Sayana Press: first LARC for subcutaneous administration

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Sayana Press is the first long-acting reversible contraceptive given by sc injection. In our New products review, Steve Chaplin presents the clinical data relating to its efficacy and adverse effects and Dr Gbolade discusses its place in contraception.

KEY POINTS

- Sayana Press is long-acting reversible contraceptive containing medroxyprogesterone acetate 104mg
- It is administered by sc injection once every 13 weeks; a single injection costs £6.90
- It is as effective as im medroxyprogesterone acetate 150mg (Depo-Provera) and is associated with similar adverse effects, notably reversible loss of bone mineral density and weight change
- After discontinuation, ovulation returns after a median of 30 weeks but may take 1 year
- There is potential for self-injection by patients and provision by a wider range of health professionals

NICE guidance on long-acting reversible contraception recommends that women should be offered a choice of methods.1 These include intrauterine devices, intrauterine progestogen-only systems and injectable preparations.

The available injectable progestogens are the etonogestrel implant (Nexplanon, which lasts for three years), a single im injection of norethisterone enantate (Noristerat, eight weeks) and 12-weekly im injections of 150mg medroxyprogesterone acetate (MPA; Depo-Provera).

Sayana Press

Sayana Press (Pfizer) is a long-acting reversible contraceptive containing MPA and formulated for sc injection into the anterior thigh or abdomen. The dose of 104mg provides contraception for 13 weeks and repeated doses should be given within seven days of this time.

No dose adjustment is required in women with renal impairment but, because MPA is cleared by hepatic metabolism, it is contraindicated in severe hepatic impairment. Other contraindications include metabolic bone disease, active thromboembolic disease and current or past cerebrovascular disease.

The risk of drug interactions is not known; MPA is not affected by enzyme-inducing drugs.

Clinical trials

In two nonrandomised noncomparative trials a total of 1787 women used Sayana Press for one year (total exposure 16 023 woman-cycles). The cumulative pregnancy rate at one year (the primary end-point) was nil, giving a Pearl Index (pregnancies per 100 woman-years of use) of 0. The trials included women with weights ranging from 35 to 165kg (mean body mass index, BMI 23–25kg/m²); the authors concluded that no dose adjustment is necessary for body weight.

In an investigator-blind trial, 535 women were randomised to use Sayana Press or Depo-Provera. The cumulative pregnancy rate at two years was 0 with Sayana Press (Pearl Index 0) and 0.75 per cent with Depo-Provera (Pearl Index 0.35). Women were offered the option of continuing contraception for a further year, during which there were no more pregnancies. Both groups of women expressed satisfaction with the method of contraception they used, with no differences between them.

Adverse effects

The nature and frequency of adverse effects associated with Sayana Press are
similar to those with Depo-Provera, except that injection-site reactions are more common (8.0 vs 0.4 per cent in one trial).

Almost all women have bleeding or spotting initially but this decreases to 40–50 per cent after six months. Amenorrhea develops in 50–60 per cent of women after six months.

Sayana Press is associated with reversible loss of bone mineral density (BMD) in the spine, hip and femoral neck of 3–4 per cent after two years’ use. In one trial, reversible loss of BMD was similar to that observed with Depo-Provera.

It may take up to one year for ovulation to return after discontinuation (median 30 weeks).

Weight change was common during use but did not affect women equally. In trials lasting one year, half of women remained within 2.2kg of their initial body weight, 12 per cent lost >2.2kg and 38 per cent gained >2.3kg. In one trial, weight gain was lower, but not significantly so, than with Depo-Provera after three years’ use (mean 4.5 vs 5.8kg).

The tolerability/side-effect profile
No serious adverse events have been reported. Bleeding patterns are similar between users of Sayana Press and Depo-Provera, with over 70 per cent of Sayana Press users experiencing spotting and/or bleeding within the first three months of use, and over 60 per cent becoming amenorrhoeic after a year.

BMD loss at the hip and spine in users of Sayana Press and Depo-Provera were similar at the end of two years and were reversible on discontinuation.

Weight changes were also similar in both groups with mean weight gain less than 2kg at the end of one year and median weight gain of 3.5kg after two years.

Injection-site reactions, including bruising, redness, blistering, pain and pruritus, seem more common in users of Sayana Press than those of Depo-Provera, ranging from 1.6 to 21 per cent.

What is its potential place in management?
Sayana Press opens up the possibility for self-injection and for a wider range of healthcare professionals, including community pharmacists, to provide injectable contraception closer to patients’ homes.

There is also the potential for its use by patients who are on anticoagulant therapy, have a bleeding disorder or are very obese with fewer concerns compared with use of Depo-Provera. Self-administration is attractive as it would decrease costs both for the patients and the NHS, and hopefully enhance the uptake and continuation rates of long-acting reversible contraceptives with the potential for a positive impact on unplanned pregnancies.

References

Declaration of interests
None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics.

Place in therapy
Sayana Press is the first long-acting reversible contraceptive injection designed and licensed for sc administration. It contains MPA 104mg in 0.65ml suspension for administration at intervals of 13 weeks +/- seven days.

The need for a new contraceptive option
Hormonal contraceptive development since the advent of the combined oral contraceptive pill just over half a century ago has focussed on progressively decreasing the steroidal content and seeking alternate routes of delivery, with the goals of providing high contraceptive efficacy while utilising the minimum effective hormonal dose and minimising side-effects. The introduction of Sayana Press marks a significant step on this journey.

It provides a slower rate of absorption relative to the im-administered Depo-Provera. This allows for lower peak serum MPA concentrations and a long duration of effect but with serum MPA levels still remaining above the threshold for inhibition of ovulation. The median time to return of ovulation after cessation of use is 30 weeks; by the end of one year after discontinuation, ovulation would have resumed in 97 per cent.

Efficacy data
No pregnancies were reported in two large phase 3 clinical trials involving 1787 women with a total of 16 023 woman-cycles of exposure to Sayana Press, giving a Pearl Index of 0. Significantly, about 33 per cent of all study participants were overweight or obese and more recent studies confirm that, in such women, MPA levels are maintained above the level required for suppression of ovulation.

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