Ulipristal

Section: 22. Medicines for reproductive health and perinatal care > 22.1. Contraceptives > 22.1.1. Oral hormonal contraceptives

ATC codes: G03AD02

Indication	Contact with health services for postcoital contraception ICD11 code: QA21.0
INN	Ulipristal
Medicine type	Chemical agent
List type	Core
Formulations	**Oral > Solid:** 30 mg tablet (ulipristal acetate)
EML status history	First added in 2017 (TRS 1006)
Sex	Female
Age	Adolescents and adults
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Ulipristal
DrugBank	Ulipristal

Expert Committee recommendation

The Expert Committee recommended the addition of ulipristal acetate to the core list of EML for emergency contraception within 5 days of unprotected sexual intercourse or contraceptive failure in women of reproductive age, on the basis of the evidence presented which supported UPA-EC as an effective and safe option for emergency contraception.

Background

Currently, levonorgestrel (LNG-EC) is included on the EML for use as an emergency oral hormonal contraceptive.

Public health relevance

Target 3.7 of the Sustainable Development Goals is to ensure, by 2030, universal access to sexual and reproductive health-care services, including family planning, information and education, and the integration of reproductive health into national strategies and programmes (1). In 2012, it was estimated that more than 85 million of pregnancies were unintended, representing approximately 40% of all pregnancies. Of these, 50% ended in abortion, 13% in miscarriage and 38% in an unplanned birth (2). In developing countries, it corresponds to 74 million unintended pregnancies as a consequence of the lack of use of effective methods of regular contraception (70%) and contraceptive failure (30%) (e.g. missed pills, broken or slipped condoms) (3, 4). In 2016, of the 20 million pregnancies occurring in adolescents aged 15–19 years living in developing countries, approximately 50% were unintended (5). Maternal causes are the second highest ranked source of mortality in this age group globally (6). In developing countries, the current use of emergency contraception (EC) is relatively low. Among sexually

active women, only 3% reported having ever used EC (7). Unintended pregnancies are usually associated with negative health, financial, social and emotional consequences. In 2012, about 50% of unintended pregnancies ended in induced abortion (2). In 2003, an estimated 42 million pregnancies were voluntarily terminated, 20 million unsafely, endangering health and life.

Benefits

The application presented the results of a 2012 systematic review (8) that included two high-quality randomized controlled trials (RCTs) comparing ulipristal acetate (UPA) and LNG in 1716 women with regular menses who requested EC following unprotected intercourse (9, 10). Both RCTs were determined to have a low risk of bias. The results showed that UPA-EC was significantly more effective in preventing pregnancy than LNG-EC (risk ratio (RR) 0.58; 95% confidence interval (CI) 0.35–0.99; P = 0.04). For use within 72 hours of unprotected sexual intercourse, UPA-EC was shown to be more effective, although the difference was only marginally significant (RR 0.63; 95% CI 0.37–1.07; P = 0.089) (8). In a meta-analysis that used a logistic-regression model, which took into account known confounding factors that may alter the treatment effect, the odds of pregnancy were significantly lower (P < 0.05) among women who used UPA-EC than those who used LNG-EC, taken within 24, 72 and 120 hours of unprotected intercourse (9). Results from a pooled analysis of three pharmacodynamic studies in which EC treatment was given at a late follicular stage (follicle ≥18 mm diameter) showed that UPA-EC was significantly better than LNG-EC (1.5 mg) at delaying follicular rupture by 5 days, whether treatment was given before the luteinizing hormone (LH) surge (RR 4; 95% CI 1.5–10.7; P = 0.0026) or after the LH surge but before the LH peak (RR 55.5; 95% CI 1.5–20.4; P = 0.0018). No treatment was effective at postponing follicular rupture when given at the time of the LH peak (11). Efficacy in obese patients Pooled data from two RCTs comparing UPA-EC and LNG-EC assessed risk of pregnancy in women categorized by body mass index (BMI) (12). Results showed that pregnancy risk was doubled in overweight women who took LNG-EC in comparison with normal or underweight women (odds ratio (OR) 2.09; 95% CI 0.86–4.87; not significant), and was more than 4 times greater in obese women (OR 4.41; 95% CI 2.05–9.44; P = 0.0002). Among the women who took UPA-EC, the risk of pregnancy in overweight women did not differ from that for women with BMI <25 kg/m² (OR 0.97; 95% CI 0.27–2.83; not significant) and the risk of pregnancy in obese women who took UPA-EC was higher but not significantly so (OR 2.62; 95% CI 0.89–7.00; not significant). Efficacy in adolescent patients As part of the Paediatric Investigation Plan agreed with the European Medicines Agency (EMA), a post-marketing phase IV observational study was conducted with the objective of assessing safety, tolerability and efficacy of UPA-EC in postmenarcheal adolescent girls and adult women. Of the 579 women included, 279 were under 18 years of age (of whom 76 were under 16 years). In the efficacy-analysis population, pregnancy occurred in seven women (of whom two were under 16 years), yielding a pregnancy rate 1.5%, similar to that observed in adult women (13).

Harms

Safety data from a comparison of adverse events (AEs) following treatment with UPA-EC (n = 1879) and LNG-EC (n = 1891) showed no differences between the two treatments. The most frequent AEs were nausea, vomiting, breast tenderness, headache, dizziness, fatigue, abdominal pain, diarrhoea, spotting/bleeding after treatment, dysmenorrhoea and back pain (8). Post-marketing experience (1.4 million women) and a meta-analysis of phase III RCTs (2221 women) reported only two serious AEs potentially related to UPA-EC use (dizziness and fainting). No increased risk of venous thromboembolic events was identified (9, 14, 15). A prospective, observational, multicentre study assessed the safety profile in adolescents under 18 years old (13). The most frequent AEs were headache, nausea and abdominal pain, changes in cycle duration and menorrhagia. These data indicate that the safety profile observed in adolescents is similar to that observed in adults. Safety and tolerability of repeated use of UPA-EC within the same menstrual cycle were assessed. Most frequent AEs were headache, nasopharyngitis, influenza and mild anaemia. All were of mild or moderate intensity. No serious AEs were reported (16).

Additional evidence

N/A

Cost / cost effectiveness

UPA-EC costs between €15–57 in Europe and US$ 40–70 in USA. The manufacturer, HRA Pharma, has proposed tiered pricing strategies to provide sustainable and affordable access. The cost–effectiveness of UPA-EC compared with LNG-EC for the avoidance of unintended pregnancy has been analysed in several studies (18–22). Potential cost-savings have been identified in several cases; in the United Kingdom, for example, the additional cost to prevent one pregnancy by giving UPA-EC rather than LNG-EC was calculated to be £311, which is lower than the cost of an unintended pregnancy (£948), regardless of the outcome (19).

WHO guidelines

UPA-EC is included in the WHO Medical eligibility criteria for contraceptive use (17).

Availability

Currently, UPA is marketed in 65 countries (19 countries of low- or lower-middle income) and is available without prescription in about 40 countries, including the European Union where it was approved by EMA in 2014.

Other considerations

Preventing unintended pregnancy and reducing adolescent childbearing through universal access to sexual and reproductive health-care services are critical to further advances in the health of women, children and adolescents.

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