

Codes ATC: **G03AD02**

Indication	Contact with health services for postcoital contraception	Code ICD11: QA21.0
INN	Ulipristal	
Type de médicament	Chemical agent	
Type de liste	Liste de base	
Formulations	Oral > Solid: 30 mg tablet (ulipristal acetate)	
Historique des statuts LME	Ajouté pour la première fois en 2017 (TRS 1006)	
Sexe	Féminin	
Âge	Adolescents et adultes	
Équivalence thérapeutique	La recommandation concerne ce médicament spécifique	
Renseignements sur le brevet	Patents have expired in most jurisdictions Lire la suite sur les brevets. 	
Wikipédia	Ulipristal 	
DrugBank	Ulipristal 	

Recommandation du comité d'experts

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.

Contexte

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

Pertinence pour la santé publique

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.

Bénéfices

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).

Torts

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).

Preuves supplémentaires

N/A

Rapport coût/efficacité

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).

Directives de l'OMS

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

Disponibilité

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.

Autres considérations

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.

1. Sustainable Development Goal 3. Ensure healthy lives and promote well-being for all at all ages. New York: United Nations; 2017 (<https://sustainabledevelopment.un.org/sdg3>, accessed 2 March 2017).
2. Sedgh G, Singh S, Hussain R. Intended and unintended pregnancies worldwide in 2012 and recent trends. *Stud Fam Plann*. 2014;45(3):301–14.
3. Singh S, Darroch JE, Ashford LS. Adding it up: the costs and benefits of investing in sexual and reproductive health 2014. New York: Guttmacher Institute; 2014 (<https://www.guttmacher.org/report/adding-it-costs-and-benefits-investing-sexual-and-reproductive-health-2014>, accessed 2 March 2017).
4. Emergency contraception fact sheet. Geneva: World Health Organization; 2016 (<http://who.int/mediacentre/factsheets/fs244/en/>, accessed 2 March 2017).
5. Darroch JE, Woog V, Bankole A, Ashford LS. Adding it up: costs and benefits of meeting the contraceptive needs of adolescents. New York: Guttmacher Institute; 2016 (https://www.guttmacher.org/sites/default/files/report_pdf/adding-it-up-adolescents-report.pdf, accessed 2 March 2017).
6. Mortality, morbidity and disability in adolescents - mortality 2014. Geneva: World Health Organization; 2014 (<http://apps.who.int/adolescent/second-decade/section3/page2/mortality.html>, accessed 2 March 2017).
7. Palermo T, Bleck J, Westley E. Knowledge and use of emergency contraception: a multicountry analysis. *Int Perspect Sex Reprod Health*. 2014;40(2):79–86.
8. Cheng L, Che Y, Gulmezoglu AM. Interventions for emergency contraception. *Cochrane Database Syst Rev*. 2012;(8):CD001324.
9. Glasier AF, Cameron ST, Fine PM, Logan SJ, Casale W, Van Horn J et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. *Lancet*. 2010;375(9714):555–62.
10. Creinin MD, Schlaff W, Archer DF, Wan L, Frezieres R, Thomas M et al. Progesterone receptor modulator for emergency contraception: a randomized controlled trial. *Obstet Gynecol*. 2006;108(5):1089–97.
11. Brache V, Cochon L, Deniaud M, Croxatto HB. Ulipristal acetate prevents ovulation more effectively than levonorgestrel: analysis of pooled data from three randomized trials of emergency contraception regimens. *Contraception*. 2013;88(5):611–8.
12. Glasier A, Cameron ST, Bliethe D, Scherrer B, Mathe H, Levy D et al. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. *Contraception*. 2011;84(4):363–7.
13. Hunter C, Ginde S, van Santen M, Perez S, Gemzell Danielsson K. Ulipristal acetate 30 mg for emergency contraception is safe and effective in both adolescents and adult women: results from an International multicenter observational study. *Eur J Contracept Reprod Health Care*. 2014;19(Suppl 1):S67–90.
14. Levy DP, Jager M, Kapp N, Abitbol JL. Ulipristal acetate for emergency contraception: postmarketing experience after use by more than 1 million women. *Contraception*. 2014;89(5):431–3.
15. Jatlaoui TC, Riley H, Curtis KM. Safety data for levonorgestrel, ulipristal acetate and Yuzpe regimens for emergency contraception. *Contraception*. 2016;93(2):93–112.
16. Jesam C, Cochon L, Salvatierra AM, Williams A, Kapp N, Levy-Gompel D et al. A prospective, open-label, multicenter study to assess the pharmacodynamics and safety of repeated use of 30 mg ulipristal acetate. *Contraception*. 2016;93(4):310–6.
17. Medical eligibility criteria for contraceptive use, fifth edition, 2015. A WHO family planning cornerstone. Geneva: World Health Organization; 2015.
18. Thomas CM, Cameron S. Can we reduce costs and prevent more unintended pregnancies? A cost of illness and cost-effectiveness study comparing two methods of EHC. *BMJ Open*. 2013;3(12):e003815.
19. Thomas CM, Schmid R, Cameron S. Is it worth paying more for emergency hormonal contraception? The cost-effectiveness of ulipristal acetate versus levonorgestrel 1.5 mg. *J Fam Plann Reprod Health Care*. 2010;36(4):197–201.
20. Rubio-Terrés C, Schmid R. Análisis coste-efectividad de la anticoncepción hormonal de emergencia con ulipristal acetato frente a levonorgestrel. *PharmacoEconomics Spanish Research Articles*. 2012;9(2):53–62 (in Spanish).
21. Schmid R. The cost-effectiveness of emergency hormonal contraception with ulipristal acetate versus levonorgestrel for minors in France. *PLoS One*. 2015;10(9):e0138990.
22. Bayer LL, Edelman AB, Caughey AB, Rodriguez MI. The price of emergency contraception in the United States: what is the cost-effectiveness of ulipristal acetate versus single-dose levonorgestrel? *Contraception*. 2013;87(3):385–90.

