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TITLE

THE MECHANISM OF ACTION OF ELLAONE: CRITICAL ISSUES IN EMA OFFICIAL DOCUMENTS

AUTHOR/S

Mozzanega B (IT) [1], Gizzo S (IT) [2], Nardelli G (IT) [3]

ABSTRACT

Context – EllaOne (micronized UPA 30mg) is marketed as an emergency contraceptive; its mechanism of action (MOA) is reported to be ovulation inhibition/delay (EMA EPAR WC500023670, p.8). We already acknowledged that it can inhibit ovulation in the first days of the fertile period, but its effect is placebo-like in the most fertile days: the peri-ovulatory days, in which most fertilizations do occur (Reprod Sci 2014;21(6):678-85). Besides, the dose of UPA sufficient to affect endometrial receptivity is far lower than that used to try ovulation delay.

Objectives & Methods –We analyse the EMA Assessment Reports (AR) EMEA/261787/2009 and EMA/73099/2015 to verify if the information in ellaOne EPAR is consistent with the data reported in ARs.

Results - In the 2009 AR it is stated (p.8) that “UPA prevents progesterone from occupying its receptor, thus the gene transcription normally turned on by progesterone is blocked, and the proteins necessary to begin and maintain pregnancy are not synthesized”. That means that UPA has both anti-implantation and abortifacient properties. The latter emerge also at p.10: “When using i.m. administration of 0.5 mg/kg 4/5 foetuses were lost in UPA treated macaques”, and are acknowledged at the pp. 45-46.

In the 2015 AR the pp.6-8 evidence that in patients treated with ellaOne every 7th or 5th day for two months ovulation was present in 91% and 72% cases respectively and the cervical mucus was permeable to sperms. However, the endometrium at the end of the treatment had a non-physiological appearance in 50% of patients.

Conclusions –EllaOne, taken either occasionally or regularly, mostly allows ovulation, but, in case of fertilization, the embryo will not find a hospitable endometrium. The CHMP is aware of this, but writes that ellaOne MOA is delaying ovulation. The information in the Package leaflet (EPAR p.23) is consequently incorrect.

INSTITUTE

[1] University of Padova, [2] University of Padova, [3] University of Padova