Desogestrel 75 µg progestin-only pill (POP) and Depot medroxyprogesterone acetate (DMPA)

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

Update July 2018
Desogestrel 75 µg
progestin-only pill (POP)

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

- General characteristics of the desogestrel 75 μg POP
- Mechanism of action
- Contraceptive efficacy
- Health benefits, migraine
- Side effects, bleeding
- Emergency contraception
- Breastfeeding
- Summary
Characteristics of POP with desogestrel

Hormone dose compared with desogestrel combined hormonal contraceptive (CHC):
- CHC: EE 30 µg/desogestrel 150 µg
- POP: EE --- /desogestrel 75 µg

- Very-low-dose daily pill
- Inhibits ovulation
- Highly efficient

- POPs have both advantages and disadvantages when compared with COCs. The pill-taking regimen is simple and fixed: no pill colour changes or days without pill-taking occur. Fertility returns promptly upon discontinuation. POPs are appropriate for women 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).
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).

- POPs may not provide as much protection against ectopic pregnancy as do COCs (McCann, 1994), and they may be associated with more functional ovarian cysts 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.
• No firm conclusion is possible concerning the comparative efficacy of POPs or whether they are as effective as COCs.
• 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.
• One poor-quality trial suggested no large effect of timing of initiation on efficacy or continuation rates.
• 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).
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.
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 dysmenorrhea
- Positive impact on endometriosis after surgery
- Positive impact on migraine with and without aura
- No negative impact on lactation

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


### Adverse events

- Irregular bleeding/amenorrhoea
- Acne 3%
- Breast pain 4%
- Headache 7.5%
- Vaginitis 3.8%
- Dysmenorrhoea 1%
- Depressed mood

22.5% discontinued because of irregular bleeding

---


This study lists adverse events occurring in more than 3% of patients.
Before using POC, ensure that the patient understands the most common side effects, especially changes in bleeding patterns.

**Definitions of vaginal bleeding (reference period: 3 months).**

1. Normal and regular blood loss: mainly related to the natural cycle or CHC use.
2. Unpredictable blood loss:
   - Frequent (more than five episodes of blood loss).
   - Prolonged (one or more episodes of blood loss lasting ≥14 days).
   - Spotting (small amount of blood loss, no need for sanitary protection).
   - Not frequent (of blood loss less than three episodes).

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.
Summary: Desogestrel 75 μg 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

- They are safe.
- They are highly effective.
- They are easy to use correctly.
- They can be delivered in both clinical and non-clinical settings.
Depot medroxyprogesterone acetate (DMPA)

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

- General characteristics of DMPA
- Contraceptive efficacy and duration of use
- Mechanism of action
- Contraindications
- Health benefits
- Safety
- Side effects and treatment
- Reasons for discontinuation
- Summary
DMPA

- 12 weekly injections of 150 mg i.m. or 104 mg s.c.
- Inhibition of ovulation
- Highly efficient and user-independent
- Slow return to fertility (50% conceive within 10 months)
<table>
<thead>
<tr>
<th>DMPA: When to start</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protects immediately from pregnancy if started on day 1–7 of the cycle</td>
</tr>
<tr>
<td>Can be started after day 7 if pregnancy is excluded; additional protection is needed (7 days)</td>
</tr>
<tr>
<td>Has no negative impact on lactation or on the baby</td>
</tr>
</tbody>
</table>
Although progestin-only injectables are safe for most women, there are some exceptions. According to the WHO MEC, progestin-only injectables are not generally recommended for women with category 3 conditions. In these situations, the risks of using this method usually outweigh the advantages. Category 3 conditions include: acute blood clot in deep veins of legs or lungs, unexplained vaginal bleeding, severe hypertension ($\geq 160/\geq 100$ mmHg), severe liver disease and most liver tumours, complicated diabetes, and breastfeeding before 6 weeks postpartum.
Not all POCs exert the same health benefits, as progestin dosages and types vary.

<table>
<thead>
<tr>
<th>Health benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reduction of heavy menstrual bleeding</td>
</tr>
<tr>
<td>• Improvement of dysmenorrhoea</td>
</tr>
<tr>
<td>• Inhibition of fibroid growth</td>
</tr>
<tr>
<td>• Protection against iron-deficiency anaemia</td>
</tr>
<tr>
<td>• Reduction of sickle cell crises in women with sickle cell anaemia</td>
</tr>
<tr>
<td>• Improvement of catamenial epilepsy</td>
</tr>
<tr>
<td>• Reduction of risk for endometrial cancer</td>
</tr>
<tr>
<td>• Reduction in symptoms of endometriosis</td>
</tr>
</tbody>
</table>

No negative impact on cardiovascular outcome according to present evidence.


Data not available for three women in the DMPA s.c. group and for two in the DMPA i.m. group.
Acne is less frequent in DMPA users than in users of other POC including LNG-IUS (clinical experience).

Peak bone mass, which can be defined as the amount of bony tissue present at the end of skeletal maturation, is an important determinant of osteoporotic fracture risk in later life.

- The majority of women using DMPA experience menstrual changes as a result of the high level of progestin. During the months after the first-second injection, episodes >7 days of unscheduled bleeding/spotting are common. This is potentially due to endometrial instability and subsequent capillary leakage from scant uterine lining. The frequency/duration of these episodes decreases with continued use. Forty-six percent of users will be amenorrhoeic by 1 year; 70% with longer use.
- Endometrial biopsy studies show a predominance of endometrial atrophy and chronic endometritis. The latter is most often due to atrophy rather than to an infectious process.
- The most reliable information on bleeding patterns among women using injectables and other hormonal contraceptives comes from a WHO-coordinated multicentre clinical trial in which women kept detailed menstrual diaries. Less than 10% of DMPA users have normal cycles in the first year of use. As indicated on the graph, many DMPA users can expect to have irregular or prolonged bleeding in the first 6 months and then infrequent
bleeding or amenorrhoea in the next 6 months and beyond. About 47% of women are amenorrhoeic (have no monthly bleeding) after 1 year of DMPA use and, although not reflected on this graph, about 80% are amenorrhoeic after 2 years of DMPA use.

- The original data from the WHO trial described the percentages of women in the trial who experienced eight types of bleeding changes at 3, 6, 9 and 12 months of DMPA use. This graph collapses those eight categories of data into four. Data from each of the four categories of prolonged bleeding were added together to form one category of prolonged bleeding. The data on frequent bleeding were added to the data on irregular bleeding and are displayed here as *irregular bleeding*. The data shown here for amenorrhoea and infrequent bleeding are as originally published.


Ref 1: The Cochrane Database found little evidence of weight gain with progestin-only contraceptives. Some differences were noted when a POC was compared with no hormonal contraceptive. Actual mean weight gain was low for 6–12 months, i.e. less than 2 kg for most studies.

However, prospective studies demonstrate that in some DMPA and implant users, there can be a relevant increase in weight, which may lead to discontinuation.

In a study carried out among 490 adolescents followed for 6 years, all groups of women gained weight, but the greatest weight gain was among injectable users. In adolescents who had weight gain >2 kg, the results were similar between those who were non-obese and those who were overweight at baseline.


DMPA and Acne

- No prospectively conducted studies are available investigating the effect of DMPA on acne.
- Especially when changing from a combined pill to a progestin-only method skin problems can appear during the first 3 months.
- Skin problems frequently resolve with longer duration of use.

Take a good history and ask actively about depressive episodes. It is not prudent to start a POC or LNG-IUS in women with major depression. If there is no other choice, close follow-up is needed. A pill might be the better option to test tolerability.
Women should achieve peak bone density during adolescence. The strongest increase in bone density occurs during the first 2 years after menarche. To achieve peak bone mass is crucial to reduce the fracture risk in later life. Women start to experience some bone loss during early menopause.
Most studies have found that DMPA users have lower bone density compared with non-users. During adolescence, DMPA prevents the achievement of peak bone density, which is of major importance in decreasing fracture risk after the menopause. A woman’s bones normally reach peak bone density during adolescence.

Women who start using DMPA as adults appear to regain most of the lost bone after they stop using DMPA. One study indicated that women who had achieved peak bone mass before the menopause (30–45 years) did not continue to lose bone density at the distal radius. However, it is not yet known whether bone loss in adolescents and young women is completely reversible.

Long-term studies are needed to determine whether DMPA use increases the risk of fracture, especially in women who begin using DMPA during adolescence. Currently, DMPA use is not the method of choice during adolescence. If no other methods are available, preventing the risks associated with unwanted pregnancy at a young age outweigh the theoretical risk of fracture later in life.
Most studies have found that DMPA users have lower bone density compared with non-users. During adolescence, DMPA prevents the achievement of peak bone density, which is of major importance in decreasing fracture risk after the menopause. A woman’s bones normally reach peak bone density during adolescence.

Women who start using DMPA as adults appear to regain most of the lost bone after they stop using DMPA. One study indicated that women who had achieved peak bone mass before the menopause (30–45 years) did not continue to lose bone density at the distal radius. However, it is not yet known whether bone loss in adolescents and young women is completely reversible.

Long-term studies are needed to determine whether DMPA use increases the risk of fracture, especially in women who begin using DMPA during adolescence. Currently, DMPA use is not the method of choice during adolescence. If no other methods are available, preventing the risks associated with unwanted pregnancy at a young age outweigh the theoretical risk of fracture later in life.


Ref 2: In this large study the continuation rate ranged from 24% to 59%. More recent studies report lower continuation rates: from 26% to 53% at 1 year, with the most frequent reason for discontinuation relating to a lack of adequate user education regarding bleeding disturbances including amenorrhoea. Counselling about the expected hormonal effects could improve the DMPA continuation rate.

Ref 1: In rural Mexico, 175 women who received detailed, structured counselling were compared with 175 women who received routine counselling: the cumulative life table discontinuation rate was 8% for women who received structured counselling vs 32% for those who received routine counselling.


* Recommendations are based on clinical experience.
DMPA: Myths

- Can stop monthly bleeding, but this is not harmful
  - Blood is not building up inside the woman
  - It is similar to not having menses during pregnancy
  - Usually not a sign of pregnancy
- Does not cause an abortion/disrupt an existing pregnancy
- Does not make women infertile

In conclusion, progestin-only injectables have characteristics that make them a desirable method for many women.
• They are safe.
• They are highly effective.
• They are easy to use correctly.
• They can be delivered in both clinical and non-clinical settings.

Appropriate counselling plays a key role in the provision of injectable contraceptives. While it is relatively simple to administer injectables correctly, providers also need to counsel patients about the characteristics of progestin-only injectable contraceptives, paying special attention to their side effects, and be able to manage side effects.