Science For A Better Life

Clinical Study Synopsis

This Clinical Study Synopsis is provided for patients and healthcare professionals to increase the transparency of Bayer's clinical research. This document is not intended to replace the advice of a healthcare professional and should not be considered as a recommendation. Patients should always seek medical advice before making any decisions on their treatment. Healthcare Professionals should always refer to the specific labelling information approved for the patient's country or region. Data in this document or on the related website should not be considered as prescribing advice.
The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

The following information is the property of Bayer AG. Reproduction of all or part of this report is strictly prohibited without prior written permission from Bayer AG. Commercial use of the information is only possible with the written permission of the proprietor and is subject to a license fee. Please note that the General Conditions of Use and the Privacy Statement of bayer.com apply to the contents of this file.

Date of study report:	23th May 2016 & 21st December 2016
Study title:	Drug Utilization Study on the Prescribing Indications for CPA/EE in 5 European Countries
Sponsor's study number:	17194
NCT number:	NCT02494297
EudraCT number:	Not applicable
Sponsor:	Bayer
Clinical phase:	Observational Study
Study objectives:	The primary objective of the study was to characterize the prescribing behaviors for CPA/EE (Cyroterone Acetate/Ethynyl Estradiol) 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
Test drug:	Diane 35 (EE/CPA, BAY86-5264)
Name of active ingredient(s):	Cyproterone acetate (CPA) in combination with ethinylestradiol (EE) [CPA/EE]
Dose:	Cyproterone acetate 2mg, Ethinylestradiol 0.035mg
Route of administration:	Oral
Duration of treatment:	According to the treating physician
Background treatment]:	Various topical therapies / keratolytics, topical antibiotics, systemic isotretinoin
Reference drug:	Not applicable
Indication:	Moderate to severe acne related to androgen sensitivity and /or hirsutism in women of reproductive age when topical therapy or systemic antibiotic treatments have failed.

Diagnosis and main criteria for inclusion:	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.
Study design:	The DUS (Drug Utilization Study) CPA/EE was a multi-national, cross-sectional study that characterized 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.
Methodology:	The treating 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 (Over The Counter) 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.
Study center(s):	5 investigational sites in 5 countries: Austria (1), Czech Republic (1), France(1), The Netherlands (1), and Spain (1)
Publication(s) based on the study (references):	None at the time of report creation.
Study period:	Study Start Date: 06-Mar-2015 Study Completion Date: 11-May-2016 (main report) 31-October-2016 (addendum France)
Early termination:	Not applicable

Number of subjects:	**Planned:** 5000 **Analyzed:** 1513 (main report) 1597 (incl. addendum France)
Criteria for evaluation	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: • brand name of prescribed CPA/EE containing drug • first use, re-use after a break, or continuous use of CPA/EE • concomitant hormonal contraceptive use • information about androgen-sensitive diseases: - duration - previous treatment - concomitant treatment - information on treatment failure • reasons for prescribing CPA/EE
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 androgensensitive 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 crosssectional 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. 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. Statistical evaluation was performed with the software package SAS®, release version 9.4, 2013.

Substantial protocol changes:	The study was conducted according to final Study Protocol from 26th January 2015, and included no substantial amendments. However, there was a protocol deviation with respect tot the original study schedule: As the approval of CNIL (Commission nationale de l'information et des libertés) 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 until 31st October 2016 in order to compensate for the delayed start. All data collected up to 8th April 2016 were included in the main report. French data were reported separately in an amended study report. ***In order to facilitate reading, the separate information on the French data (text and tables) is allways marked by "addendum".***

Subject disposition and baseline

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 2015 to the 8th April 2016, and the physicians had time to submit the last questionnaires until 14th April 2016.
For the analysis of the main report, a total o f 1,574 patients were recruited by 120 physicians. A total of 61 (3.9%) o f 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 missinginformed consent forms (n = 22). The remaining 1,513 quality-controlled computerized data sets were analyzed.

In France, 148 patients had been recruited of whom 108 (73.0%) were eligible and 40 (27.0%) were not. 68 of the eligible patients were recruited by gynecologists, 27 by dermatologists and 13 by GPs. Seven patients had to be excluded from the study because the parents' written consent would have been needed due to their age, but only their own signature was provided. Also, five patients who had been recruited after the planned end of recruitment and were not included.

Following the completion of the DUS survey CPA/EE study (main study) in April 2016, the study report was submitted to the relevant authorities for assessment within the agreed timetable.

However, due to the late start of recruitment in France, it was decided to continue the study in France in order to obtain more documented prescription events, leading to a clearer view of the prescribing behavior of French physicians. The results of the French data have been submitted in an addendum on December 21, 2016 to the relevant authorities and reflect the new set of data from France and compares it to results reported in the main study.

Results

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-starters3. 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%).

Prescription status – France (addendum)

In France, 28.7% of the eligible patients were first-time users, 59.3% continuous users, and 12.0% were restarters.
The proportion of restarters was similar to the proportion found in the overall data of the main report (14.7%), whereas the first-time users (42.0%) and continuous users (42.6%) were more evenly distributed in the main report.

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 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 1]

Table 1: - ***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%]
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

Prescribing reasons – France (addendum)

The main reason for CPA/EE prescription in France was acne (88.9%, n = 96). The second most stated reason was contraception (32.4%, n = 35) followed by seborrhea (11.1%) and hirsutism (10.2%). PCOS, androgenetic alopecia and “other reasons” were mentioned less frequently with 5.6%, 3.7% and 2.8%, respectively. In 2.8% (n = 3) contraception was the only listed reason for the prescription. The proportions for “PCOS only” and “androgenetic alopecia” only were 0.9% (n = 1) each.
In the data of the main report acne was stated less frequently as a reason for prescription (65.6%), whereas PCOS (11.4%) and contraception (66.7%) were more frequently stated as a reason for prescription. All other reasons for prescription show a similar trend in the overall data of the main report and the updated data for France. [Table 2]

Table 2: ***Prescribing reasons for CPA/EE – France (addendum)***

	CPA/EE	95%-CI
Number (%) of eligible patients	108 (100%)	
Reason		
Acne	96 (88.9%)	[80.6%;94.5%]
Seborrhea	12 (11.1%)	[5.9%;18.6%]
Hirsutism	11 (10.2%)	[4.8%;18.4%]
Androgenetic alopecia	4 (3.7%)	[0.9%;9.6%]
PCOS	6 (5.6%)	[1.3%;14.7%]
Contraception	35 (32.4%)	[17.3%;50.8%]
Other reasons	3 (2.8%)	[0.5%;8.2%]
Contraception only	3 (2.8%)	[0.6%;7.9%]

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: 15DEC2016

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% .
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%. 38 DUS CPA/EE: Final Study Report 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.

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.
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 General Practitioners (GPs) (37.4%) and Gynecologists (22.8%).

Previous treatment of acne – France (addendum)

Of the 99 patients who had a diagnosis of acne in France, 50 had mild acne (50.5% of all patients with a diagnosis of acne), 35 moderate (35.4% of all patients with a diagnosis of acne) and 14 severe acne (14.1% of all patients with a diagnosis of acne). 75.8% (n = 75) of the patients who had an acne diagnosis had received previous treatment. There was little difference in the percentage of patients who had previously been treated for acne according to the diagnostic severity of disease; previous treatment was stated in 74.0% of the patients with mild acne, 77.1% with moderate acne and 78.6% of the severely affected patients.
The percentage of mild, moderate, and severe acne in France differed from the overall data in the main report. Mild acne accounted for 36.7% of all acne diagnoses, moderate acne for 54.7% and severe acne

for 8.7%. The overall previous treatment percentage of all acne patients in the main report (57.0%) was lower than in France. The overall data in the main study showed an increasing percentage of previous acne treatment with increasing severity (42.7% previous treatment in patients diagnosed with mild acne, 63.2% moderate, 78.7% severe). 89.9% of all patients with acne in France have had their acne diagnosis for more than 12 months and 51.5% (n = 51) of the previous treatments were documented as failed or insufficient. For moderate to severe acne (i.e. without mild acne) previous treatment failure was 61.2%.
In comparison, previous treatment failure in all acne patients combined in the main report was 41.6%. For moderate to severe acne this number was 51.8%.
For patients with mild acne in France, the most frequently mentioned previous treatments were ”various topical therapies/keratolytics” (n = 11, 22.0%), which include OTC medications and washing lotions, followed by antibiotics without known form of application and systemic antibiotics (both n = 7, 14.0%). 12% (n = 6) had previously been treated with systemic isotretinoin, 8.0% (n=4) with oral contraceptives (excluding CPA/EE), anti-androgenic therapy and CPA/EE (all three categories 8.0%). In 42.0% of the cases, the previous treatment was documented as failed or insufficient.
In the overall data of the main report the most frequently mentioned previous treatments in patients with mild acne were also “various topical therapies/keratolytics” (n = 46, 12.2%) which include OTC medications and washing lotions, 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 in France the most common previous treatments were antibiotics without known form of application (n = 6, 17.1%), systemic antibiotics (n = 6, 17.1%) and systemic isotretinoin (n = 4, 11.4%). In patients with moderate acne the proportion of failed or insufficient previous treatments was 60.0%.
In the overall data of the main report, the most common previous treatments for patients with moderate acne 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%). The percentage of failed or insufficient previous treatment for these patients was stated as 49.6%. For patients with severe acne the most frequently mentioned previous treatments in the main report were systemic antibiotics (n = 7, 50.0%) and topical retinoids (n = 4, 28.6%). Patients with severe acne had the highest proportion of failed or insufficient treatments (64.3%).
In the overall data of the main report, the most common previous treatments for patients with severe acne were systemic antibiotics (n = 19, 21.3%), topical antibiotics (n = 14, 15.7%), and antibiotics combined with benzoyl peroxide (n = 10, 11.2%). These patients with severe acne had a proportion of failed or insufficient treatments of 65.2%.

Concomitant treatment of acne – France (addendum)

Overall, 30.3% (n = 30) of the patients with an acne diagnosis in France received treatment in addition to CPA/EE. There was a marked difference in concomitant treatment percentage between the three groups of severity; 18.0% (n = 9) of the patients with mild acne received concomitant treatment, whereas 31.4% (n = 11) with moderate acne, and 71.4% (n = 10) of the patients severely affected by acne received concomitant treatment. This marked difference was also found in the overall data of the main report (16.4% of the patients with mild acne received concomitant treatment, 37.9% with moderate acne and 51.7% with severe acne).
Of the 18.0% of patients (n = 9) with mild acne receiving concomitant therapy, the most frequently mentioned concomitant treatment was topical treatment with benzoyl peroxide (n = 5, 10.0%).

In the overall data of the main report, the most common treatments for patients with mild acne receiving concomitant therapy, 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 = 11) the most frequently mentioned concomitant treatments in France were systemic antibiotics (n = 5, 14.3%), topical retinoids and topical treatment with benzoyl peroxide (both n = 4, 11.4%).
In the overall data of the main report, the most common treatments for patients with moderate acne receiving concomitant therapy (n = 187), 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 who receive concomitant treatment (n = 10), the most frequently mentioned treatments in France were systemic antibiotics, topical retinoids and isotretinoin (form of application not specified (all n = 3, 21.4%)).
In the overall data of the main report, the most common treatments for patients with severe acne receiving concomitant therapy (n = 40), were systemic isotretinoin (n = 9, 10.1%), various topical

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), antiandrogenic 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 antiandrogenic 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.

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%).

Previous and concomitant treatment of hirsutism – France (addendum)

Hirsutism affected 14 patients in the French study population. Of these, four (28.6%) stated, that they had received previous treatment, nine (64.3%) had not been previously treated for their disorder. Information was missing for one (7.1%) of patient. The four previous treatments were anti-androgenic therapy, CPA/EE, systemic antibiotics and various topical therapies. Two patients with hirsutism diagnosis received concomitant treatment. Both stated various topical therapies as concomitant treatment.

In the overall data of the main report, 221 patients had a diagnosis of 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). 16 (7.2%) of the 221 patients affected by hirsutism received concomitant treatment. Laser diode hair removal (n = 5) and anti-androgenic therapy (n = 3) were reported most frequently as concomitant treatments.

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.

Concomitant use of other hormonal contraceptives and CPA/EE – France (addendum)

Of the 108 eligible patients in France, five (4.6%) were prescribed an additional hormonal contraceptive. Four of those were oral contraceptives and one non-oral contraceptive.

In comparison, in the overall data of the main report, 44 (2.9%) patients stated that they used additional hormonal contraception, of whom 42 (2.8% of the total) used oral contraceptives and two (0.1% of the total) non-oral contraceptives.

It is important to consider that these patients were reported as using 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 they start using CPA/EE.

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).
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. [Table 3]

Table 3: ***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

Utilization of CPA/EE for the indication of acne and hirsutism – France (addendum)

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 the 108 patients eligible in France, the proportion of patients with moderate or severe acne without hirsutism was 40.7% (n=44). Of the eligible patients 4.6% (n = 5) had received “previous topical treatment only” and 7.4% (n = 8) “previous systemic antibiotic treatment only”. Of the 24 patients (22.2%) who had received “previous topical and/or systemic antibiotic treatment”, failed or insufficient treatment was explicitly reported for 21 cases (16.4%).
In France, 11 patients were diagnosed with acne combined with hirsutism and three patients with hirsutism only.
Thus, 38 patients (35.2% of the total study population in France) reflect an approximation of the strict in-label use of CPA/EE in the study population of 108 patients in France: 24 patients with a diagnosis of moderate to severe acne who had “previous topical and/or systemic antibiotic treatment” and those with hirsutism (n = 14).
In comparison, for the overall 1513 patients (100%) of the main report, the proportion of patients with moderate or severe acne without hirsutism was 37.3% (n = 564). Of the total study population 13.2% (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%).
In the main report a total of 221 (14.6%) patients had a diagnosis of hirsutism, thereof 118 patients (7.8% of all patients) were diagnosed with acne with hirsutism and 103 (6.8%) were diagnosed with hirsutism without acne.
Thus, 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 in the main report: 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).
It should be considered, that the above analyses do 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. [Table 4]

Table 4***: CPA/EE use and treatment for the indication of acne and hirsutism - France***

	CPA/EE	95%-CI
Number (%) of eligible patients with	108 (100%)	
Moderate or severe acne (without hirsutism)	44 (40.7%)	[25.9%;56.9%]
Previous topical treatment only	5 (4.6%)	[1.5%;10.5%]
Previous systemic antibiotic treatment only	8 (7.4%)	[3.3%;14.1%]
Previous topical and/or systemic antibiotic treatment	24 (22.2%)	[10.7%;38.1%]
No previous topical and systemic antibiotic treatment	20 (18.5%)	[10.2%;29.7%]
Other previous treatment only	10 (9.3%)	[4.2%;17.1%]
Missing	1 (0.9%)	[0.0%;5.5%]
Acne with hirsutism	11 (10.2%)	[4.1%;20.2%]
Previous topical treatment only	0 (0.0%)	[0.0%;0.0%]
Previous systemic antibiotic treatment only	2 (1.9%)	[0.2%;6.5%]
Previous topical and/or systemic antibiotic treatment	5 (4.6%)	[1.0%;12.8%]
No previous topical and systemic antibiotic treatment	6 (5.6%)	[1.7%;13.0%]
Other previous treatment only	3 (2.8%)	[0.3%;10.4%]
Missing	0 (0.0%)	[0.0%;0.0%]
Hirsutism (without acne)	3 (2.8%)	[0.5%;8.2%]
Neither moderate or severe acne nor hirsutism	50 (46.3%)	[29.4%;63.8%]

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: 06DEC2016

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%) .
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 5]

Table 5 **- CPA/EE use and androgen-sensitive diseases**

	CPA/EE	95%-CI
Number (%) of eligible patients with	1513 (100%)	
Acne	1028 (67.9%)	[59.5%;75.6%]
Seborrhea	267 (17.6%)	[13.1%;23.0%]
Hirsutism	221 (14.6%)	[11.3%;18.4%]
Androgenetic alopecia	89 (5.9%)	[3.9%;8.4%]
PCOS	192 (12.7%)	[9.1%;17.1%]
At least one of the 5 androgen-sensitive diseases	1261 (83.3%)	[73.8%;90.5%]

Date of analysis: 12MAY2016

CPA/EE use and androgen-sensitive diseases – France (addendum)
For 97.2% (n=105) of all patients included in France, 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.
In the overall data of the main study, 83.3% of all patients included in the study were reported either to have at least one underlying androgenic disease (acne, seborrhea, hirsutism, androgenetic alopecia or PCOS) or to have been prescribed CPA/EE today for at least one of these disease entities. [Table 6]

Table 6: ***CPA/EE use and androgen-sensitive diseases – France (addendum)***

	CPA/EE	95%-CI
Number (%) of eligible patients with	108 (100%)	
Acne	99 (91.7%)	[84.2%;96.4%]
Seborrhea	32 (29.6%)	[18.8%;42.5%]
Hirsutism	14 (13.0%)	[6.0%;23.4%]
Androgenetic alopecia	6 (5.6%)	[1.9%;12.3%]
PCOS	11 (10.2%)	[3.7%;21.4%]
At least one of the 5 androgen-sensitive diseases	105 (97.2%)	[91.7%;99.5%]

Date of analysis: 06DEC2016

Discussion

The reason for conducting this study was the request by the EMA (European Medicines Agency) 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.

Discussion Main Report

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. 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.
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.

Discussion France (addendum)

In the main report, the contribution of French data was too low to allow comparison with the overall European data. The extension of the recruiting period for France has yielded additional data, which allow a better assessment of the prescribing behavior with respect to the utilization of CPA/EE.

It is reasonable to assume that a real life therapeutic strategy is not only based on the current state of acne; the preceding development of the disease severity may guide a decision to include antiandrogenic therapy even if the criteria in the label are not met at the time of prescription.
The original goal for the number of CPA/EE prescriptions, i.e. 1,000 per participating country was, like in the other four countries, not reached in France (108 prescriptions). The low number of documented prescriptions achieved may reflect the fact that CPA/EE is only rarely used or that the patients were not willing to participate. Also, the number of physicians who became active after joining the study, by signing the physician information, was low (31 of 68). Those physicians, who became active during the study, only contributed 3.5 eligible patients per physician. This number is substantially lower than in Austria (12.8), Czech Republic (17.6) and Spain (12.0). It has to be noted though, that the recruitment phase was slightly shorter in France (ten months) compared to other countries (Austria 13 months, Czech Republic 13 months, Spain 11 months).
As in the main report including all participating countries, the analysis for France shows that not all prescriptions fully reflect the updated label criteria. However, French physicians follow a stricter observance of the basic principles of the use of anti-androgenic therapy: In the majority of cases (n = 105; 97.2%) the diagnosis and/or the reason for prescription were related to androgen-dependent conditions. This degree of adherence to the pharmacological rationale for the use of CPA/EE exceeds the result found in the main report (83.3%).
Verification of previous failed treatment of acne is generally difficult to achieve as was seen here also. Documentation of this item is not explicit about the term failure, which could have various meanings, e.g. unsatisfactory response, method of application unacceptable for the patient, etc. Applying stricter criteria, but excluding precise documentation of previous treatment failure, there is no significant difference between the data from France and the data in the main report: This approximation of the strict in-label use of CPA/EE in France shows 35.2%, while the main report including data from all participating countries show 34.5%.The 14 French 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 99 French 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 108 recruited patients 99 (91.7%) had either been diagnosed with acne and/or acne was given as the reason for the prescription. Fortyfour 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 24 cases.
Overall, previous treatment failure was documented for 51.5% of the 99 cases of acne treatment.

Whether the other 48.5% 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.

Key Results

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

Prescription indications for CPA/EE:

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.

Key Results – France (addendum)

108 patients with CPA/EE prescriptions were recruited.

Prescription indications for CPA/EE:

Overall, 97.2% (n = 105) 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 (88.9%, n = 96). Other androgen-dependent conditions ranged from 11.1% (n = 12) for seborrhea to 3.7% (n = 4) for androgenetic alopecia. Contraception was reported as one of the reasons for the prescriptions in 32.4% (n = 35). In 2.8% (n = 3) of cases the prescriptions were made due to contraception only.

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

Of 38 patients (35.2% of the total study population of 108 patients) 24 (22.2%) patients had a diagnosis of moderate to severe acne with “previous topical and/or systemic antibiotic treatment” and 14 (13.0%) had hirsutism.

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

The prescription of CPA/EE together with another hormonal contraceptive was 4.6% (n = 5). Of those 4 were oral contraceptives and 1 non-oral contraceptive.

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

Of the 99 patients diagnosed with acne, 75 (75.8%) received previous treatment and in 51 (51.5%) the treatment was reported to have failed. There were 44 (44.4%) patients in the category “moderate to severe acne without hirsutism”. Of these, 24 (24.2%) received previous topical treatment and/or systemic antibiotics, which had failed in 21 (21.2%) cases.

Overall Conclusion

On an aggregate level, the study is informative with regard to the clinical scenario when prescribing CPA/EE by gynecologists, dermatologists, and GPs. The majority of prescriptions refers to the treatment of diseases with androgen-related pathophysiology.

Conclusion – France (addendum)

The extension of the recruitment period in France enabled a certain increase of local data on prescription behavior. However, the actual achieved number of documented prescriptions (108) is lower than originally intended. Therefore, general conclusions on the prescription behavior in France are only possible to a limited extent. The French data are in line with the data gathered and assessed in the main report.