

IPPF Medical Bulletin

IMAP Short Statement on the Safety of Third and Fourth Generation 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 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 oral contraceptives.

What are third and fourth generation oral contraceptives

The current classification of oral contraceptives (OCs) into four different generations relies on the progestin used: first-generation OCs includes norethisterone- and norethindrone acetate-containing pills; second-generation OCs include levonorgestrel-containing pills; third-generation pills include desogestrel-, gestodene- and norgestimate-containing pills; and fourth generation OCs 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-containing pills please visit our [Directory of Hormonal Contraception](#).

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](#)

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 oral contraceptivesⁱⁱ.
- 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 coagulations tests as a result of using third and fourth generation 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 uptake oral contraceptive pills.

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.
- 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.

The development of this document was possible thanks to the efforts and contributions of many people.

We would like to express great appreciation for the work of Julia Bunting, Marcela Rueda, Regine Sitruk-Ware, Karthik Srinivasan and the staff from our Regional Office in Europe. Finally, we gratefully acknowledge the support from

IPPF's International Medical Advisory Panel (IMAP): Pierre Buekens, Safa Elbaz, Naheed Khodakarami, Michael Mbizvo, Nuriye Ortayli and John W Townsend for their valuable guidance and reviews offered during the development process.