A Study to Evaluate the Effectiveness, Pharmacokinetics, Safety, and Acceptability of Sayana® Press when Injected Every Four Months

FHI 360 Study Number 926400

Informed Consent Form Version 4.0, last revised 19 September 2018

NCT03154125

INFORMED CONSENT FORM

A Study to Evaluate the Effectiveness, Pharmacokinetics, Safety, and Acceptability of Sayana® Press when Injected Every Four Months

FHI 360 Study Number 926400

Study Investigator: [Site to insert]

Study Sponsor: FHI 360, 359 Blackwell St, Suite 200, Durham, NC USA 27701

Funded by: [Site to insert appropriate funder: USAID or The Bill & Melinda Gates Foundation]

Introduction

The purpose of this consent form is to give you information to help you decide if you want to participate in the research study named above. This consent form may contain some words that are not familiar to you. Please ask us to explain anything you do not understand. You will also have a chance to ask questions at the end. If you decide to participate, we will ask you to sign this form and give you a signed copy of this form.

Why are we doing this study?

We are doing this study to find out if Sayana® Press will prevent women from becoming pregnant when injected every 4 months instead of every 3 months as currently prescribed.

General information about the study

Sayana Press is a new, lower-dose form of the birth control shot Depo-Provera® (also known as DMPA). DMPA has been used for over 40 years by millions of women to prevent pregnancy in many countries, including Brazil, Chile and the Dominican Republic, where this study is being conducted.

DMPA is injected into the muscle with a long needle. Sayana Press is injected with a short needle under the skin (subcutaneously). Both DMPA and Sayana Press are injected every 3 months.

Both Sayana Press and DMPA release medroxyprogesterone acetate (MPA) into the bloodstream. When MPA is above a certain level, it prevents ovulation (i.e., when your ovaries produce an egg). We know from past studies that Sayana Press is safe and effective at preventing pregnancy when injected every 3 months. The same studies also showed that MPA may prevent ovulation for 4 months or longer.

Sayana Press is approved for use in many European and African countries. However, Sayana Press is not approved for use in the United States (U.S.), Brazil, Chile or the Dominican Republic (DR). Because Sayana Press is not approved for use in your country, it can only be given as part of research.

Approximately 750 healthy, sexually active women between the age of 18 and 35 years old will take part in this study. Women in this study will receive Sayana Press injections every 4 months and will stay in the study for 12 months. If you decide to participate in this study, you will be assigned by chance (like a lottery [or other equivalent local term, for example, throwing dice]), to receive the injection at either the abdomen, upper thigh, or upper arm. A computer will pick the injection site. This means neither you nor the study staff can choose where you receive the injection.

What will happen if you take part in this study?

If you decide to participate, you will be in the study for about 12 months after you receive your first injection. After today's visit, you will come to the clinic for the following visits:

- 1 enrollment visit
- 3 follow-up visits

Screening Visit

If you agree to be in the study today, we will:

- Explain study procedures
- Ask you to sign this informed consent form
- Ask questions to see if you can be in the study
- Get your contact information
- Schedule your enrollment visit. The visit will be scheduled during the first 5 days of your next menstrual period. If you are in the first 5 days of your menstrual period today, the enrollment visit may happen today (this does not apply if you also consent to participate in the Vaginal Immunity Study).

During today's visit, you may also be tested for infections passed through sex; given a breast exam, pelvic exam, and/or Pap smear, if the study doctor thinks you need it. The visit may last about **[site to insert]**.

Enrollment Visit (Day 0)

At the enrollment visit, we will:

- Ask you to provide a urine sample for a pregnancy test
- Measure your blood pressure, height and weight
- Ask you about any medical problems or new drugs you are taking
- Ask you about your sexual activity and condom use
- Ask you about your vaginal bleeding pattern
- Draw blood from your arm (about 1 teaspoon), which may be tested to find out if you already have MPA in your blood
- Assign you by chance to receive the Sayana Press injection in the abdomen, upper thigh, or upper arm
- Give you the injection where assigned
- Tell you when to return to the clinic for your next follow-up visit

The enrollment visit may last about **[site to insert]**.

Follow-Up Visits (Month 4, Month 8 and Month 12)

You will have 3 follow-up visits at 4 months, 8 months and 12 months after the enrollment visit, that will last about **[site to insert]**. At these visits, we will:

- Measure your blood pressure and weight
- Ask you about any medical problems or new drugs you are taking
- Ask you about your bleeding patterns and if you like the study method
- Ask you about your sexual activity and condom use since your last visit
- Give you the Sayana Press injection (Months 4 and 8 only)
- Tell you when to return to the clinic for your next follow-up visit

- *Months 4 and 12 only*: Ask you to provide a urine sample for a pregnancy test. We will only ask you to provide a urine sample for a pregnancy test at month 8 if you are more than 7 days late for the visit or if you think you may be pregnant

It may be necessary for you to make additional visit(s) if you think you may be pregnant, have any medical problems or if you are worried about your study participation.

Are there any possible risks to me?

Risks of Sayana Press

Sayana Press can cause side effects, although not everyone gets them. There is no way to stop the action of the drug once it is given to you. Possible side effects may include irregular bleeding or no bleeding, headache, dizziness, breast swelling, bloating, mood changes, decreased sexual desire, weight gain or vaginal discharge. Serious health problems related to Sayana Press are very rare.

Pregnancy

When Sayana Press is injected every three months, less than 1 out of 300 women get pregnant. We do not know how well Sayana Press will prevent pregnancy when injected every four months, that is why we are doing this study. You may become pregnant during the course of the study. We will test you for pregnancy during the study at the 4 and 12-month visit, if you have signs of pregnancy, or think you might be pregnant. If you become pregnant, we will draw blood from your arm (about 1 teaspoon) to test for MPA, the active drug in Sayana Press. You will continue as a participant in the study, however, you will no longer receive the injections and you will not need to come for follow-up visits. Instead we will call you to ask about your pregnancy outcome. Due to the long-acting nature of the drug, the drug may remain in your body for some time after you get pregnant. Importantly, if you become pregnant it is very unlikely that your baby will have any health problems. Many studies have found that babies who are exposed to DMPA while in the womb do not have a higher risk of birth defects or health problems.

You may not join this study if you are currently pregnant or wish to become pregnant in the next 18 months.

Injection Site Reactions

About 1 out of every 10 women who receive Sayana Press has a mild skin reaction at the place of the injection. This reaction may include pain or tenderness, lump or dimpling. Most of these reactions go away quickly. Some women may have a permanent thickening of the skin at the place of injection but this is very rare (less than 1 out of every 1000 women). If you have any problems, we will look carefully at the place of injection for possible reactions. If necessary, a photograph of the injection site will be taken to document the changes in the skin.

Menstrual Changes

Most women have some changes in their menstrual bleeding while using Sayana Press. These changes may include irregular bleeding, spotting or no bleeding at all (which is not dangerous to your health). Some women might also experience heavy bleeding during the first few months after the injection. If your bleeding was disrupted while using Sayana Press, it should be back to normal within 12 months after the last injection.

Weight Gain

Some women gain weight while using Sayana Press (about 1.6 kg in a year). It is possible that you will gain a small amount of weight from participating in this study.

Risk of HIV

Some studies have shown that risk of getting HIV may be higher among women using DMPA, but others did not show this link. We don't know for sure if the risk of getting HIV is increased among DMPA users. Recently, the World Health Organization (WHO) – a global group that coordinates international health information - stated that women who are at high risk of HIV can use DMPA but should be informed of the possible increased risk of HIV with DMPA use. Women who are not at high risk of HIV can use DMPA without restriction. No studies have assessed the relationship between Sayana Press and HIV, but we are providing you this information because DMPA and Sayana Press contain the same active ingredient.

Neither DMPA nor the Sayana Press injection directly cause HIV infection. The main ways that a person can reduce the risk of HIV and other sexually transmitted infections (STIs) are: to not have sex; to use condoms during sex; to not share IV drug needles; or to only have one sexual partner who does not have HIV.

Sayana Press does not protect you against STIs, including HIV. If you think you are at risk of HIV or you or your partner have HIV, you cannot join the study. During the study, if you feel you may be at risk of STIs and/or HIV, you should use condoms every time you have sex.

Return to fertility

Your usual level of fertility will return when the last injection has worn off. This time varies in different women. In most women, the effect will have worn off 5 to 6 months after the last injection. Although you may be able to get pregnant quickly, it is more likely to take a year or longer after your last injection before you get pregnant.". This is why you can only join the study if you do not want to get pregnant in the next 18 months.

Bone Mineral Density

Women who use Sayana Press tend to have lower bone mineral density than women of the same age who have never used it. The effects of Sayana Press are greatest in the first 2-3 years of use. Bone mineral density generally improves after Sayana Press is stopped. It is unlikely that 3 injections of Sayana Press you will receive as a part of this study will have any effect on your bones.

Other Risks

Potential Drug Interactions

There are some medicines (prescription and non-prescription) that may cause problems when taken with Sayana Press. We will carefully review all of the medicines you are taking before giving you Sayana Press. Please tell us before you take any new medicines while you are in the study. You may tell your other health care providers that you are participating in this study if you wish.

Risk from Blood Draw

You may feel slight discomfort or feel dizzy when blood is drawn from your arm. You may have a bruise or swelling at the site of the blood draw. You may get an infection at the site of blood draw, but this is very rare.

Are there any possible benefits to me?

There are no direct study benefits to you. If Sayana Press prevents pregnancy well when injected every 4 months, this information will be helpful to women who need long-acting birth control methods.

Confidentiality

We will do our best to prevent anyone outside the study from knowing about you and your part in this study, but there is always a chance that others may learn something about you during participation. All study files that list your name will be kept in a locked file. The information you give us will be sent to FHI 360 in North Carolina, USA. When it is sent, only a number will identify you, not your name. Your name will not appear on any study report.

FHI 360 staff working on the study may look at your records to monitor the study quality and progress. The study funder (USAID), ethics review committees and/or **[site to insert Regulatory Authority, if applicable]** may also review your records.

The study data will be shared with USAID and might be used for future research. However, the shared data will not contain any identifying information about you.

We may also request to review your medical records relating to any care you receive during the study, even if you receive this care at another clinic. We will keep all the information about you confidential, to the best of our ability.

If you agree to be in the study, we will ask you how you want us to contact you during the study. If you miss a scheduled visit, we may contact you by using only the methods you approved.

The study is registered on clinicaltrials.gov, a U.S. website listing clinical studies with human participants conducted around the world. Identifying information about you will not be included on this website.

Are there any costs to you if you join the study?

There will be no costs for you to participate in this study.

Will I receive compensation during the study?

We will pay to compensate for your time and travel as follows: **[site to insert visit specific amounts]**. We will pay you at the end of each visit. We will not pay you for visits that you do not attend. Participation in the study will not affect fees, payment, billing, or reimbursement for any other services at the clinic.

What will happen if you do not join the study?

Participation in this study is voluntary, you can decide if you want to be in this study or not. If you choose to join the study, you can change your mind at any time and leave the study. Your choices will not affect any care you receive now or in the future. We will tell you if we find any new information that could affect your choice to stay in the study.

Alternatives to Participation

You do not have to participate in the study in order to receive contraception. Other contraceptive options are available outside of the study.

What if you have a problem or have questions?

If you have any questions about this study, you can contact: **[site to insert]**

What if you get sick or have a health problem?

If you experience a health problem or think you may be pregnant at any time during the study, you should come to the clinic right away. You can also contact us by phone: **[site to insert contact information].**

If you are sick or have a health problem because of being in this research study, medical care will be available to you. This medical care that is required as a result of a health problem caused by your participation in the study, will be covered by **[site to insert]**, at no cost to you.

What if you become pregnant?

If you become pregnant during the study you will no longer receive the injection and you will not need to come for regular follow-up visits. However, you will remain in the study because we want to obtain information about your pregnancy and baby. Study staff will refer you to available medical care and other services you may need. The study does not pay for this care.

What are your rights as a participant?

This research was reviewed and approved by **[site to insert IRB information]** and the Protection of Human Subjects Committee at FHI 360. These committees review research studies in order to help protect participants. If you have any questions about how you are being treated by the research staff, or your rights as a research participant, you may contact: **[site to insert IRB contact information]**

New information about the study

We will tell you about any new information we learn during the study that may affect whether you want to continue to be in the study.

PARTICIPANT AGREEMENT Participant ID # _____

I have been told what will happen if I take part in the study titled, "A Study to Evaluate the Effectiveness, Pharmacokinetics, Safety, and Acceptability of Sayana® Press when Injected Every Four Months," including the risks and benefits.

I have had a chance to ask questions, and my questions were answered to my satisfaction. I have been told that the people listed in this form will answer any questions I have in the future. Study staff will give me a copy of this consent form. By signing below, I voluntarily agree to be in this research study.

_____ _____
Printed Name of participant Date (dd/MON/yyyy)

_____
Signature of participant

I have carefully explained to the volunteer the nature and purpose of this study. The participant has been given enough time to decide whether to participate or not. The volunteer has had a chance to ask questions and receive answers about this study. The participant has demonstrated appropriate understanding of the information provided.

_____
Printed Name of Person Who Obtained Consent

_____ _____
Signature of Person Who Obtained Consent Date (dd/MON/yyyy)

ADDENDUM INFORMED CONSENT FOR PARTICIPATION IN OPTIONAL VISITS AND PROCEDURES

A Study to Evaluate the Effectiveness, Pharmacokinetics, Safety, and Acceptability of Sayana® Press when Injected Every Four Months

FHI 360 Study Number 926400

We are asking 120 women participating in this study to provide a sample of blood (no more than 1 teaspoon) at each of their study follow-up visits to test for MPA, the active drug in Sayana Press. These women will also be asked to come to the clinic for 2 extra follow-up visits. This testing will help us understand how long MPA remains in the blood.

The extra visits and blood draws are optional procedures. You do not have to agree to the optional procedures to join this study.

Additional procedures

If you agree to participate in this part of the study, at the enrollment visit, we will:

- Test the blood that we draw from your arm to make sure that you don't already have MPA in your blood
- Randomly (like flipping a coin) assign you to receive the Sayana Press injection in the abdomen, upper thigh or in the upper arm.

During your Months 4, 8, and 12 follow-up visits, in addition to the other study procedures, we will:

- Draw blood from your arm for MPA testing

Additional Visits

You will come to the clinic for 2 additional follow-up visits at Months 2 and 3. At these visits, we will:

- Draw blood from your arm for MPA testing

Risk from Blood Draw

You may feel slight discomfort or feel dizzy when blood is drawn from your arm. No more than 5 cc of blood (approximately 1 teaspoon), will be drawn at each visit. You may have a bruise or swelling at the site of the blood draw. You may get an infection at the site of blood draw, but this is very rare.

Will I receive compensation for the optional visits and procedures?

We will pay to compensate for your time and travel as follows: **[site to insert visit specific amounts]**.

PARTICIPANT AGREEMENT FOR OPTIONAL VISITS AND PROCEDURES Participant ID # _____

I have been told that I do not have to agree to the optional procedures to join this study. I have had a chance to ask questions, and my questions were answered to my satisfaction. Study staff will give me a copy of this consent form. By signing below, I voluntarily agree to take part in the optional study visits and procedures.

_____ _____
Printed Name of participant Date (dd/MON/yyyy)

_____
Signature of participant

I have carefully explained to the volunteer the nature and purpose the optional study visits and procedures. The participant has been given enough time to decide if she wants to participate. The volunteer has had a chance to ask questions and receive answers about the optional procedures. The participant has demonstrated appropriate understanding of the information provided.

_____ _____
Printed Name of Person Who Obtained Consent Date (dd/MON/yyyy)

_____
Signature of Person Who Obtained Consent