Sayana Press (DMPA-SC in Uniject) Clinical Brief

BACKGROUND

Sayana® Press is a new formulation and presentation of the injectable contraceptive Depo-Provera®, manufactured and patented by Pfizer Inc. Administered through subcutaneous injection, Sayana Press contains 30% less depot medroxyprogesterone acetate (DMPA) than the intramuscular presentation of Depo-Provera (generic: DMPA-IM). Studies have found that the contraceptive efficacy and safety profile of Sayana Press (DMPA-SC in the Uniject™ injection system) are equivalent to those of DMPA-IM. Sayana Press is indicated for the prevention of pregnancy in women of childbearing potential.

Sayana Press is presented in the Uniject injection system, an autodisable injection device, prefilled with 104 mg/0.65 mL* medroxyprogesterone acetate (MPA, the active ingredient, a synthetic form of the natural hormone progesterone) sterile aqueous suspension.[1,2]

In addition to providing three months of effective contraception, Sayana Press shares other characteristics of DMPA-IM, including:

- Rapid onset of effect: No backup contraceptive method is required during the first cycle of use.
- High efficacy: It is not compromised by body mass index (BMI).
- Convenient administration: It is easy to use.
- Discreet administration: Women can use it without telling their partners or families.
- Safety: It can be used by women for whom contraceptive use of estrogen is inappropriate or contraindicated.[3]

HOW IT WORKS

When Sayana Press is administered to a woman every three months, it inhibits the secretion of gonadotropins, preventing follicular maturation and ovulation and causing endometrial thinning. Because MPA is absorbed more slowly when administered subcutaneously, the 30% lower dose in Sayana Press allows for a lower peak MPA concentration and above-minimum serum MPA levels, compared with DMPA-IM, for suppressed ovulation over a three-month period.[4]

EFFICACY

Studies have demonstrated that the efficacy, safety, and immediacy of contraceptive effect of Sayana Press are equivalent to DMPA-IM. Clinical studies indicate that the product effectively suppresses ovulation for at least 13 weeks regardless of race, ethnicity, or BMI:

- In a randomized, evaluator-blinded study comparing efficacy, safety, and acceptability of subcutaneous DMPA with DMPA-IM over two years with an optional third year among 225 women in Brazil, Canada, and the United States, subcutaneous DMPA was well tolerated and provided comparable contraceptive efficacy and bone mineral density outcomes to those of DMPA-IM.[3]
- No pregnancies were reported in two large, open-label, Phase 3 studies that assessed one-year contraceptive efficacy, safety, and patient satisfaction for subcutaneous DMPA.[2] The studies—one in North and South America and the other in Europe and Asia—included 16,023 women-cycles of exposure to subcutaneous DMPA. Many of the women were overweight or obese.
- In a randomized, prospective, evaluator-blinded, single-center trial conducted in Los Angeles, California, with 20 African American and 38 Caucasian women, subcutaneous DMPA demonstrated the same contraceptive efficacy, pharmacokinetics, and pharmacodynamics over 12 months as DMPA-IM, regardless of women's race and BMI.[5]
- In a single-center, single-dose, open-label subcutaneous DMPA trial conducted in Singapore with 24 Asian women of five ethnic groups, ovulation suppression was maintained for at least 91 days regardless of ethnicity or injection site. The pharmacokinetic parameters for MPA in these Asian women were similar to those previously reported in Caucasian women.[6]
- The combined results of the Singapore and Los Angeles trials show no difference in suppression of ovulation with subcutaneous DMPA regardless of ethnicity or injection site.[1]

ADMINISTRATION AND DOSAGE

Sayana Press is administered once every three months (12 to 14 weeks). It is labeled for subcutaneous injection into the anterior thigh or abdomen, and recent research demonstrates that it is also effective when injected into the

Depo-Provera (DMPA-IM) contains 150 mg/mL depot medroxyprogesterone acetate. The dose is 1 mL.

back of the upper arm.[7] Sayana Press is not formulated for intramuscular injection. The dosage does not need to be adjusted for body weight.[2]

CONTRAINDICATIONS AND SIDE EFFECTS

Sayana Press is expected to have tolerability comparable to or better than the DMPA-IM formulation.[4] Based on a systematic review of the evidence, the World Health Organization's (WHO) *Medical eligibility for contraceptive use* (MEC) confirms that Sayana Press and DMPA-IM (Depo-Provera) have a similar safety profile.[8] Contraindications are identical to those for DMPA-IM.

Common side effects for both Sayana Press and DMPA-IM include: headaches; bleeding irregularities (including amenorrhea, irregular spotting or bleeding, prolonged spotting or bleeding, and heavy bleeding—irregular bleeding typically decreases over time, and amenorrhea becomes more common); increased weight; and injection-site reactions—typically mild injection-site pain, granuloma, or atrophy.

No hormonal contraceptive method protects against HIV; therefore, all couples at risk of HIV should use male or female condoms consistently and correctly. While some studies suggest that women using DMPA-IM may be at increased risk of HIV acquisition, other studies do not show this association. In March 2017, use of DMPA injectable products *among women at high risk of HIV* changed from category 1 to category 2 in WHO's MEC. This means that, for women at high risk of HIV, the advantages of using DMPA products generally outweigh the theoretical or proven risk.† The MEC offers clarifications on what information and resources should be provided to women at high risk of HIV acquisition.[8,9,10]

Currently, there are no epidemiological data available on a possible association between the lower-dose, subcutaneous formulation of DMPA and risk of HIV acquisition. In the absence of such data, researchers are reviewing and summarizing relevant data on subcutaneous DMPA (forthcoming).

Use of DMPA-IM and Sayana Press is associated with decreased bone mineral density (BMD). Most studies have found that women lose BMD while using DMPA, but regain all or partial BMD after discontinuation. It is not known whether DMPA use among adolescents affects peak bone mass levels or whether adult women with a long duration of DMPA use can regain BMD to baseline levels before menopause. The relationship between DMPA-associated changes in BMD during the reproductive years and future fracture risk is unknown. According to WHO, for women aged 18 to 45 years, there should be no restrictions on the use of DMPA, including no restrictions on the duration of its use; and the advantages for adolescents younger than 18 years of using DMPA generally outweigh the theoretical or proven risks.[8,11]

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† Category 1 of the MEC means that no restrictions are placed on the use of a contraceptive method for a specific condition (e.g., high risk of HIV).

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