

BOURNEMOUTH, DORSET AND POOLE PRESCRIBING FORUM

GUIDANCE ON THE USE OF CERAZETTE®

Background

Cerazette ® has been categorised as **green** within the “traffic light” system by the Bournemouth, Dorset and Poole Prescribing Forum for use as a possible alternative to traditional progestogen-only pills (POPs) for women within the following categories:

- Under the age of 35 years for whom a combined oral contraceptive (COC) is contra-indicated or not tolerated.
- Women of any age who cannot use COC and who consider that Cerazette ® with the 12 hour window will improve pill taking
- Women of any age for whom the COC is contraindicated but they require an oral anovulent contraceptive method
- Use prior to insertion of Implanon where there are concerns about hormonal side-effects

It was felt that there was insufficient evidence to support its general use as an alternative to traditional progestogen-only pills in lactation.

This local guidance has been prepared to support the use of Cerazette in Dorset. It has been developed in conjunction with the Bournemouth, Dorset and Poole Prescribing Forum.

What is Cerazette ®?

Cerazette® is a progestogen-only contraceptive pill containing 75micrograms of desogestrel. This is the same kind of progestogen which can be found in the combined oral contraceptive Marvelon ®. Etonogestrel, the active metabolite of desogestrel, is found in Implanon®.

How does this pill work?

Mainly by inhibiting ovulation. In one study, desogestrel 75micrograms inhibited ovulation in 97% of cycles.¹ This is quite different from other progestogen-only pills where complete inhibition of ovulation is achieved in only about half of the cycles and efficacy is thought to rely on other mechanisms e.g. effect on cervical mucus. In addition to inhibiting ovulation, Cerazette ® also produces changes to cervical mucus.

How effective is this pill?

Cerazette ® is an effective contraceptive. Women may be advised that if used consistently and correctly Cerazette ® is more than 99% effective.

One study which has addressed efficacy demonstrated a lower Pearl index with Cerazette ® than with levonorgestrel (LNG).² The following table shows the Pearl index values that were reported. In this study some of the women were breastfeeding so two Pearl indices have been included. The first are the actual figures obtained excluding gross non-compliance but including breast-feeding. The bold figures in brackets have been calculated to exclude exposure during breastfeeding. The figures in the last two columns give the range of failure rates quoted in World literature³ for POPs and COCs.

	Cerazette ²	LNG POP ²	COC overall ³	POP overall ³
Pearl Index	0.14 (0.17)	1.17 (1.41)	0.2-3.0	0.3-4.0

It should be noted that this is the only published study that has addressed efficacy. The number of pregnancies was small and the difference was not statistically significant. This study was not powered to detect differences in efficacy. Further comparative studies are therefore required to establish the comparative efficacy of Cerazette ® with other progestogen-only and combined oral contraceptive products.

How is Cerazette administered?

Tablets must be taken every day at about the same time. Contraceptive protection may be reduced if more than 12 hours have elapsed since the missed dose. In this case, an additional method of contraception should be used for the next 2 days.

How safe is Cerazette ®?

The manufacturers' Summary of Product Characteristics should be referred to for full prescribing information.

Metabolic effects

No clinically relevant effects on carbohydrate metabolism, lipid metabolism and haemostasis have been observed.

Desogestrel is one of the third generation progestogens that have been associated with an increased risk of thromboembolism. The significance of this, when desogestrel is used in the absence of oestrogen, is not known.

Lactation

Cerazette ® does not influence the production or quality of breast milk. However, small amounts of etonogestrel are excreted with the milk. Faculty of Sexual and Reproductive healthcare (FSRH) state "women who are postpartum may choose to use a POP without restriction regardless of how they are feeding their baby⁶. No adverse effects on breast feeding, infant growth or development have been noted in studies that looked at the progestogen only pill. Therefore, the Clinical Effectiveness Unit at the Faculty of Sexual and Reproductive health state that "Women can be informed that available evidence suggest that the use of progestogen only contraception whilst breast feeding does not affect breast milk volume and has been shown to have no effect on infant growth." 9

Side-effects

The most frequently reported side-effects in the clinical trials with Cerazette ® were:

- bleeding irregularity
- acne
- mood changes
- breast pain
- nausea
- Weight increase.

Other side-effects include headache, amenorrhoea, decreased libido, vaginitis, dysmenorrhoea, ovarian cysts, alopecia, fatigue and difficulty wearing contact lenses.

Bleeding irregularity has been reported in up to 50% of women using Cerazette ® and occurs more commonly than with other POPs. Careful counselling before commencing Cerazette ® is therefore important.

As a rough guide⁴, women considering Cerazette ® can be advised that by 12 months of use, over a 3-month interval:

- 5 in 10 women can expect to be amenorrhoeic or have infrequent bleeding;
- 4 in 10 women can expect to have 3 to 5 bleeding/spotting episodes;
- 1 in 10 women can expect more than 6 bleeding/spotting episodes or prolonged bleeding/spotting episodes.

Otherwise, trial data indicates that occurrence and pattern of adverse effects with desogestrel is similar to levonorgestrel.²

FSRH state that women may be advised that there is no evidence for a casual association between progestogen only pills and;

- weight change
- depression
- cardiovascular disease or breast cancer

Contra-indications:

- Known or suspected pregnancy
- Current /previous history of breast cancer
- Liver tumours; both benign adenoma and malignant hepatoma
- Recent trophoblastic disease – until the levels of human chorionic gonadotrophin have returned to normal
- Women who develop ischemic heart disease, stroke or focal migraine whilst using any POP should be advised that the risks outweigh the benefits and they should discontinue the preparation
- Women on long term liver enzyme inducing drugs such as anti-epileptics; these drugs decrease circulating levels of progestogen and women using POPs require extra precautions
- Presence or history of severe liver disease as long as liver function tests have not returned to normal
- Undiagnosed vaginal bleeding
- Hypersensitivity to any of the ingredients of Cerazette ®.

Special warnings

While Cerazette ® is associated with more complete inhibition of ovulation than traditional POPs, the possibility of ectopic pregnancy should still be considered in the event of amenorrhoea or abdominal pain.

Who is suited to this pill?

- Those women under 35 years of age^{for} whom a combined oral contraceptive (COC) is contra-indicated or not tolerated and for whom traditional POPs may be less effective.
- Women of any age who are unable to use combined hormonal contraception but consider their pill taking would improve with the 12 hour window for missed pills

Potential benefit of improved efficacy needs to be balanced on an individual patient basis against disadvantages in respect of irregular bleeding and the limited information available on long-term safety compared with traditional POPs.

Cerazette ® is unsuitable for women intolerant to any change in menstrual bleeding pattern.

Careful counselling is necessary to enable patients to make an informed choice.

Should I switch a woman under 35 who is currently on a traditional POP?

If she is amenorrhoeic, she is probably anovulent and if otherwise happy-leave her. Otherwise, discuss pros and cons of changing with each patient. Note that the patient experiencing regular menstrual periods on a traditional POP is more at risk of breakthrough pregnancy because she is relying on the mucus effects for contraception. If she is changed to Cerazette® she is likely to experience erratic bleeding which may be less acceptable to her.

How to switch pills

When changing from one POP to another or from a combined oral contraceptive pill to a progestogen-only pill, the first pill of the new pack should be started on the next day immediately after the old pack is complete. No additional contraceptive method is necessary.

What is the cost?

The annual cost of treatment compared with some other POPs is as follows:

Annual cost (MIMS October 2009)

Cerazette	£37.42
Femulen	£13.24
Micronor	£5.07
Norgeston	£10.34

SUMMARY POINTS

1. Desogestrel has been shown to be more effective at inhibiting ovulation than levonorgestrel but no significant difference in efficacy (as measured by the Pearl index) has been demonstrated.
2. The potential for improved efficacy may be of benefit for some women for whom a COC is contra-indicated or not tolerated but may not provide further benefit for women whose natural fertility is already reduced.
3. Careful counselling is needed due to erratic bleeding.
4. Long-term safety has not been established.
5. Need for pedantic pill taking still necessary.
6. Cerazette costs about seven times more than the least expensive POP.
7. It is not recommended as an alternative to a COC in routine clinical practice.
8. It may be a useful alternative to traditional POPs for women, for whom a COC is contra-indicated or not tolerated, who are:
 - under the age of 35 years;
 - Women of any age who cannot use COC and who consider that cerazette with the 12 hour window will improve pill taking
 - Women of any age for whom the COC is contraindicated but they require an oral anovulent contraceptive method
 - Use prior to insertion of Implanon where there are concerns about hormonal side-effects

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*Pearl Index – number of pregnancies that occur for each contraceptive method if used by 100 women for one year)

Note: A review of Cerazette was published in the Drug and Therapeutics Bulletin (2003; 41: (9) 68-69).

References

1. Rice, C F et al. A comparison of the inhibition of ovulation achieved by desogestrel 75 micrograms and levonorgestrel 30 micrograms daily. *Human Reproduction* 1999; 14: 982-985
2. 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 micrograms/day or levonorgestrel 30 micrograms/day. *European Journal of Contraception and Reproductive Health Care* 1998; 3: 169-178
3. *Contraception Your Questions Answered* 3rd Edition J Guillebaud 1999
4. Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. New Product Review. *Journal of Family Planning and Reproductive Health Care* 2003; 29(3): 162-164
5. Faculty of Family Planning and reproductive healthcare Clinical Effectiveness Unit UK Medical eligibility for contraceptive use 2006.
6. Faculty of Sexual and Reproductive Healthcare clinical effectiveness unit Guidance Progestogen Only Pills November 2008
7. Guillebaud; *Contraception your questions answered*. 5th edition 2009.
8. FSRH Guidance Progestagen Only Pills November 2008. FSRH Clinical Effectiveness Unit
9. FSRH Guidance Postnatal Sexual and reproductive September 2009. FSRH Clinical Effectiveness Unit

Costs correct at October 2009

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