

**Ethinylestradiol and drospirenone (Yasmin®) and thrombosis risk:
Advice from the Clinical Effectiveness Unit (CEU) of the Faculty of Sexual
and Reproductive Healthcare (FSRH)**

A drug safety bulletin has been issued by the Medicines and Healthcare products Regulatory Agency (MHRA) to highlight that the risk of thrombosis associated with combined oral contraceptive pills containing drospirenone (Yasmin®; Bayer) may be slightly higher than previously thought.¹

The article, published in Drug Safety Update, reviews current evidence on Yasmin and the risk of venous thromboembolism (VTE) in light of recently published studies and changes to Yasmin product information.

It has long been recognised that all combined hormonal contraceptives (COCs), including Yasmin, are associated with a small increase in the risk of VTE compared with no use. In women of reproductive age deep vein thrombosis and pulmonary embolism are very rare events. Therefore the absolute risk of VTE in users of all COC preparations is very low.

Observational studies of different types of COC have suggested that the degree of VTE risk may vary depending on the dose of estrogen and type of progestogen, with users of pills containing desogestrel, gestodene and cyproterone having a higher risk of VTE than users of levonorgestrel and norethisterone-containing pills. As Yasmin is a newer pill than the COCs used in earlier studies, the relative risk of VTE associated with Yasmin compared to other COCs was initially unclear.

The MHRA update reviews four recent studies which included Yasmin users. Two of these studies (EURAS and Ingenix) estimated that the risk of VTE in Yasmin users is comparable with that of COCs containing levonorgestrel.

The most recent evidence from a Danish cohort study and a Dutch case-control study supports previous studies suggesting an increased risk of VTE in users of COCs containing desogestrel, gestodene and cyproterone, and also suggests a slightly higher risk in Yasmin users compared to COCs containing levonorgestrel, norethisterone and norgestimate. Compared with levonorgestrel COCs, the Danish study estimated a relative VTE risk in Yasmin users of 1.64 [95% confidence intervals (CI) 1.27-2.10]. The Dutch study estimated a similar relative risk of 1.7 which was statistically non-significant [95% CI 0.7-3.9]. These risk estimates for Yasmin lie somewhere between the relative VTE risks associated with levonorgestrel-containing COCs and

desogestrel/gestodene COCs. Product information for Yasmin will be updated to reflect these new data.

The MHRA bulletin cautions that because of limitations in study methodology, further analyses are needed before any firm conclusions can be drawn. The Clinical Effectiveness Unit (CEU) would agree that bias and confounders cannot be completely excluded from observational studies and, therefore, the true relative risks of different combined methods remain in doubt.

MHRA advice for prescribers and women emphasizes that all hormonal contraceptives are highly effective and safe, and that when used appropriately the benefits of all COCs far outweigh the risk of VTE. The CEU would support this message and reassure women using combined hormonal contraception that their risk of VTE is very small and is less than the VTE risk associated with pregnancy. When prescribing combined contraceptive methods clinicians should take into account individual risk factors such as bodyweight and medical history. Progestogen-only or non-hormonal methods may be suitable alternatives for women considered at increased risk of VTE. More detailed prescribing guidance can be found in the UK Medical Eligibility Criteria for Contraceptive Use (UKMEC) and method-specific guidance produced by the Faculty of Sexual and Reproductive Healthcare which are freely available on the Faculty's website www.fsrh.org.uk.

Reference

1. Yasmin: update on risk of venous thromboembolism. Drug Safety Update, Volume 10, Issue 9, April 2010. <http://www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/CON076501>