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.

Title	Drug utilization study of cyproterone/ethinylestradiol (Diane®-35 and generics) in the Netherlands, UK and Italy.
Keywords	Cyproterone/ethinylestradiol, hormonal contraceptives, acne, treatment patterns
Rationale and background	Cyproterone acetate in combination with ethinylestradiol (CPA/EE) is indicated for the treatment of acne or hirsutism in women of reproductive age, when alternative treatments have failed. In 2013 MAHs were required to implement further risk minimization measures.
Research question and objectives	This interim analysis aimed to assess recent diagnosis of acne, other hyperandrogenic conditions, menstrual problems or GP consultations for contraceptive management, recent acne treatment and concomitant use of hormonal contraceptives (HC) among new users of CPA/EE in 2011-2012 for future comparison to new users in 2014.
Study Design	In this retrospective drug utilization study, new CPA/EE users in 2011 and 2012 were followed from their first CPA/EE prescription until database exit or end of index year (31 December 2011 or 31 December 2012).
Setting	CPA/EE prescriptions were identified in the PHARMO Out-patient Pharmacy Database (the Netherlands), the Health Search Database (HSD, Italy) and The Health Improvement Network (THIN, United Kingdom).
Subjects and Study Size, including dropouts	The study population for the interim analysis included 21,862 new CPA/EE users in 2011-2012.
Variables and Data sources	Type and prescriber (PHARMO only) of the first CPA/EE prescription and diagnoses of acne, other hyperandrogenic conditions, menstrual problems or GP consultations for contraceptive management and treatment of acne in the preceding year were assessed. During follow-up, the duration of CPA/EE use, concomitant use of CPA/EE and other HC and duration of concomitant use were assessed.
Results	In PHARMO, 2% of 15,252 new CPA/EE users were concomitant users of HC (median duration 78 days). Another 25% were potential concomitant users (median duration 63 days). A recent acne diagnosis was observed in 17% of users. Another 3% had a diagnosis of other hyperandrogenic conditions. Of the remaining CPA/EE users, i.e. without any hyperandrogenic diagnosis, 3% had menstrual problems and another 14% recently visited the GP for contraceptive management . Among users without an acne diagnosis, 42-45% had recently received acne treatment. In THIN, less than 1% of 5,683 new CPA/EE users were concomitant users of HC (median duration 84 days). Another 4%

	were potential concomitant users (median duration 50 days). A recent acne diagnosis was observed in 51-54% of users. Another 11% had a diagnosis of other hyperandrogenic conditions. Of the remaining CPA/EE users, 5% had menstrual problems and another 23% had an entry for contraceptive management. Among users without an acne diagnosis, 50-54% had recently received acne treatment. In HSD, 1% of 928 new CPA/EE users were concomitant users of HC. Another 3% were potential concomitant users (median duration 29 days). A recent acne diagnosis was observed for 14-17% of users. Another 7% had a diagnosis of other hyperandrogenic conditions. Of the remaining CPA/EE users, 5% had menstrual problems and another 10% received treatment by GP for contraceptive management Among users without an acne diagnosis, 6% had recently received acne treatment.
Discussion	During 2011 and 2012, concomitant use of HC was observed for up to 2% of new CPA/EE users. Additional potential concomitant users were observed, however as no new prescription was observed after the start of potential concomitant use, an actual switch was likely for these users. Many CPA/EE users in PHARMO and HSD, and a smaller proportion in THIN, had no recent diagnoses of acne, other hyperandrogenic conditions, menstrual problems or GP consultations for contraceptive management, and no recent acne treatment. Apart from the possibility that these were off-label users, the information about actual on-label indications might have been missing due to underreporting in the databases. This is an interim analysis designed for future comparison with users in 2014, after the PRAC recommendation. The final report will be delivered in 2016.
Marketing Authorisation Holder(s)	Bayer Pharma AG on behalf of a group of MAHs.
Names and affiliations of principal investigators	Irene Bezemer, PhD, International Research Program Manager. PHARMO Institute for Drug Outcomes Research, Utrecht, the Netherlands Luis Alberto García Rodríguez, MD, MSc, Director. The Health Improvement Network / Centro Español de Investigación Farmacoepidemiológica, Madrid, Spain Francesco Lapi, PharmD, PhD. Health Search, Italian College of General Practitioners (at Genomedics S.R.L.), Florence, Italy