Article 31 of Directive 2001/83/EC resulting from pharmacovigilance data

Procedure No: EMEA/H/A-31/1356

Combined hormonal contraceptives (CHCs) containing medicinal products

The following CHMP Member supports the divergent position appended to the PRAC recommendation on combined hormonal contraceptives containing medicinal products dated 10 October 2013, as stated below:

CHMP members expressing a divergent position:

Jens Heisterberg (DK)	21 November 2013	Signature: …….....
Jacqueline Genoux-Hames (LU)	21 November 2013	Signature: …….....
John Joseph Borg (MT)	21 November 2013	Signature: …….....
Pierre Demolis (FR)	21 November 2013	Signature: …….....
Harald Enzmann (DE)	21 November 2013	Signature: …….....
Jan Mueller-Berghaus (Co-opted)	21 November 2013	Signature: …….....
Jean-Louis Robert (Co-opted)	21 November 2013	Signature: …….....

Divergent statement from PRAC Members

The undersigned member of PRAC did not agree with the PRAC's opinion recommending that the Marketing Authorisation of combined hormonal contraceptives containing chlormadinone, desogestrel, dienogest, drospirenone, etonogestrel, gestodene, nomegestrol, norelgestromin or norgestimate should varied as stated by the PRAC.

These members are in full agreement with the scientific assessment made by the PRAC and based on the Rapporteur and co-rapporteur reports:

- They share the concerns over the risks of venous thromboembolic events (VTE) and arterial thromboembolic events (ATE) associated with those products.
- They agree with the well demonstrated increased risk of VTE observed with all the CHCs and the differences of risk between these contraceptives mainly driven by the type of progestogens.
- They agree with the range of risk as stated by the PRAC and compared to levonorgestrel containing CHC.
- They support the concern during the first ever year of use when the risk is highest and when restarting after a CHC-free interval of at least 4 weeks and for women with risk factors.
- They agree that there is currently no reliable evidence that newer CHCs have any higher beneficial effect or difference in tolerability

The reasons for this divergent opinion rely on the regulatory actions to take forward, focused on the wording of the section 4.1 Therapeutic indications of the SmPC and were as follows:

- The well documented differences in VTE incidence rates among users of different types of CHCs
- The lowest VTE risk is with products containing levonorgestrel, noresthisterone or norgestimate. In spite of previous reviews of benefits and risks of CHCs that have been conducted by European Member States during the past years as well as the CPMP position statement in 2001 together with a warning on VTE risk already being included in section 4.4 Special warnings and precautions for use and section 4.8 Undesirable effects of these products, VTE events of concern (number and seriousness) in the EU still persist.

Taking all these aspects into account, these members considered that there is a need for a clear recommendation in section 4.1 Therapeutic Indications for a targeted population “first ever users or women with an increased baseline risk of VTE”.

For these women, these members were in favour of implementing in the “Indication” section of chlormadinone, desogestrel, dienogest, drospirenone, gestodene, nomegestrol, (those with a higher or a yet not sufficiently evaluated VTE risk) a recommendation to prescribe a CHC with a documented low VTE risk (levonorgestrel or noresthisterone or norgestimate containing product) with the aim of reducing the number of VTE events among CHC users, in particular in first ever users or women with an increased baseline risk of VTE.