combined with benzoyl peroxide (topical)	3 (3.5%)	15 (7.4%)	0 (0.0%)	**18 (5.5%)**
Antibiotic combined with retinoid (topical)	0 (0.0%)	1 (0.5%)	0 (0.0%)	**1 (0.3%)**
Antibiotics (form of application not specified/unclear)	1 (1.2%)	2 (1.0%)	0 (0.0%)	**3 (0.9%)**
Antimycotics	1 (1.2%)	0 (0.0%)	0 (0.0%)	**1 (0.3%)**
Azelaic-acid	0 (0.0%)	2 (1.0%)	0 (0.0%)	**2 (0.6%)**
Isotretinoin (form of application not specified/unclear)	1 (1.2%)	5 (2.5%)	5 (12.8%)	**11 (3.4%)**
Isotretinoin systemic	0 (0.0%)	8 (3.9%)	7 (17.9%)	**15 (4.6%)**
Retinoids combined with benzoyl peroxide (topical)	3 (3.5%)	14 (6.9%)	0 (0.0%)	**17 (5.2%)**
Systemic antibiotics	1 (1.2%)	16 (7.8%)	2 (5.1%)	**19 (5.8%)**
Topical antibiotics	5 (5.9%)	17 (8.3%)	5 (12.8%)	**27 (8.2%)**

	Mild	Moderate	Severe	**Total**
Topical corticosteroids	0 (0.0%)	2 (1.0%)	0 (0.0%)	**2 (0.6%)**
Topical retinoids	1 (1.2%)	7 (3.4%)	0 (0.0%)	**8 (2.4%)**
Topical treatment with benzoyl peroxide	2 (2.4%)	10 (4.9%)	1 (2.6%)	**13 (4.0%)**
Various topical therapies/ keratolytics	3 (3.5%)	20 (9.8%)	2 (5.1%)	**25 (7.6%)**
Zinc tablets/various oral therapies	0 (0.0%)	1 (0.5%)	0 (0.0%)	**1 (0.3%)**
Missing	1 (1.2%)	0 (0.0%)	0 (0.0%)	**1 (0.3%)**
Missing	1 (1.2%)	6 (2.9%)	1 (2.6%)	**8 (2.4%)**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-1.6 Duration and treatment of acne by severity - gynecology

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	299 (100%)	351 (100%)	44 (100%)	**694 (100%)**
Duration (in months)				
<1	2 (0.7%)	2 (0.6%)	1 (2.3%)	**5 (0.7%)**
1 - <6	20 (6.7%)	35 (10.0%)	1 (2.3%)	**56 (8.1%)**
6 - <12	26 (8.7%)	33 (9.4%)	2 (4.5%)	**61 (8.8%)**
>=12	245 (81.9%)	277 (78.9%)	38 (86.4%)	**560 (80.7%)**
Missing	6 (2.0%)	4 (1.1%)	2 (4.5%)	**12 (1.7%)**
Previous treatment				
No	183 (61.2%)	173 (49.3%)	14 (31.8%)	**370 (53.3%)**
Yes	116 (38.8%)	178 (50.7%)	30 (68.2%)	**324 (46.7%)**
Anti androgenic therapy	1 (0.3%)	2 (0.6%)	1 (2.3%)	**4 (0.6%)**
Antibiotic combined with benzoyl peroxide (topical)	3 (1.0%)	49 (14.0%)	2 (4.5%)	**54 (7.8%)**
Antibiotics (form of application not specified/unclear)	11 (3.7%)	10 (2.8%)	4 (9.1%)	**25 (3.6%)**
Antimycotics	10 (3.3%)	4 (1.1%)	0 (0.0%)	**14 (2.0%)**
Azelaic-acid	9 (3.0%)	21 (6.0%)	4 (9.1%)	**34 (4.9%)**
CPA/EE	26 (8.7%)	37 (10.5%)	5 (11.4%)	**68 (9.8%)**
Isotretinoin systemic	5 (1.7%)	19 (5.4%)	4 (9.1%)	**28 (4.0%)**
Monoclonal antibody	1 (0.3%)	0 (0.0%)	0 (0.0%)	**1 (0.1%)**
Oral Contraceptives (not including CPA/EE)	9 (3.0%)	16 (4.6%)	0 (0.0%)	**25 (3.6%)**
Physical therapy	1 (0.3%)	1 (0.3%)	0 (0.0%)	**2 (0.3%)**
Retinoids combined with benzoyl peroxide (topical)	0 (0.0%)	2 (0.6%)	0 (0.0%)	**2 (0.3%)**
Systemic antibiotics	0 (0.0%)	8 (2.3%)	2 (4.5%)	**10 (1.4%)**
Topical antibiotics	20 (6.7%)	52 (14.8%)	7 (15.9%)	**79 (11.4%)**
Topical corticosteroids	3 (1.0%)	3 (0.9%)	0 (0.0%)	**6 (0.9%)**
Topical retinoids	3 (1.0%)	25 (7.1%)	4 (9.1%)	**32 (4.6%)**
Topical treatment with benzoyl peroxide	1 (0.3%)	4 (1.1%)	0 (0.0%)	**5 (0.7%)**
Various topical therapies/ keratolytics	42 (14.0%)	40 (11.4%)	7 (15.9%)	**89 (12.8%)**
Zinc powder	0 (0.0%)	8 (2.3%)	2 (4.5%)	**10 (1.4%)**
Zinc tablets/various oral therapies	1 (0.3%)	3 (0.9%)	0 (0.0%)	**4 (0.6%)**
Missing	1 (0.3%)	2 (0.6%)	0 (0.0%)	**3 (0.4%)**
Treatment failed / insufficient				
Yes	53 (17.7%)	123 (35.0%)	21 (47.7%)	**197 (28.4%)**
No	56 (18.7%)	49 (14.0%)	9 (20.5%)	**114 (16.4%)**
Not applicable	7 (2.3%)	5 (1.4%)	0 (0.0%)	**12 (1.7%)**
Missing	0 (0.0%)	1 (0.3%)	0 (0.0%)	**1 (0.1%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	245 (81.9%)	234 (66.7%)	24 (54.5%)	**503 (72.5%)**
Yes	43 (14.4%)	97 (27.6%)	18 (40.9%)	**158 (22.8%)**
Anti androgenic therapy	0 (0.0%)	1 (0.3%)	1 (2.3%)	**2 (0.3%)**
Antibiotic combined with benzoyl peroxide (topical)	0 (0.0%)	16 (4.6%)	4 (9.1%)	**20 (2.9%)**
Antibiotics (form of application not specified/unclear)	0 (0.0%)	1 (0.3%)	1 (2.3%)	**2 (0.3%)**
Antimycotics	6 (2.0%)	4 (1.1%)	2 (4.5%)	**12 (1.7%)**
Azelaic-acid	2 (0.7%)	5 (1.4%)	1 (2.3%)	**8 (1.2%)**
Isotretinoin (form of application not specified/unclear)	0 (0.0%)	2 (0.6%)	0 (0.0%)	**2 (0.3%)**

	Mild	Moderate	Severe	**Total**
Retinoids combined with benzoyl peroxide (topical)	0 (0.0%)	1 (0.3%)	0 (0.0%)	**1 (0.1%)**
Systemic antibiotics	2 (0.7%)	3 (0.9%)	0 (0.0%)	**5 (0.7%)**
Topical antibiotics	7 (2.3%)	27 (7.7%)	4 (9.1%)	**38 (5.5%)**
Topical corticosteroids	0 (0.0%)	2 (0.6%)	0 (0.0%)	**2 (0.3%)**
Topical retinoids	3 (1.0%)	6 (1.7%)	0 (0.0%)	**9 (1.3%)**
Topical treatment with benzoyl peroxide	3 (1.0%)	4 (1.1%)	1 (2.3%)	**8 (1.2%)**
Various topical therapies/ keratolytics	22 (7.4%)	26 (7.4%)	6 (13.6%)	**54 (7.8%)**
Zinc powder	0 (0.0%)	1 (0.3%)	0 (0.0%)	**1 (0.1%)**
Zinc tablets/various oral therapies	0 (0.0%)	1 (0.3%)	0 (0.0%)	**1 (0.1%)**
Missing	1 (0.3%)	1 (0.3%)	0 (0.0%)	**2 (0.3%)**
Missing	11 (3.7%)	20 (5.7%)	2 (4.5%)	**33 (4.8%)**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-1.7 Duration and treatment of acne by severity - dermatology

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	18 (100%)	81 (100%)	24 (100%)	**123 (100%)**
Duration (in months)				
<1	0 (0.0%)	1 (1.2%)	0 (0.0%)	**1 (0.8%)**
1 - <6	0 (0.0%)	8 (9.9%)	1 (4.2%)	**9 (7.3%)**
6 - <12	3 (16.7%)	4 (4.9%)	3 (12.5%)	**10 (8.1%)**
>=12	15 (83.3%)	68 (84.0%)	20 (83.3%)	**103 (83.7%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Previous treatment				
No	5 (27.8%)	12 (14.8%)	2 (8.3%)	**19 (15.4%)**
Yes	13 (72.2%)	69 (85.2%)	22 (91.7%)	**104 (84.6%)**
Anti androgenic therapy	1 (5.6%)	2 (2.5%)	0 (0.0%)	**3 (2.4%)**
Antibiotic combined with benzoyl peroxide (topical)	1 (5.6%)	7 (8.6%)	5 (20.8%)	**13 (10.6%)**
Antibiotic combined with retinoid (topical)	2 (11.1%)	5 (6.2%)	3 (12.5%)	**10 (8.1%)**
Antibiotics (form of application not specified/unclear)	0 (0.0%)	11 (13.6%)	4 (16.7%)	**15 (12.2%)**
Antimycotics	2 (11.1%)	4 (4.9%)	0 (0.0%)	**6 (4.9%)**
Azelaic-acid	0 (0.0%)	4 (4.9%)	4 (16.7%)	**8 (6.5%)**
CPA/EE	5 (27.8%)	4 (4.9%)	2 (8.3%)	**11 (8.9%)**
Isotretinoin (form of application not specified/unclear)	1 (5.6%)	2 (2.5%)	7 (29.2%)	**10 (8.1%)**
Isotretinoin systemic	0 (0.0%)	5 (6.2%)	2 (8.3%)	**7 (5.7%)**
Oral Contraceptives (not including CPA/EE)	5 (27.8%)	3 (3.7%)	1 (4.2%)	**9 (7.3%)**
Retinoids combined with benzoyl peroxide (topical)	0 (0.0%)	4 (4.9%)	1 (4.2%)	**5 (4.1%)**
Systemic antibiotics	2 (11.1%)	21 (25.9%)	9 (37.5%)	**32 (26.0%)**
Topical antibiotics	5 (27.8%)	17 (21.0%)	5 (20.8%)	**27 (22.0%)**
Topical retinoids	2 (11.1%)	11 (13.6%)	3 (12.5%)	**16 (13.0%)**
Topical treatment with benzoyl peroxide	1 (5.6%)	10 (12.3%)	2 (8.3%)	**13 (10.6%)**
Various topical therapies/ keratolytics	2 (11.1%)	5 (6.2%)	1 (4.2%)	**8 (6.5%)**
Zinc tablets/various oral therapies	0 (0.0%)	2 (2.5%)	0 (0.0%)	**2 (1.6%)**
Treatment failed / insufficient				
Yes	13 (72.2%)	60 (74.1%)	22 (91.7%)	**95 (77.2%)**
No	0 (0.0%)	9 (11.1%)	0 (0.0%)	**9 (7.3%)**
Not applicable	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	12 (66.7%)	21 (25.9%)	5 (20.8%)	**38 (30.9%)**
Yes	6 (33.3%)	59 (72.8%)	19 (79.2%)	**84 (68.3%)**
Anti androgenic therapy	0 (0.0%)	0 (0.0%)	1 (4.2%)	**1 (0.8%)**
Antibiotic combined with benzoyl peroxide (topical)	2 (11.1%)	10 (12.3%)	0 (0.0%)	**12 (9.8%)**
Antibiotic combined with retinoid (topical)	0 (0.0%)	1 (1.2%)	1 (4.2%)	**2 (1.6%)**
Antibiotics (form of application not specified/unclear)	0 (0.0%)	3 (3.7%)	1 (4.2%)	**4 (3.3%)**
Azelaic-acid	0 (0.0%)	2 (2.5%)	1 (4.2%)	**3 (2.4%)**
Isotretinoin (form of application not specified/unclear)	1 (5.6%)	1 (1.2%)	6 (25.0%)	**8 (6.5%)**
Isotretinoin systemic	0 (0.0%)	8 (9.9%)	7 (29.2%)	**15 (12.2%)**
Retinoids combined with benzoyl peroxide (topical)	2 (11.1%)	11 (13.6%)	0 (0.0%)	**13 (10.6%)**
Systemic antibiotics	0 (0.0%)	10 (12.3%)	2 (8.3%)	**12 (9.8%)**

	Mild	Moderate	Severe	**Total**
Topical antibiotics	0 (0.0%)	5 (6.2%)	0 (0.0%)	**5 (4.1%)**
Topical retinoids	1 (5.6%)	11 (13.6%)	1 (4.2%)	**13 (10.6%)**
Topical treatment with benzoyl peroxide	0 (0.0%)	5 (6.2%)	1 (4.2%)	**6 (4.9%)**
Various topical therapies/ keratolytics	1 (5.6%)	11 (13.6%)	2 (8.3%)	**14 (11.4%)**
Zinc tablets/various oral therapies	0 (0.0%)	0 (0.0%)	1 (4.2%)	**1 (0.8%)**
Missing	0 (0.0%)	1 (1.2%)	0 (0.0%)	**1 (0.8%)**
Missing	0 (0.0%)	1 (1.2%)	0 (0.0%)	**1 (0.8%)**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-1.8 Duration and treatment of acne by severity - general practitioner (GP)

	Mild	Moderate	Severe	**Total**
Number (%) of eligible patients with acne	60 (100%)	130 (100%)	21 (100%)	**211 (100%)**
Duration (in months)				
<1	0 (0.0%)	2 (1.5%)	2 (9.5%)	**4 (1.9%)**
1 - <6	0 (0.0%)	2 (1.5%)	0 (0.0%)	**2 (0.9%)**
6 - <12	5 (8.3%)	3 (2.3%)	2 (9.5%)	**10 (4.7%)**
>=12	52 (86.7%)	123 (94.6%)	17 (81.0%)	**192 (91.0%)**
Missing	3 (5.0%)	0 (0.0%)	0 (0.0%)	**3 (1.4%)**
Previous treatment				
No	28 (46.7%)	22 (16.9%)	3 (14.3%)	**53 (25.1%)**
Yes	32 (53.3%)	108 (83.1%)	18 (85.7%)	**158 (74.9%)**
Anti androgenic therapy	0 (0.0%)	1 (0.8%)	1 (4.8%)	**2 (0.9%)**
Antibiotic combined with benzoyl peroxide (topical)	5 (8.3%)	21 (16.2%)	3 (14.3%)	**29 (13.7%)**
Antibiotics (form of application not specified/unclear)	3 (5.0%)	6 (4.6%)	1 (4.8%)	**10 (4.7%)**
Azelaic-acid	0 (0.0%)	3 (2.3%)	0 (0.0%)	**3 (1.4%)**
CPA/EE	1 (1.7%)	3 (2.3%)	0 (0.0%)	**4 (1.9%)**
Isotretinoin (form of application not specified/unclear)	0 (0.0%)	1 (0.8%)	0 (0.0%)	**1 (0.5%)**
Isotretinoin systemic	1 (1.7%)	3 (2.3%)	1 (4.8%)	**5 (2.4%)**
Oral Contraceptives (not including CPA/EE)	0 (0.0%)	4 (3.1%)	0 (0.0%)	**4 (1.9%)**
Retinoids combined with benzoyl peroxide (topical)	1 (1.7%)	8 (6.2%)	0 (0.0%)	**9 (4.3%)**
Systemic antibiotics	6 (10.0%)	39 (30.0%)	8 (38.1%)	**53 (25.1%)**
Topical antibiotics	14 (23.3%)	31 (23.8%)	2 (9.5%)	**47 (22.3%)**
Topical retinoids	1 (1.7%)	3 (2.3%)	1 (4.8%)	**5 (2.4%)**
Topical treatment with benzoyl peroxide	4 (6.7%)	17 (13.1%)	5 (23.8%)	**26 (12.3%)**
Various topical therapies/ keratolytics	2 (3.3%)	10 (7.7%)	0 (0.0%)	**12 (5.7%)**
Treatment failed / insufficient				
Yes	25 (41.7%)	96 (73.8%)	15 (71.4%)	**136 (64.5%)**
No	6 (10.0%)	12 (9.2%)	3 (14.3%)	**21 (10.0%)**
Not applicable	1 (1.7%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	**0 (0.0%)**
Concomitant treatment				
No	44 (73.3%)	67 (51.5%)	11 (52.4%)	**122 (57.8%)**
Yes	13 (21.7%)	57 (43.8%)	9 (42.9%)	**79 (37.4%)**
Antibiotic combined with benzoyl peroxide (topical)	1 (1.7%)	7 (5.4%)	0 (0.0%)	**8 (3.8%)**
Antibiotics (form of application not specified/unclear)	1 (1.7%)	2 (1.5%)	0 (0.0%)	**3 (1.4%)**
Antimycotics	1 (1.7%)	0 (0.0%)	0 (0.0%)	**1 (0.5%)**
Azelaic-acid	0 (0.0%)	1 (0.8%)	0 (0.0%)	**1 (0.5%)**
Isotretinoin (form of application not specified/unclear)	0 (0.0%)	2 (1.5%)	0 (0.0%)	**2 (0.9%)**
Isotretinoin systemic	0 (0.0%)	3 (2.3%)	2 (9.5%)	**5 (2.4%)**
Retinoids combined with benzoyl peroxide (topical)	1 (1.7%)	3 (2.3%)	0 (0.0%)	**4 (1.9%)**
Systemic antibiotics	1 (1.7%)	11 (8.5%)	2 (9.5%)	**14 (6.6%)**
Topical antibiotics	5 (8.3%)	14 (10.8%)	4 (19.0%)	**23 (10.9%)**
Topical retinoids	1 (1.7%)	2 (1.5%)	0 (0.0%)	**3 (1.4%)**
Topical treatment with benzoyl peroxide	3 (5.0%)	9 (6.9%)	1 (4.8%)	**13 (6.2%)**
Various topical therapies/ keratolytics	1 (1.7%)	8 (6.2%)	0 (0.0%)	**9 (4.3%)**

	Mild	Moderate	Severe	**Total**
Missing	3 (5.0%)	6 (4.6%)	1 (4.8%)	**10 (4.7%)**

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2 Duration and treatment of seborrhea

	CPA/EE
Number (%) of eligible patients with seborrhea	267 (100%)
Duration (in months)	
<1	3 (1.1%)
1 - <6	10 (3.7%)
6 - <12	20 (7.5%)
>=12	227 (85.0%)
Missing	7 (2.6%)
Previous treatment	
No	140 (52.4%)
Yes	104 (39.0%)
Anti androgenic therapy	1 (0.4%)
Antibiotic combined with benzoyl peroxide topical	5 (1.9%)
Antibiotics (form of application not specified/unclear)	3 (1.1%)
Antimycotic combined with corticosteroid (topical)	1 (0.4%)
Antimycotics	13 (4.9%)
Azelaic-acid	2 (0.7%)
CPA/EE	11 (4.1%)
Isotretinoin (form of application not specified/unclear)	5 (1.9%)
Isotretinoin systemic	1 (0.4%)
Local/Topical keratolysis/therapy	30 (11.2%)
Minoxidil	1 (0.4%)
Oral contraceptives (not including CPA/EE)	2 (0.7%)
Pimecrolimus	3 (1.1%)
Retinoids combined with benzoyl peroxide topical	2 (0.7%)
Systemic antibiotics	3 (1.1%)
Topical antibiotics	4 (1.5%)
Topical corticosteroids	6 (2.2%)
Topical retinoids	2 (0.7%)
Topical treatment with benzoyl peroxide	11 (4.1%)
Zinc	1 (0.4%)
Missing	23 (8.6%)
Concomitant treatment	
No	180 (67.4%)
Yes	52 (19.5%)
Antibiotic combined with benzoyl peroxide topical	1 (0.4%)
Antibiotics (form of application not specified/unclear)	1 (0.4%)
Antimycotics	6 (2.2%)
Azelaic-acid	1 (0.4%)
Isotretinoin (form of application not specified/unclear)	1 (0.4%)
Isotretinoin systemic	1 (0.4%)
Local/Topical keratolysis/therapy	26 (9.7%)
Systemic antibiotics	1 (0.4%)
Topical antibiotics	10 (3.7%)
Topical corticosteroids	5 (1.9%)
Zinc	2 (0.7%)
Missing	35 (13.1%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2.1 Duration and treatment of seborrhea - Austria

	CPA/EE
Number (%) of eligible patients with seborrhea	35 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	0 (0.0%)
6 - <12	2 (5.7%)
>=12	28 (80.0%)
Missing	5 (14.3%)
Previous treatment	
No	28 (80.0%)
Yes	2 (5.7%)
CPA/EE	1 (2.9%)
Local/Topical keratolysis/therapy	1 (2.9%)
Missing	5 (14.3%)
Concomitant treatment	
No	27 (77.1%)
Yes	0 (0.0%)
Missing	8 (22.9%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2.2 Duration and treatment of seborrhea - Czech Republic

	CPA/EE
Number (%) of eligible patients with seborrhea	59 (100%)
Duration (in months)	
<1	1 (1.7%)
1 - <6	3 (5.1%)
6 - <12	6 (10.2%)
>=12	49 (83.1%)
Missing	0 (0.0%)
Previous treatment	
No	34 (57.6%)
Yes	13 (22.0%)
Antimycotic combined with corticosteroid (topical)	1 (1.7%)
Antimycotics	2 (3.4%)
CPA/EE	5 (8.5%)
Local/Topical keratolysis/therapy	6 (10.2%)
Missing	12 (20.3%)
Concomitant treatment	
No	41 (69.5%)
Yes	4 (6.8%)
Local/Topical keratolysis/therapy	3 (5.1%)
Topical antibiotics	1 (1.7%)
Missing	14 (23.7%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2.3 Duration and treatment of seborrhea - France

	CPA/EE
Number (%) of eligible patients with seborrhea	5 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	1 (20.0%)
6 - <12	0 (0.0%)
>=12	4 (80.0%)
Missing	0 (0.0%)
Previous treatment	
No	3 (60.0%)
Yes	2 (40.0%)
Isotretinoin systemic	1 (20.0%)
Local/Topical keratolysis/therapy	1 (20.0%)
Missing	0 (0.0%)
Concomitant treatment	
No	4 (80.0%)
Yes	1 (20.0%)
Isotretinoin systemic	1 (20.0%)
Missing	0 (0.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2.4 Duration and treatment of seborrhea - The Netherlands

	CPA/EE
Number (%) of eligible patients with seborrhea	3 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	0 (0.0%)
6 - <12	0 (0.0%)
>=12	3 (100%)
Missing	0 (0.0%)
Previous treatment	
No	1 (33.3%)
Yes	2 (66.7%)
Antimycotics	1 (33.3%)
Systemic antibiotics	1 (33.3%)
Missing	0 (0.0%)
Concomitant treatment	
No	1 (33.3%)
Yes	0 (0.0%)
Missing	2 (66.7%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2.5 Duration and treatment of seborrhea - Spain

	CPA/EE
Number (%) of eligible patients with seborrhea	165 (100%)
Duration (in months)	
<1	2 (1.2%)
1 - <6	6 (3.6%)
6 - <12	12 (7.3%)
>=12	143 (86.7%)
Missing	2 (1.2%)
Previous treatment	
No	74 (44.8%)
Yes	85 (51.5%)
Anti androgenic therapy	1 (0.6%)
Antibiotic combined with benzoyl peroxide topical	5 (3.0%)
Antibiotics (form of application not specified/unclear)	3 (1.8%)
Antimycotics	10 (6.1%)
Azelaic-acid	2 (1.2%)
CPA/EE	5 (3.0%)
Isotretinoin (form of application not specified/unclear)	5 (3.0%)
Local/Topical keratolysis/therapy	22 (13.3%)
Minoxidil	1 (0.6%)
Oral contraceptives (not including CPA/EE)	2 (1.2%)
Pimecrolimus	3 (1.8%)
Retinoids combined with benzoyl peroxide topical	2 (1.2%)
Systemic antibiotics	2 (1.2%)
Topical antibiotics	4 (2.4%)
Topical corticosteroids	6 (3.6%)
Topical retinoids	2 (1.2%)
Topical treatment with benzoyl peroxide	11 (6.7%)
Zinc	1 (0.6%)
Missing	6 (3.6%)
Concomitant treatment	
No	107 (64.8%)
Yes	47 (28.5%)
Antibiotic combined with benzoyl peroxide topical	1 (0.6%)
Antibiotics (form of application not specified/unclear)	1 (0.6%)
Antimycotics	6 (3.6%)
Azelaic-acid	1 (0.6%)
Isotretinoin (form of application not specified/unclear)	1 (0.6%)
Local/Topical keratolysis/therapy	23 (13.9%)
Systemic antibiotics	1 (0.6%)
Topical antibiotics	9 (5.5%)
Topical corticosteroids	5 (3.0%)
Zinc	2 (1.2%)
Missing	11 (6.7%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2.6 Duration and treatment of seborrhea - gynecology

	CPA/EE
Number (%) of eligible patients with seborrhea	123 (100%)
Duration (in months)	
<1	1 (0.8%)
1 - <6	5 (4.1%)
6 - <12	10 (8.1%)
>=12	101 (82.1%)
Missing	6 (4.9%)
Previous treatment	
No	75 (61.0%)
Yes	26 (21.1%)
Antibiotics (form of application not specified/unclear)	1 (0.8%)
CPA/EE	11 (8.9%)
Local/Topical keratolysis/therapy	11 (8.9%)
Minoxidil	1 (0.8%)
Oral contraceptives (not including CPA/EE)	1 (0.8%)
Systemic antibiotics	1 (0.8%)
Topical antibiotics	1 (0.8%)
Missing	22 (17.9%)
Concomitant treatment	
No	87 (70.7%)
Yes	9 (7.3%)
Antibiotics (form of application not specified/unclear)	1 (0.8%)
Local/Topical keratolysis/therapy	7 (5.7%)
Topical antibiotics	1 (0.8%)
Missing	27 (22.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2.7 Duration and treatment of seborrhea - dermatology

	CPA/EE
Number (%) of eligible patients with seborrhea	54 (100%)
Duration (in months)	
<1	1 (1.9%)
1 - <6	3 (5.6%)
6 - <12	6 (11.1%)
>=12	43 (79.6%)
Missing	1 (1.9%)
Previous treatment	
No	23 (42.6%)
Yes	31 (57.4%)
Antibiotic combined with benzoyl peroxide topical	1 (1.9%)
Antibiotics (form of application not specified/unclear)	1 (1.9%)
Antimycotic combined with corticosteroid (topical)	1 (1.9%)
Antimycotics	4 (7.4%)
Isotretinoin (form of application not specified/unclear)	5 (9.3%)
Isotretinoin systemic	1 (1.9%)
Local/Topical keratolysis/therapy	16 (29.6%)
Pimecrolimus	1 (1.9%)
Topical corticosteroids	1 (1.9%)
Topical treatment with benzoyl peroxide	1 (1.9%)
Zinc	1 (1.9%)
Missing	0 (0.0%)
Concomitant treatment	
No	32 (59.3%)
Yes	20 (37.0%)
Antimycotics	3 (5.6%)
Isotretinoin (form of application not specified/unclear)	1 (1.9%)
Isotretinoin systemic	1 (1.9%)
Local/Topical keratolysis/therapy	13 (24.1%)
Zinc	2 (3.7%)
Missing	2 (3.7%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-2.8 Duration and treatment of seborrhea - general practitioner (GP)

	CPA/EE
Number (%) of eligible patients with seborrhea	90 (100%)
Duration (in months)	
<1	1 (1.1%)
1 - <6	2 (2.2%)
6 - <12	4 (4.4%)
>=12	83 (92.2%)
Missing	0 (0.0%)
Previous treatment	
No	42 (46.7%)
Yes	47 (52.2%)
Anti androgenic therapy	1 (1.1%)
Antibiotic combined with benzoyl peroxide topical	4 (4.4%)
Antibiotics (form of application not specified/unclear)	1 (1.1%)
Antimycotics	9 (10.0%)
Azelaic-acid	2 (2.2%)
Local/Topical keratolysis/therapy	3 (3.3%)
Oral contraceptives (not including CPA/EE)	1 (1.1%)
Pimecrolimus	2 (2.2%)
Retinoids combined with benzoyl peroxide topical	2 (2.2%)
Systemic antibiotics	2 (2.2%)
Topical antibiotics	3 (3.3%)
Topical corticosteroids	5 (5.6%)
Topical retinoids	2 (2.2%)
Topical treatment with benzoyl peroxide	10 (11.1%)
Missing	1 (1.1%)
Concomitant treatment	
No	61 (67.8%)
Yes	23 (25.6%)
Antibiotic combined with benzoyl peroxide topical	1 (1.1%)
Antimycotics	3 (3.3%)
Azelaic-acid	1 (1.1%)
Local/Topical keratolysis/therapy	6 (6.7%)
Systemic antibiotics	1 (1.1%)
Topical antibiotics	9 (10.0%)
Topical corticosteroids	5 (5.6%)
Missing	6 (6.7%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3 Duration and treatment of hirsutism

	CPA/EE
Number (%) of eligible patients with hirsutism	221 (100%)
Duration (in months)	
<1	3 (1.4%)
1 - <6	8 (3.6%)
6 - <12	21 (9.5%)
>=12	187 (84.6%)
Missing	2 (0.9%)
Previous treatment	
No	162 (73.3%)
Yes	42 (19.0%)
Anti androgenic therapy	8 (3.6%)
Antibiotic combined with benzoyl peroxide (topical)	1 (0.5%)
CPA/EE	11 (5.0%)
Eflornithine	5 (2.3%)
Laser diode hair removal	4 (1.8%)
Oral contraceptives (not including CPA/EE)	5 (2.3%)
Retinoids combined with benzoyl peroxide (topical)	2 (0.9%)
Topical retinoids	2 (0.9%)
Topical treatment with benzoyl peroxide	1 (0.5%)
Various topical therapies	2 (0.9%)
Missing	1 (0.5%)
Missing	17 (7.7%)
Concomitant treatment	
No	178 (80.5%)
Yes	16 (7.2%)
Anti androgenic therapy	3 (1.4%)
Eflornithine	2 (0.9%)
Intense Pulsed Light	1 (0.5%)
Laser diode hair removal	5 (2.3%)
Topical antibiotics	1 (0.5%)
Various topical therapies	2 (0.9%)
Vitamins and nutrients	1 (0.5%)
Missing	1 (0.5%)
Missing	27 (12.2%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3.1 Duration and treatment of hirsutism - Austria

	CPA/EE
Number (%) of eligible patients with hirsutism	20 (100%)
Duration (in months)	
<1	1 (5.0%)
1 - <6	1 (5.0%)
6 - <12	2 (10.0%)
>=12	15 (75.0%)
Missing	1 (5.0%)
Previous treatment	
No	16 (80.0%)
Yes	2 (10.0%)
CPA/EE	1 (5.0%)
Oral contraceptives (not including CPA/EE)	1 (5.0%)
Missing	2 (10.0%)
Concomitant treatment	
No	17 (85.0%)
Yes	0 (0.0%)
Missing	3 (15.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3.2 Duration and treatment of hirsutism - Czech Republic

	CPA/EE
Number (%) of eligible patients with hirsutism	38 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	1 (2.6%)
6 - <12	7 (18.4%)
>=12	30 (78.9%)
Missing	0 (0.0%)
Previous treatment	
No	24 (63.2%)
Yes	8 (21.1%)
Anti androgenic therapy	1 (2.6%)
CPA/EE	6 (15.8%)
Missing	1 (2.6%)
Missing	6 (15.8%)
Concomitant treatment	
No	29 (76.3%)
Yes	2 (5.3%)
Anti androgenic therapy	1 (2.6%)
Missing	1 (2.6%)
Missing	7 (18.4%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3.3 Duration and treatment of hirsutism - France

	CPA/EE
Number (%) of eligible patients with hirsutism	1 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	1 (100%)
6 - <12	0 (0.0%)
>=12	0 (0.0%)
Missing	0 (0.0%)
Previous treatment	
No	0 (0.0%)
Yes	1 (100%)
CPA/EE	1 (100%)
Missing	0 (0.0%)
Concomitant treatment	
No	1 (100%)
Yes	0 (0.0%)
Missing	0 (0.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3.4 Duration and treatment of hirsutism - The Netherlands

	CPA/EE
Number (%) of eligible patients with hirsutism	2 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	0 (0.0%)
6 - <12	0 (0.0%)
>=12	2 (100%)
Missing	0 (0.0%)
Previous treatment	
No	1 (50.0%)
Yes	0 (0.0%)
Missing	1 (50.0%)
Concomitant treatment	
No	0 (0.0%)
Yes	0 (0.0%)
Missing	2 (100%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3.5 Duration and treatment of hirsutism - Spain

	CPA/EE
Number (%) of eligible patients with hirsutism	160 (100%)
Duration (in months)	
<1	2 (1.3%)
1 - <6	5 (3.1%)
6 - <12	12 (7.5%)
>=12	140 (87.5%)
Missing	1 (0.6%)
Previous treatment	
No	121 (75.6%)
Yes	31 (19.4%)
Anti androgenic therapy	7 (4.4%)
Antibiotic combined with benzoyl peroxide (topical)	1 (0.6%)
CPA/EE	3 (1.9%)
Eflornithine	5 (3.1%)
Laser diode hair removal	4 (2.5%)
Oral contraceptives (not including CPA/EE)	4 (2.5%)
Retinoids combined with benzoyl peroxide (topical)	2 (1.3%)
Topical retinoids	2 (1.3%)
Topical treatment with benzoyl peroxide	1 (0.6%)
Various topical therapies	2 (1.3%)
Missing	8 (5.0%)
Concomitant treatment	
No	131 (81.9%)
Yes	14 (8.8%)
Anti androgenic therapy	2 (1.3%)
Eflornithine	2 (1.3%)
Intense Pulsed Light	1 (0.6%)
Laser diode hair removal	5 (3.1%)
Topical antibiotics	1 (0.6%)
Various topical therapies	2 (1.3%)
Vitamins and nutrients	1 (0.6%)
Missing	15 (9.4%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3.6 Duration and treatment of hirsutism - gynecology

	CPA/EE
Number (%) of eligible patients with hirsutism	90 (100%)
Duration (in months)	
<1	1 (1.1%)
1 - <6	4 (4.4%)
6 - <12	12 (13.3%)
>=12	72 (80.0%)
Missing	1 (1.1%)
Previous treatment	
No	59 (65.6%)
Yes	19 (21.1%)
Anti androgenic therapy	5 (5.6%)
CPA/EE	9 (10.0%)
Laser diode hair removal	1 (1.1%)
Oral contraceptives (not including CPA/EE)	3 (3.3%)
Missing	1 (1.1%)
Missing	12 (13.3%)
Concomitant treatment	
No	69 (76.7%)
Yes	5 (5.6%)
Anti androgenic therapy	2 (2.2%)
Laser diode hair removal	1 (1.1%)
Various topical therapies	1 (1.1%)
Missing	1 (1.1%)
Missing	16 (17.8%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3.7 Duration and treatment of hirsutism - dermatology

	CPA/EE
Number (%) of eligible patients with hirsutism	31 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	2 (6.5%)
6 - <12	3 (9.7%)
>=12	26 (83.9%)
Missing	0 (0.0%)
Previous treatment	
No	22 (71.0%)
Yes	8 (25.8%)
CPA/EE	1 (3.2%)
Eflornithine	5 (16.1%)
Laser diode hair removal	2 (6.5%)
Missing	1 (3.2%)
Concomitant treatment	
No	26 (83.9%)
Yes	4 (12.9%)
Eflornithine	2 (6.5%)
Intense Pulsed Light	1 (3.2%)
Laser diode hair removal	1 (3.2%)
Missing	1 (3.2%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-3.8 Duration and treatment of hirsutism - general practitioner (GP)

	CPA/EE
Number (%) of eligible patients with hirsutism	100 (100%)
Duration (in months)	
<1	2 (2.0%)
1 - <6	2 (2.0%)
6 - <12	6 (6.0%)
>=12	89 (89.0%)
Missing	1 (1.0%)
Previous treatment	
No	81 (81.0%)
Yes	15 (15.0%)
Anti androgenic therapy	3 (3.0%)
Antibiotic combined with benzoyl peroxide (topical)	1 (1.0%)
CPA/EE	1 (1.0%)
Laser diode hair removal	1 (1.0%)
Oral contraceptives (not including CPA/EE)	2 (2.0%)
Retinoids combined with benzoyl peroxide (topical)	2 (2.0%)
Topical retinoids	2 (2.0%)
Topical treatment with benzoyl peroxide	1 (1.0%)
Various topical therapies	2 (2.0%)
Missing	4 (4.0%)
Concomitant treatment	
No	83 (83.0%)
Yes	7 (7.0%)
Anti androgenic therapy	1 (1.0%)
Laser diode hair removal	3 (3.0%)
Topical antibiotics	1 (1.0%)
Various topical therapies	1 (1.0%)
Vitamins and nutrients	1 (1.0%)
Missing	10 (10.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4 Duration and treatment of androgenetic alopecia

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	89 (100%)
Duration (in months)	
<1	2 (2.2%)
1 - <6	10 (11.2%)
6 - <12	12 (13.5%)
>=12	62 (69.7%)
Missing	3 (3.4%)
Previous treatment	
No	43 (48.3%)
Yes	37 (41.6%)
5-alpha-reductase inhibitor	1 (1.1%)
Anti androgenetic therapy	3 (3.4%)
CPA/EE	5 (5.6%)
Corticosteroids	1 (1.1%)
Estrogen combined with corticosteroid	2 (2.2%)
Herbal medicines and various topical treatments	3 (3.4%)
Minoxidil	21 (23.6%)
Oral contraceptives (not including CPA/EE)	3 (3.4%)
Tacrolimus	1 (1.1%)
Vitamins and nutrients	5 (5.6%)
Missing	9 (10.1%)
Concomitant treatment	
No	60 (67.4%)
Yes	17 (19.1%)
5-alpha-reductase inhibitor	1 (1.1%)
Anti androgenetic therapy	3 (3.4%)
CPA/EE	1 (1.1%)
Corticosteroids	1 (1.1%)
Estrogen combined with corticosteroid	1 (1.1%)
Herbal medicines and various topical treatments	2 (2.2%)
Minoxidil	9 (10.1%)
Tacrolimus	1 (1.1%)
Vitamins and nutrients	2 (2.2%)
Missing	12 (13.5%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4.1 Duration and treatment of androgenetic alopecia - Austria

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	3 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	0 (0.0%)
6 - <12	0 (0.0%)
>=12	2 (66.7%)
Missing	1 (33.3%)
Previous treatment	
No	2 (66.7%)
Yes	0 (0.0%)
Missing	1 (33.3%)
Concomitant treatment	
No	2 (66.7%)
Yes	0 (0.0%)
Missing	1 (33.3%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4.2 Duration and treatment of androgenetic alopecia - Czech Republic

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	25 (100%)
Duration (in months)	
<1	1 (4.0%)
1 - <6	3 (12.0%)
6 - <12	6 (24.0%)
>=12	14 (56.0%)
Missing	1 (4.0%)
Previous treatment	
No	14 (56.0%)
Yes	8 (32.0%)
CPA/EE	1 (4.0%)
Corticosteroids	1 (4.0%)
Estrogen combined with corticosteroid	2 (8.0%)
Minoxidil	5 (20.0%)
Tacrolimus	1 (4.0%)
Vitamins and nutrients	1 (4.0%)
Missing	3 (12.0%)
Concomitant treatment	
No	18 (72.0%)
Yes	2 (8.0%)
Corticosteroids	1 (4.0%)
Estrogen combined with corticosteroid	1 (4.0%)
Minoxidil	1 (4.0%)
Tacrolimus	1 (4.0%)
Vitamins and nutrients	1 (4.0%)
Missing	5 (20.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4.3 Duration and treatment of androgenetic alopecia - France

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	1 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	0 (0.0%)
6 - <12	1 (100%)
>=12	0 (0.0%)
Missing	0 (0.0%)
Previous treatment	
No	0 (0.0%)
Yes	1 (100%)
Vitamins and nutrients	1 (100%)
Missing	0 (0.0%)
Concomitant treatment	
No	0 (0.0%)
Yes	1 (100%)
Minoxidil	1 (100%)
Missing	0 (0.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4.4 Duration and treatment of androgenetic alopecia - The Netherlands

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	2 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	0 (0.0%)
6 - <12	0 (0.0%)
>=12	2 (100%)
Missing	0 (0.0%)
Previous treatment	
No	0 (0.0%)
Yes	2 (100%)
Anti androgenetic therapy	1 (50.0%)
CPA/EE	1 (50.0%)
Herbal medicines and various topical treatments	1 (50.0%)
Missing	0 (0.0%)
Concomitant treatment	
No	0 (0.0%)
Yes	2 (100%)
Anti androgenetic therapy	1 (50.0%)
CPA/EE	1 (50.0%)
Herbal medicines and various topical treatments	1 (50.0%)
Missing	0 (0.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4.5 Duration and treatment of androgenetic alopecia - Spain

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	58 (100%)
Duration (in months)	
<1	1 (1.7%)
1 - <6	7 (12.1%)
6 - <12	5 (8.6%)
>=12	44 (75.9%)
Missing	1 (1.7%)
Previous treatment	
No	27 (46.6%)
Yes	26 (44.8%)
5-alpha-reductase inhibitor	1 (1.7%)
Anti androgenetic therapy	2 (3.4%)
CPA/EE	3 (5.2%)
Herbal medicines and various topical treatments	2 (3.4%)
Minoxidil	16 (27.6%)
Oral contraceptives (not including CPA/EE)	3 (5.2%)
Vitamins and nutrients	3 (5.2%)
Missing	5 (8.6%)
Concomitant treatment	
No	40 (69.0%)
Yes	12 (20.7%)
5-alpha-reductase inhibitor	1 (1.7%)
Anti androgenetic therapy	2 (3.4%)
Herbal medicines and various topical treatments	1 (1.7%)
Minoxidil	7 (12.1%)
Vitamins and nutrients	1 (1.7%)
Missing	6 (10.3%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4.6 Duration and treatment of androgenetic alopecia - gynecology

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	37 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	5 (13.5%)
6 - <12	7 (18.9%)
>=12	23 (62.2%)
Missing	2 (5.4%)
Previous treatment	
No	19 (51.4%)
Yes	9 (24.3%)
Anti androgenetic therapy	1 (2.7%)
CPA/EE	3 (8.1%)
Corticosteroids	1 (2.7%)
Estrogen combined with corticosteroid	1 (2.7%)
Herbal medicines and various topical treatments	1 (2.7%)
Minoxidil	3 (8.1%)
Oral contraceptives (not including CPA/EE)	1 (2.7%)
Tacrolimus	1 (2.7%)
Vitamins and nutrients	2 (5.4%)
Missing	9 (24.3%)
Concomitant treatment	
No	23 (62.2%)
Yes	3 (8.1%)
Anti androgenetic therapy	1 (2.7%)
Corticosteroids	1 (2.7%)
Estrogen combined with corticosteroid	1 (2.7%)
Minoxidil	1 (2.7%)
Tacrolimus	1 (2.7%)
Vitamins and nutrients	1 (2.7%)
Missing	11 (29.7%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4.7 Duration and treatment of androgenetic alopecia - dermatology

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	36 (100%)
Duration (in months)	
<1	1 (2.8%)
1 - <6	2 (5.6%)
6 - <12	3 (8.3%)
>=12	29 (80.6%)
Missing	1 (2.8%)
Previous treatment	
No	12 (33.3%)
Yes	24 (66.7%)
Anti androgenetic therapy	2 (5.6%)
CPA/EE	2 (5.6%)
Estrogen combined with corticosteroid	1 (2.8%)
Herbal medicines and various topical treatments	2 (5.6%)
Minoxidil	17 (47.2%)
Oral contraceptives (not including CPA/EE)	2 (5.6%)
Vitamins and nutrients	1 (2.8%)
Missing	0 (0.0%)
Concomitant treatment	
No	22 (61.1%)
Yes	13 (36.1%)
5-alpha-reductase inhibitor	1 (2.8%)
Anti androgenetic therapy	2 (5.6%)
CPA/EE	1 (2.8%)
Herbal medicines and various topical treatments	1 (2.8%)
Minoxidil	8 (22.2%)
Vitamins and nutrients	1 (2.8%)
Missing	1 (2.8%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-4.8 Duration and treatment of androgenetic alopecia - general practitioner (GP)

	CPA/EE
Number (%) of eligible patients with androgenetic alopecia	16 (100%)
Duration (in months)	
<1	1 (6.3%)
1 - <6	3 (18.8%)
6 - <12	2 (12.5%)
>=12	10 (62.5%)
Missing	0 (0.0%)
Previous treatment	
No	12 (75.0%)
Yes	4 (25.0%)
5-alpha-reductase inhibitor	1 (6.3%)
Minoxidil	1 (6.3%)
Vitamins and nutrients	2 (12.5%)
Missing	0 (0.0%)
Concomitant treatment	
No	15 (93.8%)
Yes	1 (6.3%)
Herbal medicines and various topical treatments	1 (6.3%)
Missing	0 (0.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the missing day of disease, the 1st was set; if the month was missing additionally, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5 Duration and treatment of PCOS

	CPA/EE
Number (%) of eligible patients with PCOS	192 (100%)
Duration (in months)	
<1	11 (5.7%)
1 - <6	15 (7.8%)
6 - <12	13 (6.8%)
>=12	149 (77.6%)
Missing	4 (2.1%)
Previous treatment	
No	132 (68.8%)
Yes	43 (22.4%)
Anti androgenic therapy	5 (2.6%)
CPA/EE	4 (2.1%)
Folic acid and inositol	5 (2.6%)
Metformin	3 (1.6%)
Oral contraceptives (not including CPA/EE)	25 (13.0%)
Progestins	1 (0.5%)
Topical antibiotics	1 (0.5%)
Missing	17 (8.9%)
Concomitant treatment	
No	148 (77.1%)
Yes	13 (6.8%)
Anti androgenic therapy	2 (1.0%)
CPA/EE	1 (0.5%)
Folic acid and inositol	2 (1.0%)
Metformin	3 (1.6%)
NSAID	2 (1.0%)
Oral contraceptives (not including CPA/EE)	1 (0.5%)
Vitamins and nutrients	2 (1.0%)
Missing	31 (16.1%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5.1 Duration and treatment of PCOS - Austria

	CPA/EE
Number (%) of eligible patients with PCOS	25 (100%)
Duration (in months)	
<1	3 (12.0%)
1 - <6	1 (4.0%)
6 - <12	2 (8.0%)
>=12	16 (64.0%)
Missing	3 (12.0%)
Previous treatment	
No	23 (92.0%)
Yes	1 (4.0%)
Oral contraceptives (not including CPA/EE)	1 (4.0%)
Missing	1 (4.0%)
Concomitant treatment	
No	22 (88.0%)
Yes	0 (0.0%)
Missing	3 (12.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5.2 Duration and treatment of PCOS - Czech Republic

	CPA/EE
Number (%) of eligible patients with PCOS	23 (100%)
Duration (in months)	
<1	5 (21.7%)
1 - <6	5 (21.7%)
6 - <12	1 (4.3%)
>=12	12 (52.2%)
Missing	0 (0.0%)
Previous treatment	
No	13 (56.5%)
Yes	2 (8.7%)
Anti androgenic therapy	2 (8.7%)
Missing	8 (34.8%)
Concomitant treatment	
No	13 (56.5%)
Yes	2 (8.7%)
Anti androgenic therapy	2 (8.7%)
Missing	8 (34.8%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5.3 Duration and treatment of PCOS - France

	CPA/EE
Number (%) of eligible patients with PCOS	0 (0.0%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	0 (0.0%)
6 - <12	0 (0.0%)
>=12	0 (0.0%)
Missing	0 (0.0%)
Previous treatment	
No	0 (0.0%)
Yes	0 (0.0%)
Missing	0 (0.0%)
Concomitant treatment	
No	0 (0.0%)
Yes	0 (0.0%)
Missing	0 (0.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5.4 Duration and treatment of PCOS - The Netherlands

	CPA/EE
Number (%) of eligible patients with PCOS	0 (0.0%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	0 (0.0%)
6 - <12	0 (0.0%)
>=12	0 (0.0%)
Missing	0 (0.0%)
Previous treatment	
No	0 (0.0%)
Yes	0 (0.0%)
Missing	0 (0.0%)
Concomitant treatment	
No	0 (0.0%)
Yes	0 (0.0%)
Missing	0 (0.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5.5 Duration and treatment of PCOS - Spain

	CPA/EE
Number (%) of eligible patients with PCOS	144 (100%)
Duration (in months)	
<1	3 (2.1%)
1 - <6	9 (6.3%)
6 - <12	10 (6.9%)
>=12	121 (84.0%)
Missing	1 (0.7%)
Previous treatment	
No	96 (66.7%)
Yes	40 (27.8%)
Anti androgenic therapy	3 (2.1%)
CPA/EE	4 (2.8%)
Folic acid and inositol	5 (3.5%)
Metformin	3 (2.1%)
Oral contraceptives (not including CPA/EE)	24 (16.7%)
Progestins	1 (0.7%)
Topical antibiotics	1 (0.7%)
Missing	8 (5.6%)
Concomitant treatment	
No	113 (78.5%)
Yes	11 (7.6%)
CPA/EE	1 (0.7%)
Folic acid and inositol	2 (1.4%)
Metformin	3 (2.1%)
NSAID	2 (1.4%)
Oral contraceptives (not including CPA/EE)	1 (0.7%)
Vitamins and nutrients	2 (1.4%)
Missing	20 (13.9%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5.6 Duration and treatment of PCOS - gynecology

	CPA/EE
Number (%) of eligible patients with PCOS	85 (100%)
Duration (in months)	
<1	9 (10.6%)
1 - <6	9 (10.6%)
6 - <12	5 (5.9%)
>=12	59 (69.4%)
Missing	3 (3.5%)
Previous treatment	
No	55 (64.7%)
Yes	16 (18.8%)
Anti androgenic therapy	2 (2.4%)
CPA/EE	1 (1.2%)
Folic acid and inositol	2 (2.4%)
Oral contraceptives (not including CPA/EE)	10 (11.8%)
Progestins	1 (1.2%)
Missing	14 (16.5%)
Concomitant treatment	
No	59 (69.4%)
Yes	6 (7.1%)
Anti androgenic therapy	2 (2.4%)
Folic acid and inositol	2 (2.4%)
Vitamins and nutrients	2 (2.4%)
Missing	20 (23.5%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5.7 Duration and treatment of PCOS - dermatology

	CPA/EE
Number (%) of eligible patients with PCOS	16 (100%)
Duration (in months)	
<1	0 (0.0%)
1 - <6	1 (6.3%)
6 - <12	0 (0.0%)
>=12	15 (93.8%)
Missing	0 (0.0%)
Previous treatment	
No	8 (50.0%)
Yes	8 (50.0%)
CPA/EE	1 (6.3%)
Folic acid and inositol	2 (12.5%)
Metformin	2 (12.5%)
Oral contraceptives (not including CPA/EE)	2 (12.5%)
Topical antibiotics	1 (6.3%)
Missing	0 (0.0%)
Concomitant treatment	
No	14 (87.5%)
Yes	2 (12.5%)
CPA/EE	1 (6.3%)
Metformin	1 (6.3%)
Missing	0 (0.0%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B4-5.8 Duration and treatment of PCOS - general practitioner (GP)

	CPA/EE
Number (%) of eligible patients with PCOS	91 (100%)
Duration (in months)	
<1	2 (2.2%)
1 - <6	5 (5.5%)
6 - <12	8 (8.8%)
>=12	75 (82.4%)
Missing	1 (1.1%)
Previous treatment	
No	69 (75.8%)
Yes	19 (20.9%)
Anti androgenic therapy	3 (3.3%)
CPA/EE	2 (2.2%)
Folic acid and inositol	1 (1.1%)
Metformin	1 (1.1%)
Oral contraceptives (not including CPA/EE)	13 (14.3%)
Missing	3 (3.3%)
Concomitant treatment	
No	75 (82.4%)
Yes	5 (5.5%)
Metformin	2 (2.2%)
NSAID	2 (2.2%)
Oral contraceptives (not including CPA/EE)	1 (1.1%)
Missing	11 (12.1%)

Note: Patient may have more than one entry for previous and concomitant treatment.
Note: For the day of disease, the 1st was set. If the month was missing, the 31st of December was used for calculation of the duration.
Date of analysis: 12MAY2016

Table B5 - Concomitant use of hormonal contraceptives and CPA/EE

	CPA/EE
Number (%) of eligible patients with	1513 (100%)
No additional HC	1469 (97.1%)
Additional HC	44 (2.9%)
Oral contraceptive	42 (2.8%)
Non-oral contraceptive	2 (0.1%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B5.1 Concomitant use of hormonal contraceptives and CPA/EE - Austria

	CPA/EE
Number (%) of eligible patients with	282 (100%)
No additional HC	282 (100%)
Additional HC	0 (0.0%)
Oral contraceptive	0 (0.0%)
Non-oral contraceptive	0 (0.0%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B5.2 Concomitant use of hormonal contraceptives and CPA/EE - Czech Republic

	CPA/EE
Number (%) of eligible patients with	563 (100%)
No additional HC	542 (96.3%)
Additional HC	21 (3.7%)
Oral contraceptive	21 (3.7%)
Non-oral contraceptive	0 (0.0%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B5.3 Concomitant use of hormonal contraceptives and CPA/EE - France

	CPA/EE
Number (%) of eligible patients with	24 (100%)
No additional HC	22 (91.7%)
Additional HC	2 (8.3%)
Oral contraceptive	2 (8.3%)
Non-oral contraceptive	0 (0.0%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B5.4 Concomitant use of hormonal contraceptives and CPA/EE - The Netherlands

	CPA/EE
Number (%) of eligible patients with	32 (100%)
No additional HC	32 (100%)
Additional HC	0 (0.0%)
Oral contraceptive	0 (0.0%)
Non-oral contraceptive	0 (0.0%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B5.5 Concomitant use of hormonal contraceptives and CPA/EE - Spain

	CPA/EE
Number (%) of eligible patients with	612 (100%)
No additional HC	591 (96.6%)
Additional HC	21 (3.4%)
Oral contraceptive	19 (3.1%)
Non-oral contraceptive	2 (0.3%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B5.6 Concomitant use of hormonal contraceptives and CPA/EE - gynecology

	CPA/EE
Number (%) of eligible patients with	936 (100%)
No additional HC	901 (96.3%)
Additional HC	35 (3.7%)
Oral contraceptive	35 (3.7%)
Non-oral contraceptive	0 (0.0%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B5.7 Concomitant use of hormonal contraceptives and CPA/EE - dermatology

	CPA/EE
Number (%) of eligible patients with	167 (100%)
No additional HC	164 (98.2%)
Additional HC	3 (1.8%)
Oral contraceptive	2 (1.2%)
Non-oral contraceptive	1 (0.6%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B5.8 Concomitant use of hormonal contraceptives and CPA/EE - general practitioner (GP)

	CPA/EE
Number (%) of eligible patients with	410 (100%)
No additional HC	404 (98.5%)
Additional HC	6 (1.5%)
Oral contraceptive	5 (1.2%)
Non-oral contraceptive	1 (0.2%)
Missing	0 (0.0%)
Missing	0 (0.0%)

Date of analysis: 12MAY2016

Table B6 - CPA/EE use and treatment for the indication of acne and hirsutism

	CPA/EE	95%-CI
Number (%) of eligible patients with	1513 (100%)	
Moderate or severe acne (without hirsutism)	564 (37.3%)	[29.8%;45.3%]
Previous topical treatment only	199 (13.2%)	[6.5%;22.8%]
Previous systemic antibiotic treatment only	34 (2.2%)	[1.2%;3.8%]
Previous topical and/or systemic antibiotic treatment	301 (19.9%)	[12.8%;28.7%]
No previous topical and systemic antibiotic treatment	263 (17.4%)	[12.5%;23.2%]
Other previous treatment only	60 (4.0%)	[2.6%;5.7%]
Missing	1 (0.1%)	[0.0%;0.4%]
Acne with hirsutism	118 (7.8%)	[5.7%;10.4%]
Previous topical treatment only	43 (2.8%)	[1.6%;4.6%]
Previous systemic antibiotic treatment only	6 (0.4%)	[0.1%;1.0%]
Previous topical and/or systemic antibiotic treatment	64 (4.2%)	[2.6%;6.5%]
No previous topical and systemic antibiotic treatment	54 (3.6%)	[2.3%;5.3%]
Other previous treatment only	13 (0.9%)	[0.4%;1.6%]
Missing	1 (0.1%)	[0.0%;0.4%]
Hirsutism (without acne)	103 (6.8%)	[4.8%;9.4%]
Neither moderate or severe acne nor hirsutism	728 (48.1%)	[39.4%;56.9%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B6.1 CPA/EE use and treatment for the indication of acne and hirsutism - Austria

	CPA/EE	95%-CI
Number (%) of eligible patients with	282 (100%)	
Moderate or severe acne (without hirsutism)	93 (33.0%)	[19.9%;48.3%]
Previous topical treatment only	7 (2.5%)	[0.8%;5.6%]
Previous systemic antibiotic treatment only	3 (1.1%)	[0.1%;3.8%]
Previous topical and/or systemic antibiotic treatment	16 (5.7%)	[2.3%;11.4%]
No previous topical and systemic antibiotic treatment	77 (27.3%)	[17.8%;38.7%]
Other previous treatment only	9 (3.2%)	[0.9%;7.9%]
Missing	0 (0.0%)	[0.0%;0.0%]
Acne with hirsutism	12 (4.3%)	[1.3%;10.1%]
Previous topical treatment only	4 (1.4%)	[0.2%;5.0%]
Previous systemic antibiotic treatment only	1 (0.4%)	[0.0%;2.1%]
Previous topical and/or systemic antibiotic treatment	5 (1.8%)	[0.3%;5.9%]
No previous topical and systemic antibiotic treatment	7 (2.5%)	[0.4%;8.2%]
Other previous treatment only	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Hirsutism (without acne)	8 (2.8%)	[1.0%;6.1%]
Neither moderate or severe acne nor hirsutism	169 (59.9%)	[41.6%;76.4%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B6.2 CPA/EE use and treatment for the indication of acne and hirsutism - Czech Republic

	CPA/EE	95%-CI
Number (%) of eligible patients with	563 (100%)	
Moderate or severe acne (without hirsutism)	254 (45.1%)	[27.9%;63.2%]
Previous topical treatment only	122 (21.7%)	[6.3%;46.6%]
Previous systemic antibiotic treatment only	0 (0.0%)	[0.0%;0.0%]
Previous topical and/or systemic antibiotic treatment	140 (24.9%)	[8.8%;48.4%]
No previous topical and systemic antibiotic treatment	114 (20.2%)	[9.5%;35.4%]
Other previous treatment only	22 (3.9%)	[1.8%;7.4%]
Missing	1 (0.2%)	[0.0%;1.0%]
Acne with hirsutism	29 (5.2%)	[2.7%;8.8%]
Previous topical treatment only	8 (1.4%)	[0.2%;5.0%]
Previous systemic antibiotic treatment only	0 (0.0%)	[0.0%;0.0%]
Previous topical and/or systemic antibiotic treatment	8 (1.4%)	[0.2%;5.0%]
No previous topical and systemic antibiotic treatment	21 (3.7%)	[1.5%;7.7%]
Other previous treatment only	6 (1.1%)	[0.3%;2.7%]
Missing	1 (0.2%)	[0.0%;1.0%]
Hirsutism (without acne)	9 (1.6%)	[0.7%;3.2%]
Neither moderate or severe acne nor hirsutism	271 (48.1%)	[28.8%;67.9%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B6.3 CPA/EE use and treatment for the indication of acne and hirsutism - France

	CPA/EE	95%-CI
Number (%) of eligible patients with	24 (100%)	
Moderate or severe acne (without hirsutism)	14 (58.3%)	[22.7%;88.4%]
Previous topical treatment only	2 (8.3%)	[0.6%;31.5%]
Previous systemic antibiotic treatment only	1 (4.2%)	[0.1%;21.1%]
Previous topical and/or systemic antibiotic treatment	8 (33.3%)	[4.8%;76.5%]
No previous topical and systemic antibiotic treatment	6 (25.0%)	[7.9%;50.8%]
Other previous treatment only	6 (25.0%)	[7.9%;50.8%]
Missing	0 (0.0%)	[0.0%;0.0%]
Acne with hirsutism	1 (4.2%)	[0.1%;21.1%]
Previous topical treatment only	0 (0.0%)	[0.0%;0.0%]
Previous systemic antibiotic treatment only	1 (4.2%)	[0.1%;21.1%]
Previous topical and/or systemic antibiotic treatment	1 (4.2%)	[0.1%;21.1%]
No previous topical and systemic antibiotic treatment	0 (0.0%)	[0.0%;0.0%]
Other previous treatment only	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Hirsutism (without acne)	0 (0.0%)	[0.0%;0.0%]
Neither moderate or severe acne nor hirsutism	9 (37.5%)	[6.1%;80.3%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B6.4 CPA/EE use and treatment for the indication of acne and hirsutism - The Netherlands

	CPA/EE	95%-CI
Number (%) of eligible patients with	32 (100%)	
Moderate or severe acne (without hirsutism)	17 (53.1%)	[17.1%;86.8%]
Previous topical treatment only	3 (9.4%)	[2.0%;25.0%]
Previous systemic antibiotic treatment only	0 (0.0%)	[0.0%;0.0%]
Previous topical and/or systemic antibiotic treatment	6 (18.8%)	[7.2%;36.4%]
No previous topical and systemic antibiotic treatment	11 (34.4%)	[5.1%;77.4%]
Other previous treatment only	4 (12.5%)	[1.3%;40.5%]
Missing	0 (0.0%)	[0.0%;0.0%]
Acne with hirsutism	2 (6.3%)	[0.2%;27.8%]
Previous topical treatment only	1 (3.1%)	[0.0%;30.0%]
Previous systemic antibiotic treatment only	0 (0.0%)	[0.0%;0.0%]
Previous topical and/or systemic antibiotic treatment	1 (3.1%)	[0.0%;30.0%]
No previous topical and systemic antibiotic treatment	1 (3.1%)	[0.0%;21.0%]
Other previous treatment only	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Hirsutism (without acne)	0 (0.0%)	[0.0%;0.0%]
Neither moderate or severe acne nor hirsutism	13 (40.6%)	[6.5%;84.0%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B6.5 CPA/EE use and treatment for the indication of acne and hirsutism - Spain

	CPA/EE	95%-CI
Number (%) of eligible patients with	612 (100%)	
Moderate or severe acne (without hirsutism)	186 (30.4%)	[23.4%;38.1%]
Previous topical treatment only	65 (10.6%)	[6.8%;15.6%]
Previous systemic antibiotic treatment only	30 (4.9%)	[2.5%;8.6%]
Previous topical and/or systemic antibiotic treatment	131 (21.4%)	[15.6%;28.2%]
No previous topical and systemic antibiotic treatment	55 (9.0%)	[5.5%;13.6%]
Other previous treatment only	19 (3.1%)	[1.3%;6.3%]
Missing	0 (0.0%)	[0.0%;0.0%]
Acne with hirsutism	74 (12.1%)	[8.0%;17.3%]
Previous topical treatment only	30 (4.9%)	[2.5%;8.6%]
Previous systemic antibiotic treatment only	4 (0.7%)	[0.1%;2.0%]
Previous topical and/or systemic antibiotic treatment	49 (8.0%)	[4.5%;13.0%]
No previous topical and systemic antibiotic treatment	25 (4.1%)	[2.3%;6.7%]
Other previous treatment only	7 (1.1%)	[0.4%;2.5%]
Missing	0 (0.0%)	[0.0%;0.0%]
Hirsutism (without acne)	86 (14.1%)	[9.8%;19.3%]
Neither moderate or severe acne nor hirsutism	266 (43.5%)	[33.8%;53.5%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B6.6 CPA/EE use and treatment for the indication of acne and hirsutism - gynecology

	CPA/EE	95%-CI
Number (%) of eligible patients with	936 (100%)	
Moderate or severe acne (without hirsutism)	354 (37.8%)	[26.6%;50.1%]
Previous topical treatment only	122 (13.0%)	[3.6%;30.3%]
Previous systemic antibiotic treatment only	5 (0.5%)	[0.1%;1.6%]
Previous topical and/or systemic antibiotic treatment	142 (15.2%)	[5.4%;31.2%]
No previous topical and systemic antibiotic treatment	212 (22.6%)	[15.1%;31.7%]
Other previous treatment only	39 (4.2%)	[2.5%;6.5%]
Missing	1 (0.1%)	[0.0%;0.6%]
Acne with hirsutism	58 (6.2%)	[4.0%;9.1%]
Previous topical treatment only	17 (1.8%)	[0.7%;3.7%]
Previous systemic antibiotic treatment only	2 (0.2%)	[0.0%;0.8%]
Previous topical and/or systemic antibiotic treatment	21 (2.2%)	[1.0%;4.3%]
No previous topical and systemic antibiotic treatment	37 (4.0%)	[2.2%;6.6%]
Other previous treatment only	11 (1.2%)	[0.5%;2.3%]
Missing	1 (0.1%)	[0.0%;0.6%]
Hirsutism (without acne)	32 (3.4%)	[1.9%;5.6%]
Neither moderate or severe acne nor hirsutism	492 (52.6%)	[39.4%;65.4%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B6.7 CPA/EE use and treatment for the indication of acne and hirsutism - dermatology

	CPA/EE	95%-CI
Number (%) of eligible patients with	167 (100%)	
Moderate or severe acne (without hirsutism)	98 (58.7%)	[46.2%;70.4%]
Previous topical treatment only	30 (18.0%)	[8.9%;30.7%]
Previous systemic antibiotic treatment only	15 (9.0%)	[2.8%;20.3%]
Previous topical and/or systemic antibiotic treatment	72 (43.1%)	[31.7%;55.1%]
No previous topical and systemic antibiotic treatment	26 (15.6%)	[6.6%;29.2%]
Other previous treatment only	14 (8.4%)	[2.3%;20.1%]
Missing	0 (0.0%)	[0.0%;0.0%]
Acne with hirsutism	11 (6.6%)	[2.0%;15.3%]
Previous topical treatment only	5 (3.0%)	[0.3%;10.6%]
Previous systemic antibiotic treatment only	1 (0.6%)	[0.0%;3.7%]
Previous topical and/or systemic antibiotic treatment	8 (4.8%)	[0.7%;15.0%]
No previous topical and systemic antibiotic treatment	3 (1.8%)	[0.4%;5.2%]
Other previous treatment only	0 (0.0%)	[0.0%;0.0%]
Missing	0 (0.0%)	[0.0%;0.0%]
Hirsutism (without acne)	20 (12.0%)	[2.6%;30.8%]
Neither moderate or severe acne nor hirsutism	38 (22.8%)	[15.0%;32.1%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016

Table B6.8 CPA/EE use and treatment for the indication of acne and hirsutism - general practitioner (GP)

	CPA/EE	95%-CI
Number (%) of eligible patients with	410 (100%)	
Moderate or severe acne (without hirsutism)	112 (27.3%)	[19.5%;36.3%]
Previous topical treatment only	47 (11.5%)	[6.4%;18.5%]
Previous systemic antibiotic treatment only	14 (3.4%)	[1.5%;6.7%]
Previous topical and/or systemic antibiotic treatment	87 (21.2%)	[14.2%;29.8%]
No previous topical and systemic antibiotic treatment	25 (6.1%)	[3.1%;10.5%]
Other previous treatment only	7 (1.7%)	[0.6%;3.8%]
Missing	0 (0.0%)	[0.0%;0.0%]
Acne with hirsutism	49 (12.0%)	[6.7%;19.1%]
Previous topical treatment only	21 (5.1%)	[2.0%;10.6%]
Previous systemic antibiotic treatment only	3 (0.7%)	[0.1%;2.8%]
Previous topical and/or systemic antibiotic treatment	35 (8.5%)	[3.9%;15.8%]
No previous topical and systemic antibiotic treatment	14 (3.4%)	[1.4%;6.9%]
Other previous treatment only	2 (0.5%)	[0.1%;1.8%]
Missing	0 (0.0%)	[0.0%;0.0%]
Hirsutism (without acne)	51 (12.4%)	[8.2%;17.9%]
Neither moderate or severe acne nor hirsutism	198 (48.3%)	[35.3%;61.4%]

Note: Exact 95% CI for proportions are given, variance inflation is considered in terms of effective sample size (Clopper & Pearson, 1934, Korn & Graubard, 1998)
Date of analysis: 12MAY2016