The European Agency for the Evaluation of Medicinal Products
Post-authorisation evaluation of medicines for human use

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Position Statement

CPMP concludes its assessment of 'third generation' combined oral contraceptives and the risk of venous thromboembolism

The EMEA Committee for Proprietary Medicinal Products (CPMP), has today published the outcome of its assessment on the risk of venous thromboembolism associated with the use of so-called 'third generation' combined oral contraceptives containing the progestins desogestrel or gestodene (mono-, bi- or tri-phasic formulation).

The CPMP assessment is the result of an ongoing review which began in 1995 based on three independent epidemiological studies that indicated an increased risk of venous thromboembolism associated with the use of combined oral contraceptives containing desogestrel or gestodene, compared to combined oral contraceptives containing the progestin levonorgestrel.

The EMEA previously issued CPMP public statements in 1995 and, taking into account newly emerging data, in 1996 and 1997. Further to the initial studies, the CPMP has evaluated additional epidemiological studies and studies on blood clotting mechanisms. The CPMP has taken into account all available information up to mid-September 2001 in performing this assessment.

The CPMP concludes in its public assessment report that:

- Venous thromboembolism is a rare side effect of all combined oral contraceptives . The level of this risk is low, and overall the balance of benefits and risks remains favourable with all available combined oral contraceptives. Thus, there is no reason for women currently using any brand of combined oral contraceptives to stop taking it on basis of these findings.
- On the basis of a careful scientific evaluation, it has been found that women using a combined oral contraceptive containing desogestrel or gestodene with 30µg of ethinylestradiol have a small increased risk of venous thromboembolism compared to women using combined oral contraceptives containing levonorgestrel with the same amount of ethinylestradiol. For combined oral contraceptives containing desogestrel or gestodene with 20µg of ethinylestradiol the epidemiological data do not suggest a lower risk of venous thromboembolism than for those containing 30µg of ethinylestradiol.
- There is an excess risk of venous thromboembolism during the first year a woman ever uses any combined oral contraceptive. The impact of the relative risk of venous thromboembolism of combined oral contraceptives containing desogestrel or gestodene compared to those containing levonorgestrel on the number of additional cases would be greatest in the first year a woman ever uses a combined oral contraceptive. This should be taken into account when a combined oral contraceptive is prescribed for and used by a woman for the first time.
- The increased risk of venous thromboembolism associated with combined oral contraceptives is less than the risk of venous thromboembolism associated with pregnancy.

The CPMP reminds health-care professionals that, in relation to the risk of venous thromboembolism, contraindications for use of combined oral contraceptives include a history of or existing venous thromboembolic diseases and history of or recent myocardial infarction or stroke. Known risk factors to take into account when prescribing combined oral contraceptives include obesity, the post-partum

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period (i.e. time after having given birth), recent surgical operation and family history of venous thrombosis. Furthermore, discontinuation of combined oral contraceptives should be considered in the event of surgical operation, or immobilisation for any reason.

The CPMP, after having considered all options of safety measures, recommends amendment of the relevant sections of the prescribing information of national marketing authorisations to reflect the outcome of this scientific evaluation. The recommendations are set out in full in the public assessment report.

For further details, see the public assessment report, which is available together with information for users and health-care professionals, on the web site of the EMEA (www.emea.eu.int). Further information will also be available on the web sites of the national competent authorities (see below).

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