Progestin-only pill (POP)
Desogestrel 75 μg (DSG)
Drospirenone 4 mg (DRSP)

An advanced slide kit complementing the WHO training tool is available from:
www.fptraining.org

Update January 2020
POP: Contents

- General characteristics
- Mechanism of action
- Contraceptive efficacy
- Health benefits, migraine
- Adverse events, bleeding
- Emergency contraception
- Breastfeeding
- Summary
### General characteristics

<table>
<thead>
<tr>
<th>Desogestrel 75 µg</th>
<th>Drospirenone 4 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormone dose compared with combined hormonal contraceptive (CHC):</td>
<td></td>
</tr>
<tr>
<td>CHC: EE 30(20)µg/desogestrel 150 µg</td>
<td></td>
</tr>
<tr>
<td>POP: EE --- /desogestrel 75 µg</td>
<td></td>
</tr>
<tr>
<td>CHC: EE 30(20)µg/drospirenone 3 mg</td>
<td></td>
</tr>
<tr>
<td>POP: EE --- /drospirenone 4 mg</td>
<td></td>
</tr>
</tbody>
</table>

- Very-low-dose daily pills
- Inhibit ovulation
- Highly efficient

---

Suppression of ovarian function is less strong in comparison with CHC

- Ovulation is inhibited
- The low dose allows, however, more follicular development
- Women have higher oestradiol concentration in comparison with DMPA users
- Occasionally follicles will develop and not rupture, resulting in ovarian cysts

Ref 1


- **POPs have both advantages and disadvantages when compared with COCs.** The pill-taking regimen (of DSG) is simple and fixed: no pill colour changes or days without pill-taking occur. The 24+4 pill-taking regimen (of DRSP) includes a pill-free interval of 4 days. Fertility returns promptly upon discontinuation. POPs are appropriate for all women, but especially those who cannot or should not take estrogen in COCs; for example, a woman older than 35 years who smokes cigarettes (ACOG, 2006).

- **Lacking estrogen,** POPs may have a lower risk of complications. A WHO case–control study found no significant increase in the risk of stroke, myocardial infarction and VTE among POP users compared with non-users (WHO, 1998). A cohort study from Denmark also found no statistically significant association between POPs and VTE (Lidegaard, 2009).

- **Although the literature is unclear concerning the potential impact of COCs on lactation,** no concern exists for POPs (Moggia, 1991; Dunson, 1993; McCann, 1994; Bjarnadóttir, 2001; FFPRHC, 2004). No data are available concerning a potential effect on infant brain or liver.

- **Like DMPA injections for contraception (Manchikanti, 2007),** POPs may reduce the frequency of sickle cell crises.

- **Less restrictive screening for use may facilitate wider distribution by non-clinicians,**
or over-the-counter provision.

- Disadvantages include the recommendation for careful compliance and the disruption of normal menstrual patterns (FSRH, 2008). These changes include irregular bleeding, short or long cycles, bleeding and spotting, prolonged bleeding, or no bleeding at all. Overall, POPs are associated with more days of bleeding and spotting compared with COCs (Raymond, 2011).
• Randomised controlled trials published to date are inadequate to compare POPs with each other or with COCs. Since POPs are commonly used during breastfeeding, when fertility is low, the impact of better efficacy of any pill would be small in this setting. No trial has addressed the question of consistent timing of ingestion.

• Any potential benefit of better contraceptive efficacy with desogestrel 75 μg vs LNG 30 μg (Collaborative, 1998) may be offset by worse bleeding patterns. These include prolonged bleeding and absence of bleeding. For every one pregnancy that might be prevented with desogestrel, five women will discontinue early because of irregular bleeding. The trade-off between efficacy and continuation may be viewed differently in different settings, and amongst women in the same settings. For some women efficacy will be the chief consideration, while for others regular bleeding will be more important.

• Little information was available about the advice given as to the timing of administration of the pills or whether back-up contraception should be used in case of a late or missed pill. Although accurate timing of administration is considered important for POPs, little empirical evidence supports this hypothesis, and interindividual variation in the metabolism of progestins is wide (Goldzieher, 1994; Wallach, 2000).

• Calculations on pooled studies with 1571 patients gave an overall Pearl index (based on 14 329 cycles) of 0.7258 (95%CI 0.3133 to 1.4301) for the DRSP-only pill (Palacios et al. 2019 Acta OG Scan 1549-1557). The PI in another study was
POP are efficient but the dose is very low
So: Caution with concomitant use of enzyme-inducing drugs such as St John’s wort

Recommendation:
Use back-up method

Grey points/squares, cycles with St John’s wort

3-ketodesogestrel levels are significantly lower in users of a CHC containing EE 20 µg / desogestrel 150 µg during concomitant treatment with St John’s wort. This resulted in this study in more intracyclic bleeding episodes. Users of the much lower dosed POP will be more vulnerable to increased metabolism and loss of efficacy.

Ref 1,2


St John’s wort (Hypericum perforatum) is a popular herbal medicine marketed as a dietary supplement and widely used for the treatment of mild-to-moderate depression. St John’s wort was reported to have efficacy comparable to that of selective serotonin reuptake inhibitors and tricyclic antidepressants for the treatment of mild-to-moderate depression, as well as a better side effect profile.


This study did not reveal any clinically significant changes in etonogestrel pharmacokinetics, suggesting that oral desogestrel may be used by women after RYGB surgery. Peak serum concentrations (Cmax) increased after 52±2 weeks compared with preoperative values (0.817 ng/ml versus 0.590 ng/ml, P=0.024).
Health benefits

- Very low impact on plasma lipids, carbohydrate metabolism and haemostasis
- No increase in risk of VTE or arterial thrombotic event (ATE)
- Positive impact on dysmenorrhoea
- Positive impact on migraine with and without aura (DSG)
- No negative impact on lactation (DSG)

No data on DRSP yet

Ref 1-10

7. Merki-Feld GS et al. Positive effects of the progestin desogestrel 75 μg on migraine
frequency and use of acute medication are sustained over a treatment period of 180 days. J Headache Pain 2015; 16: 522.


The desogestrel study lists adverse events occurring in more than 3% of patients, the drospirenone study adverse events in more than 3% of the users.

### Adverse events

<table>
<thead>
<tr>
<th>Desogestrel</th>
<th>Drospirenone</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Irregular bleeding/amenorrhoea</td>
<td>• Irregular bleeding/metrorrhagia 4.8%</td>
</tr>
<tr>
<td>• Acne 3%</td>
<td>• Acne 6.3%</td>
</tr>
<tr>
<td>• Breast pain 4%</td>
<td>• Cystitis 2.9%</td>
</tr>
<tr>
<td>• Headache 7.5%</td>
<td>• Headache 4.5%</td>
</tr>
<tr>
<td>• Vaginitis 3.8%</td>
<td></td>
</tr>
<tr>
<td>• Dysmenorrhoea 1%</td>
<td></td>
</tr>
<tr>
<td>• Nausea 3.3%</td>
<td></td>
</tr>
</tbody>
</table>

22.5% discontinued desogestrel, because of irregular bleeding

Ref 1,2
A total of 713 participants with 7638 DRSP treatment cycles were analyzed. The proportion of participants with any bleeding decreased from 72.7% in Cycle 1 to 40% in Cycle 6 and 32.1% in Cycle 13. Unscheduled bleeding decreased from 49.1% in Cycle 1 to 27.8% in Cycle 6 and to 22.8% in Cycle 13. Prolonged bleeding was reported by 6.5% during Cycles 2 to 4 decreasing to 4.2% during Cycles 11 to 13.

This report describes the improvement in bleeding profile of women using the new DRSP-only oral contraceptive in comparison to DSG:
The proportion of women with unscheduled bleeding was statistically significantly lower in the DRSP group than in the DSG group (p = 0.0001, Chi-square test). Importantly: Scheduled bleeding or spotting was defined as any bleeding or spotting that occurred during hormone-free intervals (defined as days 25–28 ± 1). Up to eight consecutive bleeding/spotting days were considered as scheduled bleeding days. Unscheduled bleeding or spotting day was defined as any bleeding/spotting that occurred while taking active hormones (days 2–23), except days which were classified
as scheduled bleeding days. As desogestrel is administered without any free period, no scheduled bleeding is expected.
Direct evidence demonstrates no harmful effect of POC on breastfeeding performance, and generally demonstrates no harmful effects on infant growth, health or development; however, these studies have been inadequately designed to determine whether a risk of long-term effects exists.

No data on DRSP available yet, but the amount of DRSP 4 mg in breast milk is negligible as it is only 0.11% of the daily use of the 4 mg.

They are safe.
They are highly effective.
They are easy to use correctly.
They can be delivered in both clinical and non-clinical settings.

Summary POP

• Safe and highly effective
• Low-doses: avoid medication which increase metabolism
• Easy to use
• Can be used by women with cardiovascular risk factors
• Bleeding irregularity may be a concern for some women and needs appropriate counselling
• The POP can be provided in both clinical and non-clinical settings