

NEW DRUG EVALUATION

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CERAZETTE®

Cerazette® is a progestogen-only oral contraceptive (POP) containing desogestrel. Unlike other POPs it inhibits ovulation as well as thickening cervical mucus. Limited published evidence suggest that when compared to levonorgestrel 30 mcg/day differences in efficacy were not statistically significant and it is not better tolerated than levonorgestrel. Cerazette® is more expensive compared with other POPs and its role in the management of contraception is currently unclear.

What is it?

Cerazette® (Organon) is a progestogen-only oral contraceptive containing desogestrel, a third generation progestogen. Each tablet contains 75 mcg and like other POPs should be taken at the same time each day. Desogestrel is also available in the combined oral contraceptives (COC) Mercilon® and Marvelon®, in which it is taken at a dose of 150 mcg/day. Unlike other progestogen-only formulations, the primary mechanism of action of desogestrel is claimed to be inhibition of ovulation¹ but it also causes thickening of cervical mucus. The manufacturers claim that Cerazette® 'offers the efficacy of a combined pill, with the reassurance of an oestrogen free pill'.

How effective is it?

The effects of desogestrel 75 mcg and levonorgestrel 30 mcg on ovulation were compared in a 12-month randomised double-blind trial (n=71).² Ovulation was confirmed by ultrasonography followed by a rise in serum progestogen >30 nmol/l. The women were evaluated during the 7th and 12th treatment periods. Overall, 1.7% of cycles were ovulatory in women taking desogestrel compared with 28% in those receiving levonorgestrel.

The contraceptive efficacy of desogestrel and levonorgestrel has been reported in a double-blind published study.³ Women were randomised in a ratio of 3:1 to desogestrel (n=989) or levonorgestrel (n=331) for 13 cycles. Efficacy was reported as the Pearl Index (PI, number of pregnancies per 100 woman-years of use). There were three pregnancies among women taking

desogestrel (PI 0.41) and four among those taking levonorgestrel (PI 1.55). Of these two in the desogestrel group and one in the levonorgestrel group were thought to be due to user rather than method failure giving PIs of 0.14 and 1.17 respectively. (The Pearl index reported for low dose combined oral contraceptives is 0.12-0.54).³ Although the study demonstrated a lower PI with desogestrel compared with levonorgestrel the results were not statistically significant. However the study was designed primarily to detect a difference between the two groups in bleeding patterns and not efficacy. Desogestrel users had a higher incidence of both amenorrhoea and infrequent bleeding, and frequent bleeding and prolonged bleeding. Slightly more women discontinued desogestrel due to 'irregular bleeding' than levonorgestrel (22% vs. 18%, p=ns)

How safe is it?

The commonest adverse effects associated with desogestrel are acne 3.1%, headache 7.5%, nausea 3.3%, breast pain 4.0%, dysmenorrhoea 1.2% and vaginitis 3.8%.³ In one comparative study desogestrel and levonorgestrel were associated with similar frequencies of adverse effects.³ In this study, 10.5% of women taking desogestrel and 9.2% taking levonorgestrel discontinued contraception due to adverse effects, p=ns.

Although combined oral contraceptives are associated with an increased incidence of venous thromboembolism (VTE, deep venous thrombosis and pulmonary embolism), the clinical relevance for desogestrel used as a contraceptive in the absence of an

estrogenic component is unknown. Cerazette® should be discontinued in the event of a thrombosis.¹

Desogestrel, like levonorgestrel, has small and clinically insignificant effects on haemostasis⁴, lipid and carbohydrate metabolism^{5,6}, and thyroid and adrenal function.⁶

What other options are there?

Six other progestogen-only contraceptives are available. Femulen® (etynodiol diacetate 500 mcg), Micronor®, Noriday® (norethisterone 350 mcg), Microval®,

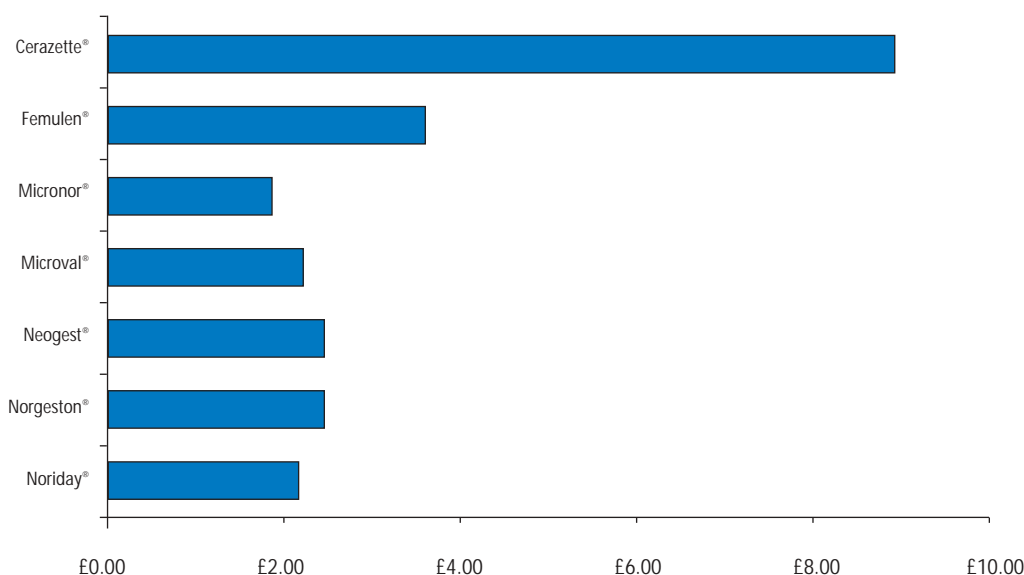
Norgeston® (levonorgestrel 30 mcg) and Neogest® (levonorgestrel 37.5 mcg).

When should it be used?

When desogestrel was compared to levonorgestrel, any advantage in terms of contraceptive efficacy was not statistically significant. There was also no evidence that it was better tolerated than levonorgestrel. There are no published studies comparing desogestrel with other POPs and COCs. Currently its role in the management of contraception is unclear.

How much does it cost?

Cost for 3 month's treatment (prices from MIMS March 2003)



NB Doses shown are for general comparison only and do not imply therapeutic equivalence.

REFERENCES

- 1 Organon Laboratories. Cerazette SPC. June 1998.
- 2 Rice CF, Killick SR, Dieben T, et al. A comparison of the inhibition of ovulation achieved by desogestrel 75 mcg and levonorgestrel 30 mcg daily. Human Reproduction 1999;14:982-5. (RCT)
- 3 Collaborative Study Group on the Desogestrel-containing Progestogen-only Pill. A double-blind study comparing the contraceptive efficacy, acceptability and safety of two progestogen-only pills containing desogestrel 75 mcg/day or levonorgestrel 30 mcg/day. Eur J Contraception Repr Health Care 1998;3:169-78. (RCT)
- 4 Winkler UH, Howie H, Buhler K, et al. A randomized controlled double-blind study of the effects on hemostasis of two progestogen-only pills containing 75 mcg desogestrel or 30 mcg levonorgestrel. Contraception 1998;57:385-92. (RCT)
- 5 Barkfeldt J, Virkkunen A, Dieben T. The effects of two progestogen-only pills containing either desogestrel (75 mcg/day) or levonorgestrel (30 mcg/day) on lipid metabolism. Contraception 2001;64:295-9. (RCT)
- 6 Kivela A, Ruuskanen M, Agren U, et al. The effects of two progestogen-only pills containing either desogestrel (75 mcg/day) or levonorgestrel (30 mcg/day) on carbohydrate metabolism and adrenal and thyroid function. Eur J Contraception Repr Health Care 2001;6:71-7. (RCT)

KEY RCT - randomised controlled trial, CT-controlled trial, O-open study, MA-meta analysis, R-review, U-unpublished, A- abstract, E-editorial

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