

Interaction between ella (Ulipristal Acetate) and Hormonal Contraception (Progestins)

BOTTOM LINE

Some agencies recommend *against* using UPA in women who have recently taken progestins.^{1,2} This seems the most prudent course of action in the absence of clinical data and is reflected in the medSask Emergency Contraception guidelines.

WHAT IS ELLA?

ella (ulipristal acetate) is the most recent product introduced to the Canadian market for emergency contraception (EC). It is a selective progesterone receptor modulator which displays competitive inhibition and partial agonism at the progesterone receptor and inhibits or delays ovulation.³

WHAT IS THE INTERACTION BETWEEN ELLA AND PROGESTINS?

Because UPA reversibly binds to the progesterone receptor, progestins with greater affinity to the receptor could interfere with UPA-EC's effectiveness; conversely, UPA-EC could interfere with the effectiveness of hormonal contraception (HC) of lower-affinity progestins. Research has confirmed that concurrent use of UPA-EC in the presence of desogestrel (DSG), the progestin component in certain HC products, decreases the ability of UPA-EC to delay ovulation.⁴ The manufacturer acknowledges this interaction in the monograph by recommending HC not be started within five days of taking UPA-EC.³ However, what is not acknowledged is the possibility that HC taken before or at the time of UPA-EC could also interfere with UPA-EC's effectiveness. No data are available as no studies have been undertaken to address this question and use of HC was an exclusion criteria in the UPA-EC trials.⁵⁻⁷ It seems logical that if DSG administered after UPA-EC can interfere with UPA-EC's effectiveness, it could also interfere if in systemic circulation at the time of administration of UPA-EC.

It needs to be noted the dose of DSG in the above trial was 0.75 mg and the highest strength of DSG available in Canada is 0.15 mg⁸; furthermore, data are only available for 41 women and this was a pharmacodynamic study assessing the surrogate marker of follicular rupture.⁴ No data are available regarding any other progestogens. Until clinical data are available to answer the question, it seems prudent to take the worst-case-scenario approach in which the interaction is considered clinically relevant with all progestogens.

WHAT CONTRACEPTIVES ARE INCLUDED?

All types of HC in Canada contain a progestin.⁸ Combined oral contraceptives, the contraceptive vaginal ring, the contraceptive patch, levonorgestrel intrauterine systems, depo-medroxyprogesterone acetate, and progestin-only pills are included.

HOW SHOULD THE INTERACTION BETWEEN ULIPRISTAL AND PROGESTINS BE MANAGED?

Ulipristal acetate has been shown to delay or prevent ovulation for five days.¹ In order to avoid this interaction, progestins should be avoided for at least five days after taking UPA-EC.¹⁻³ In addition, the Society of Obstetricians and Gynecologists of Canada recommends back-up contraception for an additional seven days after starting or resuming HC.¹

Because the potential interaction of progestins taken before UPA-EC is theoretical, only one management strategy has been identified which recommends UPA-EC not be used in women who have taken progestogen-containing products in the last seven days.² As such, UPA-EC should be avoided in most cases of contraceptive failure due to missed doses of HC. For those who are late for the depo-medroxyprogesterone injection, the copper intrauterine device (IUD) or levonorgestrel should be recommended because return to ovulation is variable⁹ and the duration of concentrations sufficient to cause the (theoretical) interaction are unknown.²

WHEN THEN CAN ELLA BE USED IN ORDER TO AVOID THE INTERACTION WITH PROGESTINS?

- when no contraception or non-hormonal contraception is being used
- for women who are late re-starting their oral contraceptive, contraceptive patch or contraceptive ring (i.e. have been without hormonal contraception for more than seven days).

IS THERE ALSO AN INTERACTION BETWEEN LEVONORGESTREL AND PROGESTINS?

There is no evidence to suggest an interaction between levonorgestrel and progestins.^{1,2} Levonorgestrel can be used in women who have used hormonal contraception in the last seven days; after taking levonorgestrel, any form of HC may be continued/started on the same day.^{1,2}

ADDITIONAL CONSIDERATIONS

- Patient preference should play a role in the selection of EC with consideration given to the potential inconvenience to the patient if resuming or starting HC has to be delayed due to the interaction between UPA-EC and HC.
- It is prudent to consider the expected time to ovulation after failure/incorrect use of the various methods of HC in order to assess whether or not EC is warranted.

Until data are available to prove otherwise, the best methods of EC for women who have been taking HC within the last week or those on depo-medroxyprogesterone are copper IUDs or levonorgestrel EC products.

**Prepared by Roberta Panchuk, Pharmacy Intern. Reviewed by Carmen Bell BSP, Karen Jensen MSc, BSP
medSask | February 2018**



References:

1. Gilbert E, Dunn S, Black A. Addendum to the Canadian Consensus on Contraception – Emergency Contraception: 1) Excluding pre-existing pregnancy when inserting copper IUD and 2) Initiation of hormonal contraception after emergency contraception. *J Obstet Gynaecol Can* 2016; 38(12):1150-1151.
2. The Faculty of Sexual & Reproductive Healthcare. FSRH guideline: emergency contraception. [updated Dec 2017; cited 23 Feb 2018] Available at <https://www.fsrh.org/standards-and-guidance/current-clinical-guidance/emergency-contraception/>
3. Product monograph for ella. Actavis Specialty Pharmaceuticals, Co. Markham, ON L6G 0B5. May 2016.
4. Brache V, Cochon L, Duijkers IJM. A prospective, randomized, pharmacodynamics study of quick-starting a desogestrel progestin-only pill following ulipristal acetate for emergency contraception. *Hum Reprod*. 2015; 30(12): 2785-2793.
5. Glasier AF, Cameron ST, Fine PM, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomized non-inferiority trial and meta-analysis. *Lancet*. 2010; 375(9714): 555-62.
6. Creinin MD, Schlaff W, Archer DF, et al. Progesterone receptor modulator for emergency contraception: a randomized controlled trial. *Obstet Gynecol*. 2006; 108(5): 1089-97.
7. Fine P, Mathe H, Ginde S. Ulipristal acetate taken 48-120 hours after intercourse for emergency contraception. *Obstet Gynecol*. 2010; 115(2 Pt 1):257-63.
8. Regier L, Jensen B, Downey S. Hormonal contraception: supplementary tables. RxFiles drug comparison charts. Saskatoon, SK: Saskatoon Health Region. [updated 01 Jan 2018; accessed 23 Feb 2018]. Available from: www.RxFiles.ca
9. Paulen ME, Curtis KM. When can a woman have repeat progestogen-only injectables – depot medroxyprogesterone acetate or norethisterone enantate? *Contraception* 2009;80:391–408.