HAUTE AUTORITÉ DE SANTÉ

GYNAECOLOGY
New medicinal product
July 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

OPTIKINZY (norgestimate/ethinylestradiol), hormone contraceptives for systemic use

Insufficient clinical benefit to justify reimbursement for contraception.

Main points

- OPTIKINZY has been granted an MA for oral contraception.
- The data do not allow us to formally conclude that there is no difference in terms of risk of thromboembolism between oestroprogestative contraceptives containing levonorgestrel and those containing norgestimate (OPTIKINZY).
- No efficacy or tolerance advantage of OPTIKINZY over levonorgestrel-containing oestroprogestative oral contraceptives has been demonstrated.

Therapeutic strategy

- In women of child-bearing age, the choice of contraception must take into consideration their desires, changes in personal situation, the progressive decrease in fertility with age, the increase in vascular risk factors and changes to contraindications. Cardiovascular risk increases with age and changes the benefit-to-risk ratio of the various methods.
- Contraindications change with age, in particular concerning the use of oestroprogestative contraceptives in the event of headaches or if the subject smokes:
  - under the age of 35: oestroprogestative contraceptives are contraindicated in the event of migraines with aura. If the subject smokes, the risk of arterial thrombosis must be taken into consideration and the patient must be informed of the available help for quitting smoking;
  - over the age of 35: oestroprogestatives are contraindicated in women who smoke or who suffer from migraines, with or without aura. Substitution with a progestative method alone, or by another means of contraception, is recommended.
- Amongst the available methods, oestroprogestative contraceptives can be used in women who do not present with contraindications (primarily venous or arterial thromboembolism, liver, cancer, etc.) and taking into account the risk factors of thrombosis (in particular personal or family history of venous or arterial thrombosis, known biological thrombophilia, prolonged immobilisation, obesity, age > 35 years, hypertension, diabetes, dyslipidaemia, smoking, migraine).
- Women must be informed:
  - of the various methods of oestroprogestative contraception initiation and use according to their route of administration: taken daily, always at the same time for the oral route;
  - of the steps to take if the pill is forgotten for more than 12 h and concerning emergency contraception;
  - of the contraceptive efficacy of these methods;
  - of their potential disadvantages (mastodynia, cycle disorders, etc.);
  - of their risks, particularly the risk of venous or arterial thromboembolic accidents, especially during the first year after initiation of the method, or following an interruption and resumption of the method (inform the subject of the suggestive of these complications and which must lead the subject to seek medical advice);
  - of the need to inform all physicians of the use of hormonal contraception in the event of intercurrent treatment, surgery, prolonged immobilisation, or of long trips in sitting position (plane, train, coach, car, etc.);
  - of the risk of reduced efficacy in the event of diarrhoea or vomiting, or if combined with certain medicines (including St John's wort, some anticonvulsants, antiproteases, rifampicin/rifabutin, bosentan, griseofulvin, modafinil and orlistat);
- **Role of the medicinal product in the therapeutic strategy**

OPTIKINZY has no role in the therapeutic strategy.

Clinical data

- A network meta-analysis concluded that the risk of thromboembolic events caused by combined oral contraceptives (COCs) containing norgestimate combined with 35 µg ethinylestradiol did not differ statistically from that of oral contraceptives containing levonorgestrel combined with 20 or 30 µg ethinylestradiol.
- Two nested case-control studies were published simultaneously, with conflicting results:
  - one concluded that there was an increase in venous thromboembolic risk compared to similar non-users for COCs containing norgestimate and for those containing levonorgestrel, and that there was no significant difference between the two types of COC.
  - the other concluded that there was an increase in intermediate risk between that associated with levonorgestrel-containing COCs and those containing desogestrel, with a significantly higher risk for COCs containing norgestimate compared to those containing levonorgestrel
  - the meta-analysis of the two studies, with significant heterogeneity concerning norgestimate, do not allow any conclusions to be drawn concerning this discrepancy.
- A meta-analysis of observational studies concluded that the risk of thromboembolic events caused by COCs containing norgestimate did not differ statistically from that of COCs containing levonorgestrel. This study, however, included the publication concerning the two nested case-control studies, taking into consideration the result of a supplementary sub-group analysis of the two combines studies, despite the existence of significant heterogeneity. This raises questions concerning the validity of the results of this meta-analysis.
- In 2014, a European assessment report concluded that combined hormonal contraceptives containing the progestatives levonorgestrel, norethisterone or norgestimate presented the lowest risk of thromboembolic events.
- In 2017, ANSM reported that the risk of pulmonary embolism, ischaemic stroke and myocardial infarction was significantly lower with combined oral contraceptives containing 20 µg ethinylestradiol than with those containing 30-40 µg. Consequently, ANSM recommends the first-line use of COCs containing levonorgestrel combined with 20 µg oestrogens.
- These data do not allow us to formally conclude that there is no difference in terms of risk of thromboembolism between COCs containing levonorgestrel and OPTIKINZY.

Benefit of the medicinal product

- The actual clinical benefit* of OPTIKINZY is insufficient to justify public funding cover.
- Not approved for non-hospital pharmacy reimbursement or for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 25 July 2018 (CT-16826) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.