European Medicines Agency starts review of third- and fourth-generation combined oral contraceptives

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Information on Medicinal Product

Combined hormonal contraceptives are medicinal products used for contraception which contain two types of hormones; an oestrogen and a progestogen. The review includes all contraceptives containing the following progestogens: chlormadinone, desogestrel, dienogest, drospirenone, etonogestrel, gestodene, nomegestrol, norelgestromin and norgestimate. The combined hormonal contraceptives being reviewed are referred to as 'third generation' or 'fourth generation' and are available as pills, skin patches and vaginal rings.

In Malta several products containing third and fourth generation progestogens are authorised nationally; Minesse, Mercilon, Cilest, Yaz, Eloine, Qlaira, Palandra, Yasmin, Yasminelle, Aliane, Clairette, Sunya, Katya and Acnocin. Zoely, Ioa and Evra are also authorised in Malta via the centralized procedure.

Information from European Medicines Agency about the safety concern

The review of these contraceptives was requested by the French medicines agency ANSM following concerns in France about the risk of venous thromboembolism (VTE or blood clots in veins). The risk of VTE with combined hormonal contraceptives is known to depend on both the level of oestrogen and the type of progestogen they contain.

A Dutch study published in the British Medical Journal in 2009[1] found that, overall, taking the pill was associated with a five-fold increased risk of experiencing a clot. However, on closer analysis, a variation in risk emerged: women taking pills containing a progestogen called levonorgestrel had the lowest risk of thrombosis at four times that of women not on the pill; those on contraceptives containing desogestrel (for example, Mercilon) had the highest risk, at seven

[1] Lidegaard O, Løkkegaard E, Svendsen AL et al Hormonal contraception and risk of venous thromboembolism: national follow-up study; BMJ 2009; available online at http://www.bmj.com/content/339/bmj.b2890

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times that of those not taking the pill; and women taking a pill with norgestimate (for example, Cilest) had an almost sixfold extra risk as did those on drospirenone (for example, Yasmin). Therefore while the overall risk with the products under review is low, the relative risk is higher for the third and fourth generation oral contraceptives than the risk associated with the progestogen levonorgestrel.

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) will now review all available data on the risk of VTE with these contraceptives and issue an opinion on whether the currently available product information provides the best information possible for patients and doctors to take appropriate healthcare decisions. For more information see this EMA **press release**. The review will also cover the risk of arterial thromboembolism (blood clots in arteries, which can potentially cause a stroke or heart attack). This risk is very low and is not currently known to be higher with any particular type of progestogen.

In Malta

For Patients

Information about the risks of venous thrombo-embolism is included in leaflets for patients and prescribers, and has been continuously updated. Combined oral contraceptives are kept under close monitoring by the Medicines Authority and by the Marketing Authorisation Holders of the products and there is no reason for any woman to stop taking her contraceptive. If there are any concerns about the hormonal contraceptive being used this can be discussed with the doctor.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on all oral contraceptives. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority yellow card scheme or online at http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.>

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

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