Progestogen-only oral contraceptives

Steve Chaplin BPharm, MSc and Anne MacGregor MD, MICR, FFSRH

Progestogen-only oral contraceptives are a useful alternative to combined oral contraceptives but adherence is more important.

Steve Chaplin

There are 10 brands of progestogen-only oral contraceptives (POPs) comprising three progestogens: the newer desogestrel, and the older levonorgestrel and norethisterone (see Table 1). Femulen, which contained etynodiol diacetate, was discontinued in 2013.

Desogestrel prevents conception by inhibiting ovulation; the traditional agents act primarily by making the cervical mucus impermeable to sperm. There is insufficient evidence to compare the effectiveness of desogestrel and the traditional agents.1

POPs may be preferred to combined oral contraceptives (COCs) for women unable to take an oestrogen, who have risk factors for thromboembolism or who are breastfeeding.2

Adherence to correct dose timing is important for effectiveness.

Common adverse effects include gastrointestinal disturbances, weight change, breast discomfort, depression, altered libido and irregular bleeding.

KEY POINTS

- The POPs desogestrel, levonorgestrel and norethisterone are available in 10 brands
- The desogestrel POP acts primarily by inhibiting ovulation; norethisterone and levonorgestrel POPs act primarily by making the cervical mucus impermeable to sperm
- POPs may be preferred to COCs for women unable to take an oestrogen, who have risk factors for thromboembolism or who are breastfeeding
- Adherence to correct dose timing is important for effectiveness
- Common adverse effects include gastrointestinal disturbances, weight change, breast discomfort, depression, altered libido and irregular bleeding

Administration

POPs are taken continuously at about the same time each day. The first tablet should be taken up to, and including, day five of the cycle. If started later, additional contraceptive precautions are required for two days. After pregnancy, POPs can be started up to and including day 21 post-partum without the need for additional contraceptive precautions; if started later, additional contraceptive precautions are required for two days. When switching from a COC, if use of the POP begins on day 1–3 of the hormone free interval, no additional precautions are required.

The duration of contraception is shorter for POPs than COCs if a dose is missed or absorption is reduced. The advantage of desogestrel over norethisterone or levonorgestrel is that contraception is assured for longer. If a dose of norethisterone or levonorgestrel is delayed by more than three hours (>27 hours after the last pill taken), it should be taken immediately and the next dose should be taken as scheduled. This interval is 12 hours (>36 hours after the last pill taken) for desogestrel. For all POPs additional contraception is necessary for the next two days. If unprotected intercourse occurs before two further tablets have been taken correctly, emergency contraception should be considered.

In the event of vomiting within two hours of a dose taken at the correct time, a second pill can be taken within three hours (12 hours for desogestrel) without loss of contraception. If the interval is longer or the woman continues to vomit, additional contraception will be necessary. If very severe watery diarrhoea lasts for 24 hours, additional measures will be needed for two days after the diarrhoea has resolved.

Drug interactions

The clearance of progestogens is increased by drugs that induce hepatic
Progestogen-only oral contraceptives

**Drug Points**

Required while taking these drugs and for levels of selegiline and these should not antagonise the anticoagulant effect of warfarin. John's Wort. Additional contraception is necessary four weeks after discontinuing them.

Conversely, progestogens increase blood levels of selegiline and these should not be taken together. Progestogens may antagonise the anticoagulant effect of phenindione (but not warfarin). Healthcare has published detailed guidance on the indications and contraindication of POPs for a full list of the UKMEC, see Table 1. Daily dosage and cost of currently available POPs

<table>
<thead>
<tr>
<th>Progestogen</th>
<th>Daily dose (µg)</th>
<th>Cost per 28 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desogestrel</td>
<td>75</td>
<td>£1.12 (Zelleta)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>£1.17 (Cerelle, Nacrez)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>£1.74 (Aizea)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>£2.89 (Desomono, Desorex)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>£3.18 (Cerazette)</td>
</tr>
<tr>
<td>Norethisterone</td>
<td>350</td>
<td>£0.60 (Micronor)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>£0.70 (Noriday)</td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>30</td>
<td>£0.74 (Norgestion)</td>
</tr>
</tbody>
</table>

Table 1. Daily dosage and cost of currently available POPs

micosomal enzymes, reducing the effectiveness of contraception. Examples include some antiepileptic drugs, some protease inhibitors, griseofulvin and St John’s Wort. Additional contraception is required while taking these drugs and for four weeks after discontinuing them. Conversely, progestogens increase blood levels of selegiline and these should not be taken together. Progestogens may antagonise the anticoagulant effect of phenindione (but not warfarin).

Cautions and contraindications

POPs are contraindicated (UK Medical Eligibility Criteria for Contraceptive Use, UKMEC 4) in women with breast cancer. The Faculty of Sexual and Reproductive Healthcare has published detailed guidance on the indications and contraindication of POPs (for a full list of the UKMEC, see references 2 and 3). Overall, the risks of taking a POP generally outweigh benefits for women who have severe liver cirrhosis, liver tumours, or systemic lupus erythematosus with positive (or unknown) anti-phospholipid antibodies. Women with a history of breast cancer more than five years previously with no evidence of disease, or women who develop ischaemic heart disease or stroke may be prescribed a POP under specialist supervision if a non-hormonal contraception is unacceptable (UKMEC3).

Adverse effects

Irregular bleeding is a common adverse effect (more frequent than with COCs) and amenorrhoea may also occur. Desogestrel is associated with a higher frequency of irregular bleeding than other POPs, with frequency increased in 20–30 per cent of women and reduced in 20 per cent. Persistent ovarian cysts are not uncommon with POP use. Other adverse effects reported by users but without evidence of a causal association include gastrointestinal disturbances (nausea, vomiting, change in appetite), weight change, headache, dizziness, breast discomfort, depression, skin disorders and altered libido.

There is some evidence of a small increase in the risk of breast cancer among POP users (but this may be due to earlier diagnosis). Age when stopping use, rather than duration of use, may be a more important risk factor. The excess risk declines after stopping until there is no excess risk by 10 years.

Reference


Declaration of interests

Steve Chaplin has none to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics

Place in therapy

**Anne MacGregor**

Correctly taken, progestin-only pills (POPs) are very effective, preventing more than 99 per cent of pregnancies. Unlike combined pills, they have the advantage of being taken every day without a pill-free interval. One disadvantage is that traditional POPs only have a three-hour window for maintaining efficacy (12-hour window for the newer desogestrel POP), although efficacy is restored after two days of pill taking.

Unscheduled bleeding is the most common side-effect of POPs. Desogestrel, which inhibits ovulation in the majority of women, is often associated with either an irregular bleeding profile or amenorrhoea. Traditional POPs, which rely on their cervical mucous effect to prevent pregnancy, have less effect on bleeding patterns and many women continue a regular menstrual cycle. If unscheduled bleeding is a significant problem and disease or pathology has been excluded, anecdotal reports suggest that it is worth trying a different progestogen before abandoning the method.

With very few absolute contraindications, POPs are safe for the majority of women, particularly those who cannot take oestrogens. Specifically women with hypertension, venous thromboembolism (VTE), stroke or heart disease, migraine with aura, or who are breastfeeding, can all take POPs. POPs can be “quick-started” at any time of the cycle, without checking BP or weight, which are mandatory before prescribing combined oral contraceptives (COCs). Additional precautions are needed for the first two days with a pregnancy test done after three weeks, if indicated. POPs are also useful as a “bridging” method until the preferred method of contraception can be started. POPs can be continued until age 55 years, when natural fertility is assumed to have ceased.

Declaration of interests

Professor MacGregor has none to declare.

Anne MacGregor is honorary professor at the Centre for Neuroscience & Trauma, Barts and the London School of Medicine and Dentistry; associate specialist, Barts Sexual Health Centre, St Bartholomew’s Hospital, London