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IMAP Short Statement on the Safety of Third and Fourth Generation Combined Oral Contraceptives

Based on the analysis conducted by the United States Food and Drugs Administration (FDA) (2013) and the recommendations contained on the publications "Family Planning: a Global Handbook for Providers" by WHO (2011) and Medical Eligibility Criteria (WHO, 2010),[i] IMAP Members provide guidance to IPPF's Member Associations on the safety of third and fourth generation combined oral contraceptives. This statement is developed in response to recent public alarm in European countries, where women sued manufacturers for potential fatal blood clots (Venous Thromboembolism) as a result of using Meliane (Gestodene-containing oral contraceptive pill). The conclusions presented below do not apply to implants, IUS or other products containing the active components in third and fourth generation combined oral contraceptives.

An additional review is currently being conducted by the European Medicines Agency (EMA) on the risk of VTE and arterial thromboembolism with combined hormonal contraceptives containing third and fourth generation progestogens. An update from the EMA on the use of these products is expected in 2013. In addition, the WHO will be considering evidence related to VTE risk associated with combined oral contraceptives with various progestogens as part of the update of Medical Eligibility Criteria and Selected Practice Recommendations, anticipated to be finalized in 2014. This statement will be updated as these recommendations are made in order to communicate the latest regional and international consensus on this issue

What are third and fourth generation combined oral contraceptives

The current classification of combined oral contraceptives (COCs) into four different generations relies on the progestin used: first-generation COCs includes norethisterone- and norethindrone acetate-containing pills; second-generation COCs include levonorgestrel-containing pills; third-generation pills include desogestrel-, gestodene- and norgestimate-containing pills; and fourth generation COCs include drospirenone- or any other new progestin-containing pills.

Examples of gestodene-containing pills include:
Arianna, Careza, Femiane, Femoden, Logest, Meliane, Secret 28.

Examples of drospirenone-containing pills include:
Aliane, Damsel, Fennelle, Jasminelle, Yadine, Yasmin, Yasminelle 21, Yasminelle 28 and Yaz.

Note: to learn more about gestodene- and drospirenone-contaning pills please visit our Directory of Hormonal Contraception.

What is Venous Thromboembolism

The term venous thromboembolism (VTE) refers to both deep vein thrombosis (DVT) – a blood clot in one of the deep veins of the body; and pulmonary embolism – a blood clot that travels through the bloodstream and lodges in one of the lungs.

Evidence on third and fourth generation pills

- Recent epidemiological studies reviewed by the FDA have not shown the magnitude of increased risk of Venous Thromboembolism (VTE) reported in earlier studies as a result of using third and fourth generation combined oral contraceptives[ii].
- Earlier studies reporting increased risk of VTE produced conflicting results and had methodological limitations that call into question the validity of their findings and conclusions about the magnitude of the additional risk associated with using these products.
- Changes in the results of coagulation tests as a result of using third and fourth generation combined oral contraceptives suggested in earlier studies have not been shown to be directly responsible for an increase in VTEs.
- Medical Eligibility Criteria (WHO, 2010) indicates that women with history of deep venous thrombosis (VT) or pulmonary embolism (PE), acute DVT/PE, DVT/PE and established on anti-coagulant therapy, or women who have been through a major surgery with prolonged immobilization are not eligible to take combined oral contraceptive pills.

[i] The analysis from the United States Food and Drug Administration regarding third and fourth generation pills focus specifically on drugs containing desogestrel. Gestodene-containing drugs are not currently registered in United States.

[ii] United States Food and Drug Administration, Department of Health and Human Services. Docket No. FDA-2007-P-0190 United States Food and Drug Administration, Department of Health and Human Services. Docket No. FDA-2007-P-0190

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Recommendations

- Member Associations can advise women to continue using the third and fourth generation pills as currently there is no clinical evidence of increased risk for VTE. Member Associations should open the space to discuss clients' concerns regarding third and fourth generation pills. Counselling women about the potential risk is appropriate, if they are informed about what signs, symptoms and risk markers they should pay attention to. Clients should be informed that the risk of blood clots is higher in women using any combined hormonal contraceptive than those who are not using them but is also significantly lower than the risk of developing blood clots in pregnancy and the postpartum period.
- Member Associations may continue providing third and fourth generation pills as part of their contraceptives method mix. However, it is recommended that providers follow closely the criteria stated on the Medical Eligibility Criteria (WHO, 2010) to assess women's eligibility to take any contraceptive including oral contraceptives.
- Member Associations should support information, communication and education activities to overcome the negative messages around oral contraceptives spread as a result of the recent public alarm in Europe.