Frequently Asked Questions About Sayana® Press

Sayana Press pilot introduction

WHAT IS SAYANA PRESS?

Sayana Press is a lower-dose formulation and presentation of the popular contraceptive, Depo-Provera®, manufactured by Pfizer, Inc. Sayana Press provides three months of contraceptive protection per dose. It is delivered in the Uniject™ injection system, a small prefilled autodisable device. It contains 104 mg of depot medroxyprogesterone acetate (DMPA) per 0.65 mL dose and is administered via subcutaneous (SC) injection.

Further product information is available in the sections below.

WHY IS FAMILY PLANNING IMPORTANT?

An estimated 222 million women and girls worldwide want to prevent unintended pregnancy but are not using modern contraception.¹² Many lack accurate information about family planning methods or may face objections from their partners about using contraception. Those who are poor or who live in hard-to-reach places face particular challenges, without easy access to clinics or health care providers offering contraceptive options. Women worldwide have expressed the need for a contraceptive method that can be easily administered in low-resource, non-clinic settings.¹²

Access to modern contraception improves health and can save lives. About one in three maternal deaths could be avoided by delaying motherhood, spacing births, preventing unintended pregnancies, and avoiding unsafely performed abortions.²⁻⁴

Women’s health improves when they can optimally space and time their births.¹² Healthier mothers mean healthier children and improved child survival. Families can better care for and educate those children, and communities benefit when women can participate in broader economic and community activities.

HOW CAN SAYANA PRESS INCREASE ACCESS TO FAMILY PLANNING?

Injectable contraceptives are among the world’s most popular family planning options.⁵ They are safe, effective, and discreet, but until now, they have not been widely available outside clinic settings. Women in rural and remote communities often must travel long distances to reach clinics that offer injectable contraceptives.

Sayana® Press has the potential to give more women access to this family planning method through health facilities and providers based closer to where women live. It provides three months of safe, effective pregnancy prevention with a single injection. It is easy to transport, and easy to use with minimal training—ideal for community-based health workers and potentially for women themselves to administer.

Increasing the range of family planning options available to women and girls also makes it easier for them to find an approach that best meets their needs.

Sayana, Sayana Press, and Depo-Provera are registered trademarks of Pfizer, Inc. Uniject is a trademark of BD.
WHAT IS THE SAYANA PRESS PILOT INTRODUCTION PROJECT?
PATH is coordinating an innovative public-private partnership to introduce Sayana Press, as part of a global effort to reach more women and girls in low-resource settings with family planning services. Five countries in Africa and South Asia (Bangladesh, Burkina Faso, Niger, Senegal, and Uganda) are introducing Sayana Press in 2014, and their experiences will help inform global decision-making on whether and how to include Sayana Press in family planning programs.

WHEN WILL WOMEN HAVE ACCESS TO SAYANA PRESS?
Women in the five project countries will have access to Sayana Press as pilot product introductions begin in 2014. The project activities will continue through 2016. Ministries of health, PATH, and key partners will systematically collect data from the pilot introduction experiences, including the number of doses administered and the percentage of Sayana Press users who are new to modern family planning.

WHAT IS PFIZER’S ROLE IN THE PROJECT?
Pfizer, Inc. is the product manufacturer. The product price for the pilot introduction project was negotiated between the project donors and Pfizer.

WHY IS SAYANA PRESS BEING INTRODUCED IN AFRICA AND SOUTH ASIA?
Sayana Press pilot introduction countries were primarily identified based on ministry of health interest, support, and engagement in the initiative. Other factors in the country selection process included each country’s contraceptive and family planning goals and their interest in Sayana Press as a method that could help meet their needs.

Self-injection of Sayana Press

WHAT DO WE KNOW ABOUT SELF-INJECTION OF SAYANA PRESS?
Qualitative research suggests that self-injection of Sayana Press is both feasible and acceptable among many women.6–8 Research indicates that women are capable of successfully self-administering injectable contraception via the Uniject system.9 Women can also self-inject Sayana®, which is the same formulation as Sayana Press, but in a glass prefilled syringe.10–12 Findings also suggest that many women would prefer to self-administer.7,8,10–12

Research is still needed to assess operational feasibility of home and self-injection of Sayana Press in low-resource settings, including considerations for implementing a sustainable home-based delivery program. PATH plans to work closely with ministries of health in Senegal and Uganda to build the evidence base on the program parameters required to support self-injection, as well as its impact and cost-effectiveness. This research will help determine the training requirements and programmatic design that will optimize women's ability to manage self-injection. PATH will also assess whether self-injection of Sayana Press contributes to longer contraceptive continuation and is cost-effective (relative to the provider-administered DMPA intramuscular formulation [IM]) to inform country and global decisions regarding introduction and scale-up of this delivery mode.

IS SAYANA PRESS BEING USED FOR HOME AND SELF-INJECTION?
Sayana Press is not currently labeled for self-injection.

Sayana Press registration, cost, and shelf life

WHERE IS SAYANA PRESS REGISTERED?
Pfizer registered depo-subQ provera 104™, the same drug in Sayana Press, with the US Food and Drug Administration (FDA) in 2004. Sayana and Sayana Press are also registered with the UK Medicines and Healthcare Products Regulatory Agency (MHRA). Sayana Press is registered in a number of countries in other parts of the world, including all pilot introduction countries.*

*Sayana Press was approved in the European Union via procedure number UK/H/0960/002UK/H/0960/002. The UK was the Reference Member State. A Public Assessment Report is available at the Heads of Medicines Agency website and the MHRA webpage: http://www.mhra.gov.uk/home/groups/par/documents/websiteresources/con126147.pdf.
WILL PFIZER SEEK WORLD HEALTH ORGANIZATION PREQUALIFICATION FOR SAYANA PRESS?

Products that have attained approval from a globally recognized stringent regulatory authority are not typically required by procurement agencies to also secure World Health Organization (WHO) prequalification. Pfizer is unlikely to seek WHO prequalification because the drug contained in Sayana Press has been approved by the FDA and regulatory authorities in Europe.

WHAT IS THE PRICE OF SAYANA PRESS?

There is not currently a published price for Sayana Press. As with most medicines, price depends on current and anticipated demand and purchase volumes. Experience with early Sayana Press pilot introductions will help provide ministries of health and partners with more information about the potential benefits and value of the product.

Sayana Press units for the pilot introduction and evaluation project are being purchased with funds from the Bill & Melinda Gates Foundation, the UK Department for International Development, and the US Agency for International Development.

WHAT IS THE STABILITY AND SHELF LIFE OF SAYANA PRESS?

The product has a three-year shelf life from the date of production, when unopened. Once opened, the product should be used immediately or discarded.

WHAT ARE THE TEMPERATURE REQUIREMENTS FOR TRANSPORT AND STORAGE OF SAYANA PRESS?

Sayana Press is stable at most room temperatures. The recommended storage temperature for Sayana Press is between 15°C and 30°C (59°F and 86°F). The recommended storage temperature for DMPA IM is between 20°C and 25°C (68°F and 77°F). It should not be frozen, refrigerated, or exposed to extreme heat.

Clinical product information

IS SAYANA PRESS AS EFFECTIVE AS DMPA IM FOR CONTRACEPTIVE PROTECTION?

Studies demonstrate that Sayana Press, manufactured and patented by Pfizer, Inc., provides efficacy, safety, and immediacy of contraceptive effect equivalent to the IM presentation of DMPA, registered by Pfizer as Depo-Provera. Sayana Press is a single-dose presentation of the SC formulation of the drug, consisting of 104 mg/0.65 mL DMPA in the Uniject™ injection system. This drug is also available in a single-dose, prefilled glass syringe, registered by Pfizer as Sayana.†

In clinical trials, Sayana effectively suppressed ovulation for at least three months in all subjects regardless of ethnicity, race, and body mass index. In three multinational clinical studies conducted in North and South America, Europe, and Asia, no pregnancies were detected among 2,042 women using the injectable contraceptive for up to one year.13,14

WHAT IS THE DIFFERENCE BETWEEN SAYANA PRESS AND DMPA IM?

A key advantage of Sayana Press is its availability in the Uniject injection system, which provides ease of administration and the potential to benefit system-level logistics in terms of storage, transport, and distribution.15 The Sayana Press formulation is expected to have comparable (if not improved) tolerability to the IM formulation, as it requires a 30 percent lower total dose and side effects are generally dose-dependent.

WHAT IS THE DIFFERENCE BETWEEN INTRAMUSCULAR AND SUBCUTANEOUS INJECTION?

IM injections are given deep into the muscles, whereas SC injections pierce the epidermal and dermal layers of the skin and deliver the drug into the loose subcutaneous tissue. Following SC injection, the drug enters capillaries by diffusion or filtration.16 Because of the distance between the surface of the skin and the muscle, DMPA IM administration requires a

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†Both Sayana and Sayana Press contain 104 mg/0.65 mL DMPA, and are administered by subcutaneous injection; the dose is 0.65 mL. Depo-Provera is 150 mg/mL DMPA and is administered by intramuscular injection; the dose is 1 mL.
longer needle that is 1.5 inches in length. DMPA SC injections use needles that are 3/8 inches in length. Advantages of SC injections include:

- Improved safety profile—because larger blood vessels are located deeper, SC injections are less likely than IM injections to pierce a blood vessel.
- Ease of administration—there is more surface area available for SC injections and they require fewer landmarks compared with IM injections; SC injections are administered with shorter needles.

HAS DMPA SC BEEN SHOWN TO PROVIDE CONTRACEPTIVE EFFICACY IN DIFFERENT RACIAL/ETHNIC GROUPS?
Yes. Studies of DMPA SC conducted in North and South America, Europe, and Asia demonstrated equal contraceptive effectiveness across races and ethnicities. Sayana and Sayana Press contain the same dose of DMPA SC used in these studies and are expected to perform identically.

WHAT ARE THE MOST COMMON SIDE EFFECTS OF SAYANA PRESS?
The Sayana Press formulation contains a lower dose of the active ingredient (104 mg/0.65 mL DMPA) than Depo-Provera (150 mg/mL DMPA) formulation administered intramuscularly. 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 may become more common.
- Weight gain.
- Injection-site reactions—typically mild injection-site pain, inflammation, or atrophy.

WHAT IS THE RELATIONSHIP BETWEEN HORMONAL CONTRACEPTION USE AND WOMEN’S RISK FOR CONTRACTING HIV?
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 progestin-only injectable contraception may be at increased risk of HIV acquisition, other studies do not show this association. A WHO expert group reviewed all available evidence and agreed that the data were not sufficiently conclusive to change current medical eligibility guidance, which states that women at risk of HIV may safely use progestin-only injectables. However, due to the inconclusive nature of existing evidence on possible increased risk of HIV acquisition, women using progestin-only injectable contraception should be strongly advised to also always use condoms, male or female, and other HIV preventive measures.

DOES SAYANA PRESS AFFECT BONE MINERAL DENSITY?
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 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, the advantages for adolescents under age 18 of using DMPA generally outweigh the theoretical or proven risks.

DOES BODY MASS INDEX AFFECT THE EFFICACY OF DMPA SC?
No. Clinical studies to date demonstrate that the contraceptive efficacy of the active ingredient in Sayana Press is not affected by body mass index (weight-to-height ratio).

IN WHICH PARTS OF THE BODY CAN SAYANA PRESS BE INJECTED?
Pfizer’s current package insert for Sayana Press labels the product for injection in the abdomen or thigh. Research conducted in 2012 indicates that administration through injection in the back of the upper arm provides sufficient medroxyprogesterone acetate levels for contraceptive protection for three months (13 weeks) plus at least a two-week window for reinjection.

CAN A WOMAN SWITCH BETWEEN DMPA IM AND SC?
Yes. Because the active ingredient in the IM and SC formulations is identical, it is safe to switch back and forth between these two formulations on a regular dosing schedule (i.e., every three months) with the same level of contraceptive protection. Sayana Press is expected to perform identically to other presentations of DMPA SC.
WHERE HAVE CLINICAL TRIALS BEEN CONDUCTED?

Clinical trials of Sayana have been conducted in North and South America (Brazil, Canada, Chile, Mexico, Peru, and the United States); Europe (Bulgaria, Estonia, Latvia, Lithuania, Norway, Poland, Romania, Russia, and the United Kingdom); and Asia (Indonesia, Pakistan, and Russia). Pharmacokinetics studies were conducted in Los Angeles, California (including Caucasian and African American participants), and Singapore (including a diverse group of Asian participants).

WHAT WILL HAPPEN IF SAYANA PRESS IS ADMINISTERED INTRAMUSCULARLY?

To ensure three months of contraceptive protection, Sayana Press must be administered subcutaneously rather than intramuscularly. The short needle (3/8 inches) used with Sayana Press minimizes the likelihood of inadvertent intramuscular injection.

SAYANA PRESS AND CONTRACEPTIVE IMPLANTS BOTH CONTAIN PROGESTIN. HOW ARE THEY DIFFERENT AND WHAT ARE THE IMPLICATIONS OF THE DIFFERENCES?

While Sayana Press is delivered via a subcutaneous injection every three months, contraceptive implants are small flexible rods or capsules that are placed under the skin of the upper arm through a minor surgical procedure. Like Sayana Press, implants are estrogen-free and contain a progestin hormone (like the natural hormone progesterone) to thicken cervical mucus and disrupt the menstrual cycle. However, progestin is released from implants very slowly providing pregnancy protection for three to five years, depending on the type of implant. Implants are very effective, with less than 1 pregnancy per 100 women using implants over the first year. Potential implant side effects are similar to those associated with Sayana Press, including menstrual bleeding changes, headaches, abdominal pain, or breast tenderness.

Some women may prefer the convenience of implants for longer-term protection, but implants must be inserted and removed by a trained provider—making it important for providers and facilities to be accessible to clients. Sayana Press can offer women more control over when to initiate or stop their contraception because it is designed for use by health workers at lower levels in the health care system (who are often more accessible to clients) or, potentially, by women themselves.

The Uniject injection system

WHAT IS UNIJECT?

Uniject is a prefilled autodisable injection device that was developed to meet challenges of widespread distribution of vaccines and other medications in low-resource settings.

WHAT ARE THE KEY BENEFITS OF UNIJECT FOR DELIVERING SAYANA PRESS?

- Easy to use: Can be used by health workers who do not normally give injections.
- Single dose: Minimizes wastage and facilitates outreach to individual patients.
- Prefilled: Eliminates the need to prepare a vial and syringe, is easy to inject, and simplifies procurement and logistics.
- All in one: Eliminates the need to bundle vials and syringes and prevents potential mismatches at the service delivery point.
- Nonreusable: Minimizes patient-to-patient transmission of bloodborne pathogens through needle reuse.
- Compact size: For easy transport, storage, and disposal.

WHERE AND HOW HAS UNIJECT BEEN USED IN THE PAST?

BD (Becton, Dickinson and Company) produces bulk empty Uniject devices and provides these to vaccine and pharmaceutical producers. Since 2000, more than 88 million Uniject devices have been used to administer injectable medicines throughout Africa, Asia, and Latin America. For example, Uniject is used throughout Indonesia to deliver hepatitis B vaccine to newborns.

Global injectable contraceptive use

HOW WIDELY USED ARE INJECTABLE CONTRACEPTIVES GLOBALLY?

Injectable contraceptives, in addition to implants, have been shown to be the most commonly used form of contraceptives in sub-Saharan Africa, South Central Asia, and Southeast Asia. Approximately 35 million women use injectable contraceptives worldwide.
Approximately 73 million doses of injectable contraceptives (all types) were ordered by global donors in 2012. Approximately 578 million doses were ordered between 2000 and 2012.33

**WHEN WAS DEPO-PROVERA APPROVED BY THE FDA FOR CONTRACEPTIVE USE?**

Depo-Provera (150 mg/mL of DMPA for intramuscular injection) has been registered in the United States since 1992.34 Depo-Provera has been prequalified by WHO since 2010 after being evaluated on a stringent set of criteria.35

**IN APPROXIMATELY HOW MANY COUNTRIES IS DEPO-PROVERA REGISTERED FOR CONTRACEPTIVE USE?**

Depo-Provera is registered in approximately 85 countries across several continents.36 Other injectables containing DMPA first became available in 1971, and are now registered in 179 countries.37

**REFERENCES**

17. Woods AD, Kabat AG. *Administration of pharmaceuticals by injection: General concepts and major parenteral routes for procedures*. n.d.


