Faculty of Sexual & Reproductive Healthcare

Statement from the Clinical Effectiveness Unit

Strengthening of warnings about use of Dianette® and other brands of co-cyprindiol

June 2013

Following a recent safety review, a letter has been issued to healthcare professionals from the manufacturers of Dianette® and other cyproterone acetate 2 mg/ ethinylestradiol 35 mcg (co-cyprindiol) products. The review by the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) followed concerns about the risk of thrombosis associated with co-cyprindiol. With the agreement of the EMA and Medicines and Healthcare products Regulatory Authority (MHRA), a letter has been issued to raise awareness of the thrombosis risks and the outcome of the review.

The increased risk of venous and arterial thromboembolism (VTE and ATE) in users of estrogen-containing contraceptives is well established. For some time it has also been evident that the combination of estrogen with cyproterone and some other progestogenic hormones is associated with a 1.5-2 fold increased incidence of VTE compared with levonorgestrel-containing combined pills. Concerns were raised in France earlier this year when the co-cyprindiol product Diane-35® was linked to the death of four women over a 25-year period. This led to suspension of sales of the drug by French authorities.

The information circulated by the pharmaceutical companies is not in response to the publication of any new data. The recommendations of the PRAC review apply across Europe, thus encouraging greater consistency in prescribing practice. The recommendations will not affect current UK availability of co-cyprindiol or alter existing advice to UK prescribers. Faculty of Sexual and Reproductive Healthcare (FSRH) guidance on Combined Hormonal Contraception[1] highlights the increased risk of thrombosis associated with use of co-cyprindiol pills (Dianette® and Clairette®) and advises that although co-

cyprindiol can be used for contraception it should not be used solely for this purpose.

As with combined hormonal contraceptives, women being prescribed Dianette® should be alerted to the fact that users of these products are at an increased risk of thrombosis compared with non-users and users of levonorgestrel-containing combined pills. However, the absolute risk is still low and is less than the risk associated with pregnancy. When prescribed appropriately the benefits of using combined hormonal contraception and co-cyprindiol outweigh the risks of VTE, particularly in women who derive non-contraceptive benefits from use. Health professionals wishing to prescribe Dianette® or other ethinylestradiol/cyproterone acetate containing products should be guided by the UK Medical Eligibility Criteria for Contraceptive Use[2], http://www.fsrh.org/pdfs/UKMEC2009.pdf and the Summary of Product Characteristics for the individual product. More detailed information on the risks associated with combined hormonal contraceptive products and ethinylestradiol/cyproterone acetate containing products can be found on pages 11-12 of FSRH guidance.
http://www.fsrh.org/pdfs/CEUGuidanceCombinedHormonalContraception.pdf

Reference List

(1) Faculty of Sexual and Reproductive Health Care. Combined Hormonal Contraception. 2011. http://www.fsrh.org/pdfs/CEUGuidanceCombinedHormonalContraception.pdf

(2) Faculty of Sexual and Reproductive Health Care. UK Medical Eligibility for Contraceptive Use. 2009.
http://www.fsrh.org/pdfs/UKMEC2009.pdf