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 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.

HOW CAN SAYANA PRESS INCREASE ACCESS TO FAMILY PLANNING?

Injectable contraceptives are among the world's most widely used family planning options.[1] They are safe, effective, and discreet, but until now, they have not been extensively 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 health workers 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 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.

WHERE HAS SAYANA PRESS BEEN INTRODUCED?

PATH, the United Nations Population Fund (UNFPA), and additional partners are coordinating pilot introductions led by the Ministries of Health of Burkina Faso, Niger, Senegal, and Uganda. The first Sayana Press introduction launched in Burkina Faso in July 2014. Since then, Sayana Press has been introduced in at least five additional countries (e.g., Bangladesh, Democratic Republic of Congo, and Nigeria) by a range of public- and private-sector organizations.

WHAT ARE THE RESULTS AND LESSONS LEARNED FROM THE FIRST INTRODUCTIONS?

With Ministry of Health (MOH) leadership, Sayana Press introductions have made injectable contraceptives a routine part of community-level health care for the first time in Burkina Faso, Niger, and Senegal, giving women convenient access in their own villages. In Uganda, the Sayana Press pilot introduction activities build on MOH commitment to expand community-based delivery of injectable contraceptives.

In order to track the progress of Sayana Press introduction in the first four countries, PATH works with MOHs and other partners to collect and report monitoring data and review early programmatic experience with Sayana Press to help understand results to date and synthesize lessons learned. For example:

- Introduction strategies (e.g., the number of health workers trained and how quickly they are trained, which delivery channels offer Sayana Press) drive volumes of doses administered and trends in consumption.
- Consumption may also be affected by other factors, including communication activities and stockouts.
- Sayana Press seems to appeal to and/or be accessible to young women in the four countries.
- Introduction strategies that prioritize more peripheral delivery channels (e.g., remote locations, community health workers) reach a higher percentage of new users of family planning than facility-based delivery.

To learn more about the potential effectiveness of Sayana Press administered by health workers, PATH is also conducting studies in Burkina Faso and Uganda to measure differences in contraceptive continuation among women who use Sayana Press and those who use intramuscular DMPA (DMPA IM). In other words, the studies will assess whether women who receive Sayana Press injections from health workers use the method for a longer period of time than women who receive DMPA IM injections from health workers. In the Burkina Faso study, women obtain their injectable contraceptives from clinic-based providers, and women in the Uganda study obtain the method from community-based health workers.

PATH will use the continuation data, as well as cost data, to compare the effectiveness and cost-effectiveness of Sayana Press and DMPA IM from different types of family planning health workers, whether community- or clinic-based. Those results are anticipated in 2017.

WHAT IS PFIZER'S ROLE IN THE PRODUCT INTRODUCTIONS?

Pfizer Inc. is the product manufacturer. The product price for the pilot introduction project was negotiated between the project donors and Pfizer. Pfizer is not directly involved in PATH-led Sayana Press activities.

WHY IS SAYANA PRESS BEING INTRODUCED IN AFRICA AND SOUTH ASIA?

Sayana Press pilot introduction countries were primarily identified based on MOH interest, support, and engagement in the initiative. Other factors in the country identification 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. Introductions of Sayana Press also aim to support the London Summit on Family Planning's (FP2020) coordinated effort to ensure that voluntary family planning services reach an additional 120 million women and girls in the world's poorest countries by 2020.[2]

Self-injection of Sayana Press

WHAT DO WE KNOW ABOUT SELF-INJECTION OF SAYANA PRESS?

Previous qualitative research suggests that self-injection of Sayana Press is both feasible and acceptable among many women.[3–5] Research from high-resource settings indicates that women are capable of successfully self-administering injectable contraception via the Uniject injection system.[6] Women can also self-inject Sayana®, which is the same formulation as Sayana Press, in a glass prefilled syringe.[7–9] Findings suggest that many women would prefer to self-administer.[4,5,7–9]

PATH is working closely with the governments of Senegal and Uganda to conduct research on self-injection of Sayana Press. At the end of 2015, early results from the first PATH-MOH self-injection study in Uganda are promising: most women can competently self-inject after they are trained to do so.

Results from the PATH-MOH studies will help inform potential program design to support women living in low-resource settings to self-inject Sayana Press safely and effectively, and to understand the potential impact of the practice.

WHAT HOME AND SELF-INJECTION RESEARCH STUDIES ARE CURRENTLY ONGOING?

PATH and MOH operational feasibility studies were designed to assess the feasibility of home and self-injection in settings like Senegal and Uganda, including considerations for implementing sustainable home-based delivery programs. The Uganda study was completed in December 2015, and the Senegal study will be completed in mid-2016.

Effectiveness and cost-effectiveness studies in Senegal and Uganda in 2016–2017 will assess whether women who self-inject with Sayana Press continue using injectable contraceptives longer than women who use DMPA IM administered by a provider. This information, along with the relative costs of these two approaches, will be analyzed to establish the effectiveness and cost-effectiveness of self-injected Sayana Press compared to provider-administered DMPA IM.

FHI 360, in collaboration with the Malawi MOH and the US Agency for International Development (USAID)/Malawi, through the Advancing Partners and Communities project, is conducting a one-year randomized clinical trial to assess whether adult women are able to self-inject Sayana Press every three months after enrollment. Results from the study are anticipated in early 2017.

DOES SAYANA PRESS HAVE REGULATORY APPROVAL FOR SELF-INJECTION?

In 2015, the UK Medicines & Healthcare products Regulatory Agency (MHRA) authorized Sayana Press for self-injection in the United Kingdom.[10] Pfizer has indicated that it will seek regulatory approval to add self-injection to the existing Sayana Press registrations in a number of additional countries, such as Burkina Faso, Senegal, and Uganda.

The World Health Organization (WHO) also recommends self-administration of Sayana Press "in contexts where mechanisms to provide the woman with appropriate information and training exist, referral linkages to a healthcare provider are strong, and where monitoring and follow-up can be ensured."[11]

Sayana Press registration, cost, and shelf life

WHERE IS SAYANA PRESS REGISTERED?

Sayana and Sayana Press are registered with the MHRA. Sayana Press is registered in a number of countries in other parts of the world, including all pilot introduction countries.* Pfizer also registered depo-subQ provera 104™, the same drug in Sayana Press, with the US Food and Drug Administration (FDA) in 2004.

WHAT IS THE PRICE OF SAYANA PRESS?

In November 2014, Pfizer Inc., the Bill & Melinda Gates Foundation, and the Children's Investment Fund Foundation agreed to a new public-private collaboration through which Sayana Press will be sold for US$1 per dose to qualified purchasers.[12] The agreement will help ensure that women in 69 of the world's poorest countries have access to this new contraceptive option at reduced or no cost.

Sayana Press units for the pilot introduction and research studies are being purchased with funds from donors including the Bill & Melinda Gates Foundation, the UK Department for International Development, and USAID.

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 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.

HAS SAYANA PRESS BEEN ENDORSED BY THE WORLD HEALTH ORGANIZATION?

WHO included Sayana Press in its fifth edition of the *Medical eligibility criteria for contraceptive use* (MEC).[13] The MEC provides guidance for health providers on which women and girls can use a particular family planning method. The product is referenced in the MEC as DMPA-SC, the non-branded name. Based on a systematic review of the evidence, the MEC confirms that Sayana Press and DMPA IM (Depo-Provera) have a similar safety profile.

Once a new product or method is included in the MEC, guidelines regarding its use can then be included in subsequent revisions to WHO's *Selected practice recommendations for contraceptive use* (SPRs). Revised SPRs that include Sayana Press/subQ MPA in Uniject are anticipated in 2016.

*Sayana Press was approved in the European Union via procedure number UK/H/0960/002UK/H/0960/002. The United Kingdom 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.

WHAT IS THE STABILITY AND SHELF LIFE OF SAYANA PRESS?

Sayana Press now has an approved five-year shelf life from the date of production, when unopened. The shelf life of Sayana Press units depends on when they were manufactured, as the shelf life was recently updated officially from three years to five years. If the shelf life is in question, refer to the product label. Once opened, the product should be immediately used 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). Sayana Press 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.[14,15]

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.[16] The Sayana Press formulation is expected to have comparable (if not improved) tolerability over 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 SC tissue. Following SC injection, the drug enters capillaries by diffusion or filtration.[17] Because of the distance between the surface of the skin and the muscle, DMPA IM administration requires a longer needle, 1.5 inches in length. DMPA SC injections use needles that are 3/8 inch in length.[18] 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.[19]
- 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.

LEXICON OF INJECTABLE DMPA PRODUCTS

MPA: Medroxyprogesterone acetate, the active contraceptive agent.

DMPA: Depot MPA. When injected intramuscularly or subcutaneously, MPA forms a reservoir or depot that releases the drug over time.

DMPA IM: Generic name for the intramuscular form of DMPA.

DMPA SC: Generic name for the subcutaneous form of DMPA.

Depo-Provera®: Pfizer Inc. brand of DMPA IM, available in vials or prefilled syringes.

Depo-subQ provera 104™: Pfizer brand of DMPA SC in prefilled syringes.

Sayana®: Pfizer Limited (UK) brand of DMPA SC in prefilled syringes, licensed in the United Kingdom and some other countries.

Sayana® Press: Pfizer Limited brand of DMPA SC in the Uniject injection system.

[†]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 contains 150 mg/mL DMPA and is administered by intramuscular injection; the dose is 1 mL.

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.[14,16,20–22] 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 the Depo-Provera formulation (150 mg/mL DMPA) 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 OF 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.[23,24]

In order to generate more evidence on this topic, the Evidence for Contraceptive Options and HIV Outcomes study is an open-label, randomized clinical trial that will compare three reversible methods of contraception to evaluate whether there is a link between use of any of these methods and increased risk of acquiring HIV infection.[25] Study results are expected in 2018.

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 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.[13,26]

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.[27]

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 for women 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).[20] Pharmacokinetics studies have been conducted in Los Angeles, California (including Caucasian and African American participants), and Singapore (including a diverse group of Asian participants).[21,22]

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 inch) used with Sayana Press minimizes the likelihood of inadvertent IM 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 SC 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, and breast tenderness.[28]

Some women may prefer the convenience of implants for longer-term protection, but implants must be inserted and removed by a trained health 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.[29]

The Uniject injection system

WHAT IS UNIJECT?

Uniject is a prefilled autodisable injection system that was developed to meet challenges of widespread distribution of vaccines and other medications in low-resource settings.[30,31]

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

WHY IS FAMILY PLANNING IMPORTANT?

An estimated 222 million women and girls worldwide want to prevent unintended pregnancy but are not using modern contraception.[32,33] 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.[32,33]

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.[33,34,35]

Women's health improves when they can optimally space and time their births.[32,33] 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 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.[1,35,36] Approximately 35 million women use injectable contraceptives worldwide.[37]

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.[38]

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

Depo-Provera (150 mg/mL of DMPA for IM injection) has been registered in the United States since 1992.[39] Depo-Provera has been prequalified by WHO since 2010 after being evaluated on a stringent set of criteria.[40]

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

Depo-Provera is registered in approximately 85 countries across several continents.[41] Other injectables containing DMPA first became available in 1971, and are now registered in 179 countries.[42]

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