



Faculty of Sexual & Reproductive Healthcare
New Product Review from the Clinical Effectiveness Unit
Subcutaneous Depot Medroxyprogesterone Acetate
(Sayana Press®)

June 2013

Product Summary

Description

- Progestogen-only injectable contraceptive licensed for subcutaneous (SC) use.
- Contains 104mg of medroxyprogesterone acetate (MPA) in 0.65ml suspension.
- Bioequivalent to IM depot medroxyprogesterone acetate (IM DMPA, Depo-Provera®).
- Administered at intervals of 13 weeks +/- 7days

Mechanism of action

- Primary mechanism of action is to prevent ovulation.

Administration

- Via a new delivery system (Unijet™)
- The single dose pre-filled injector should be shaken vigorously to ensure a uniform suspension.
- The injector needs to be activated according to the manufacturer's instructions
- The needle should be pointing downwards and the medication should be injected, over 5-7 seconds, into the upper anterior thigh or the anterior abdomen.

Efficacy

- No pregnancies were reported in 16023 women cycle exposures

Safety and side effects

- No serious adverse events have been reported.
- Rates of loss of bone mineral density, amenorrhoea, weight gain and return to fertility similar to those seen with IM DMPA.
- Mild to moderate injection site reactions have been reported (redness, bruising, blistering, pruritis and skin changes including indurations, atrophy and scarring).

Benefits

- Sayana Press® may be preferable to IM DMPA in patients at risk of haematoma due to bleeding disorders or anticoagulation.
- Potential for self administration (outside product licence)

Storage

- Should be stored at room temperature

Cost

- £6.90

Background

Injectable progestogen-only contraception is a popular and effective method of contraception and until now, in the UK has largely been administered as Depo-Provera®, an intramuscular (IM) injection of 150mg medroxyprogesterone acetate (DMPA).

Sayana Press® (Pfizer Limited) is an injectable progestogen-only contraceptive newly launched onto the UK market. It is designed to administer medroxyprogesterone acetate (MPA) via the subcutaneous (SC) route. Sayana Press® contains 104 mg of MPA in 0.65ml suspension for injection. Although it contains less DMPA than Depo-Provera, pharmacokinetic studies show that the two products are bioequivalent. Sayana Press® will not replace IM DMPA but will give women more contraceptive options.

This review is intended to inform health professionals and is not a guidance document. It evaluates the available evidence and summarises the manufacturer's recommendations for use of SC DMPA.

FSRH guidance on this topic is currently being updated and will be published in 2013.

What is the mechanism of action for SC DMPA?

The main mechanism of action of SC DMPA is to inhibit the secretion of gonadotrophins, which in turn prevents follicular maturation and ovulation. ⁽¹⁾

SC DMPA has been shown to be effective in preventing pregnancy, with no pregnancies reported in 16023 women cycle exposures ⁽²⁾ and one randomised controlled trial reporting no pregnancies over three years of use ⁽³⁾.

The circulatory level of MPA required for contraceptive efficacy is consistently maintained in women with body mass indices >30kg/m². Therefore, no dose adjustment is required in obese women ^(2,5).

How should SC DMPA be used?

The Summary of Product Characteristics (SPC) ⁽¹⁾ states that if Sayana Press® is administered on day 1-5 of the cycle no additional contraceptive precautions are required. If administered at any other times in the cycle extra precautions should be used for 7 days. The SPC states that subsequent doses should be administered every 13 weeks +/- 7 days.

- Sayana Press® is supplied in a single-dose pre-filled injector which should be stored at room temperature. Prior to use it should be shaken vigorously to ensure a uniform suspension. The injector must be activated prior to use. It is activated by piercing an internal seal, which allows the medicine to come out of the needle when the injector's reservoir is squeezed (see manufacturer's instructions for more detailed information) ⁽¹⁾. To ensure that the full injection is given, the medication should be injected slowly over approximately 5-7 seconds with the needle pointing downwards, into the upper anterior thigh or the anterior abdomen, avoiding bony areas or the umbilicus. ⁽¹⁾

Although Sayana Press® is currently not licensed for self administration; studies have found that self administration of SC DMPA is feasible and acceptable to women ^(6,7,8). In one study the majority of women found the injection easy and convenient and were likely to

recommend self-injection to other women ⁽⁶⁾. Another study found that 80% of injections were given on time and no injections were given >14 weeks ⁽⁷⁾. In this study 46% of subjects agreed that subcutaneous injection was less painful than IM injection, 46% were unsure and 8% disagreed. In both studies 20% of self injections were met with difficulty, mainly due to resistance and device issues. Both studies showed similar continuation rates of self-administration at 12 months (74% (95% CI 62-86%) and 88%).

Are there any side effects or safety issues?

No serious adverse events have been reported.

Changes in bone mineral density (BMD) were studied in a randomised trial comparing SC DMPA to IM DMPA ⁽³⁾. By the end of the second year, 28.3% and 37.7% of SC DMPA users had a $\geq 5\%$ decrease in bone mineral density from the baseline in their total hip and lumbar spine respectively. Overall no significant differences in loss of bone mineral density were seen between the SC and IM groups⁽³⁾. Advice in relation to bone health is as per current guidance⁽⁹⁾.

As with IM DMPA, the incidence of irregular bleeding in SC DMPA users decreases over a 12 month treatment period whilst the incidence of amenorrhoea increases with the majority being amenorrhoeic by month 12 ⁽¹⁰⁾.

Changes in weight have been studied. In two non-comparative trials the mean weight changes at 12 months of SC DMPA use were 1.7kg (± 4.5 SD) (Americas trial) and 1.4kg (± 3.6 SD) (European/Asia trial) ^(2, 11). A study comparing SC DMPA and IM DMPA showed similar changes in weight at 36 months between the groups (4.5 \pm 8.5kg and 5.8 \pm 8.7kg respectively) ⁽³⁾. Although increases in weight were seen in these studies there were large individual variations with some women losing and some gaining considerable weight. No significant differences in weight gain were seen between baseline BMI subgroups in these studies.

Of women who received one SC injection of MPA, 97.4% (38/39) had return of ovulation by 12 months, with the median time of return to ovulation being 30 weeks ⁽⁴⁾. As with IM DMPA, women should be advised about the potential delay in return to fertility.

Injection site reactions with SC DMPA have been reported ^(2,3,6,7) and appear to be more common than in IM users ⁽³⁾. SC injection site reaction rates ranged from 1.6% - 21% in these studies and included injection site redness, pain, pruritis, bruising and blistering ^(2,3,6,7). These reactions were generally thought to be mild to moderate. In one study mild SC injection site skin changes, including indurations, scarring and atrophy, were seen in 9% of participants. ⁽⁷⁾

Are there any restrictions on use?

The UK Medical Eligibility Criteria for Contraceptive Use (UKMEC)⁽¹²⁾ is a set of agreed criteria for safe provision of contraception to men or women with a range of medical conditions. At the time of publication SC DMPA was not available in the UK. However, the CEU would recommend that the UKMEC classifications for IM DMPA are used for SC DMPA ⁽¹²⁾.

Are there any drug interactions?

No interaction studies have been undertaken with SC DMPA. As the clearance of medroxyprogesterone acetate is approximately equal to hepatic blood flow⁽¹⁾ it is unlikely that drugs that induce hepatic enzymes will significantly affect the kinetics of DMPA. Studies with IM DMPA support this theory⁽¹³⁾. The SPC for Sayana Press® indicates that no drug interactions would be expected and no dose adjustment would be required in patients taking liver enzyme-inducing drugs⁽¹⁾.

Cost

The unit price of Sayana Press for the NHS will be £6.90. The price for Depo-Provera is £6.01. (Personal communication with Pfizer 11/03/2013).

What does SC DMPA add to the range of contraceptives already available?

Patient satisfaction with SC DMPA is similar to that of IM DMPA users^(3,8). Self administration of SC DMPA may be an option, although it is not licensed for such use. Subcutaneous administration may be less likely to cause haematoma than IM injection in patients who are on anticoagulant therapy or have a bleeding disorder⁽¹²⁾. There may be advantages of subcutaneous administration in very obese women for whom there is concern about IM DMPA reaching muscle.

Acknowledgement

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