

## EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

California law, under Health & Safety Code Section 24172, requires that any person asked to take part as a subject in research involving a medical experiment, or any person asked to consent to such participation on behalf of another, is entitled to receive the following list of rights written in a language in which the person is fluent. This list includes the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of the signed and dated written consent form as provided for by California law.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

\_\_\_\_\_  
Signature of Subject  
(or Subject's conservator, guardian or other  
representative as provided for by California law)

\_\_\_\_\_  
Date

STUDY: Ustekinumab Vs. Placebo for Radiographic Axial Spondyloarthritis  
PROTOCOL NO: CNTO1275AKS3002  
STERLING IRB ID: 5139C-019/Shibuya  
DATE OF IRB REVIEW: 11/11/15

## **PARTICIPANT INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE MEDICAL INFORMATION**

**STUDY TITLE:** A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Ustekinumab in the Treatment of Anti-TNF $\alpha$  Refractory Subjects With Active Radiographic Axial Spondyloarthritis

**PROTOCOL NO:** CNTO1275AKS3002

**STUDY DOCTOR:** Barry E Shibuya, MD

**STUDY SITE:** Fremont Rheumatology  
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**TELEPHONE:** 510-791-1300  
510-585-3055 (After office hours)

**SPONSOR:** Janssen Research & Development, LLC

### **Read this information carefully**

You are being asked to participate in a medical research study. Your participation in this research study is strictly voluntary, meaning that you may or may not choose to take part. To decide whether or not you want to be part of this research, the risks and possible benefits of the study are described in this form so that you can make an informed decision. This process is known as informed consent. This consent form describes the purpose, procedures, possible benefits and risks of the study. This form explains how your medical information will be used and who may see it. You may have a copy of this form to review at your leisure or to ask advice from others.

The study doctor or study staff will answer any questions you may have about this form or about the study. Please read this document carefully and do not hesitate to ask anything about this information. This form may contain words that you do not understand. Please ask the study doctor or study staff to explain the words or information that you do not understand. After reading the consent form, if you would like to participate, you will be asked to sign this form. You will be given a signed copy of your consent form to take home and keep for your records.

Doctor Shibuya is doing this study for Janssen Research & Development, LLC (the Sponsor).

An independent ethics committee, Sterling Institutional Review Board, has reviewed the study.

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## WHAT IS THE PURPOSE OF THE STUDY?

You are asked to volunteer to take part in a drug research study because you have active Radiographic Axial Spondyloarthritis.

Axial spondyloarthritis (or AxSpA) refers to an inflammatory disease, which affects mainly the spine and sacroiliac joints (a pair of joints connecting the spine to the pelvis). Radiographic Axial Spondyloarthritis is a later stage disease, also known as Ankylosing Spondylitis. The term “radiographic” means “visible on X-ray,” and this refers to changes or damage in the bones visible on X-ray.

This research study tests the safety and effectiveness of a drug, ustekinumab.

The purpose of this study is to see if ustekinumab is useful for treating research participants with Radiographic Axial Spondyloarthritis who have active symptoms despite standard treatments.

## HOW MANY PEOPLE WILL TAKE PART IN THE RESEARCH STUDY?

About 483 men and women at least 18 years of age will take part in this worldwide study.

## WHAT IS THE STUDY DRUG?

Ustekinumab has been approved by the Food and Drug Administration (FDA) for use in patients with the following conditions: moderate to severe Plaque Psoriasis and Psoriatic Arthritis. It is currently sold as STELARA<sup>®</sup>. Ustekinumab is not approved in any country to treat patients with Radiographic Axial Spondyloarthritis. Therefore, it is only available in a research study like this one.

If you have little or no improvement by Week 16 of the study, you will be offered to change from the study drug to a commercially available drug called golimumab (sold as SIMPONI<sup>®</sup>). Golimumab, given as a subcutaneous (under the skin) injection, has been approved by the U.S. Food and Drug Administration (FDA) and other regulatory authorities for the treatment of Rheumatoid Arthritis, Ankylosing Spondylitis (Radiographic Axial Spondyloarthritis), Psoriatic Arthritis, and Ulcerative Colitis.

## HOW LONG WILL I BE IN THIS STUDY AND WHAT CAN I EXPECT?

You will be in the study for about 72 weeks. The study is divided into 3 phases:

1. **Screening:** If you would like to be in this study, your study doctor will first check that you are eligible. This is called screening. Screening must be completed within 8 weeks before you get the study drug.
2. **Study Drug:** This period lasts for 52 weeks. During this time you will get the study drug as explained in the section “What happens if I agree to take part in this research study and am eligible?”

- **If you stop the study drug early (but agree to continue your participation in the study):**
  - **before** Week 24, you will return for all visits through Week 24.
  - **after** Week 24 and **before** Week 52, you will return for a follow-up visit at your earliest opportunity.
- 3. **Safety Follow-up:** You will return to the study clinic 12 weeks after your last dose of study drug to complete a follow-up visit.

Extra visits may be scheduled if needed.

### **WHAT ABOUT THE MEDICATION(S) I TAKE NOW FOR ACTIVE RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS?**

Some medications are not allowed during the study. Your study doctor will review your medications with you. He or she will let you know if any of them are not allowed during this study. Do not stop taking any of your current medicine unless your study doctor tells you to do so. Also, inform your study doctor about all prescription and over-the-counter drugs you take or before starting any new prescription medications. This includes anti-inflammatories, vitamins, herbs, and other kinds of therapies.

The use of some complementary therapies such as Chinese medicine, acupuncture, Ayurvedic medicine etc., is not allowed.

### **WHAT HAPPENS IF I AGREE TO TAKE PART IN THIS RESEARCH STUDY AND AM ELIGIBLE?**

Not everyone will get ustekinumab at the beginning of the study. If you are eligible to participate in the study, you will either receive ustekinumab or placebo by subcutaneous injection (under the skin). The placebo looks just like ustekinumab, and is given in the same way, but has no active drug in it.

There are 3 study drug groups during the first part of the study. You will be put into one of the 3 study drug groups: ustekinumab 45 mg, ustekinumab 90 mg, or placebo (until Week 24). The study drug group you will be assigned to will be decided by chance, like flipping a coin. You may receive either ustekinumab or placebo (inactive substance).

The chance that you will get ustekinumab 45 mg is 1 out of 3; the chance that you will get ustekinumab 90 mg is 1 out of 3; and the chance that you will get placebo is 1 out of 3. This means that 2 out of 3 people participating in this study will receive the study drug.

### **Early escape**

At Week 16, if repeatedly at Week 12 and Week 16 you have less than a 10% improvement in both back pain and morning stiffness, you will begin receiving golimumab 50 mg every 4 weeks through Week 52. You may begin self-administration at home of subcutaneous (under the skin)

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injection of golimumab 50 mg. This part of the study is "open label", meaning you and your study doctor and his/her staff will know what drug you are receiving.

Note: If you qualify for early escape, you will visit the site less frequently and you will undergo fewer procedures and less blood will be drawn.

At Week 24, if you are still receiving placebo and did not meet early escape criteria, you will begin receiving ustekinumab (either 45 mg or 90 mg by chance) at Weeks 24 and 28 followed by every 12 weeks through Week 52. If you were already assigned to ustekinumab 45 mg or 90 mg and did not meet early escape, you will receive placebo at Week 24 and continue on your assigned dose of ustekinumab (45 mg or 90 mg) with a dose at Week 28 followed by every 12 weeks throughout Week 52.

While the study is ongoing, neither you nor your study doctor (or his/her staff) will know which study drug group you are in (unless qualifying for an early escape at Week 16); however if needed for a medical emergency, your study doctor can quickly find out which treatment group you are in.

You will be responsible to take the same actions as part of this research study no matter which study drug you are receiving.

**From this point on, all reference to the words “study drug” can mean ustekinumab 45 mg, ustekinumab 90 mg, golimumab 50 mg, or placebo.**

#### **WHAT PROCEDURES WILL BE DONE IF I VOLUNTEER FOR THE STUDY?**

If you agree to participate in this research study, your study doctor will do tests to see if you are eligible for this study. Even though you have been selected to participate for the reasons listed above, it is possible that these tests will show that you are not eligible. The tests will also ensure that you do not have any medical problems that may increase your risk of having a medical problem related to the study drug. If the tests show that you are not eligible, you will not be able to participate in the study. Your study doctor will let you know of the results as soon as possible.

If you decide to take part in this research study, you agree to take the study drug and visit your study doctor as instructed.

Below is a list of all the things that happen during the study. There is also a table later in this form to show what happens at each visit.

- **Review medical history**
- **Review of medications**
- **Physical exam.** The physical exam will not include a breast, pelvic, or rectal exam.
- **Measure your height and weight**
- **Vital signs:** Your blood pressure and pulse will be collected.
- **Electrocardiogram (also called ECG):** Sticky patches will be placed on your chest. These patches are connected to a machine which will show the electrical activity of your heart.

- **X-Ray** (picture) of your chest and joints in your back:
  - Your study doctor will use the X-ray picture of your chest to make sure you do not have signs of tuberculosis (TB) or other problems. TB is a bacterial disease that usually affects the lungs. If you have had a chest X-ray within 3 months of starting study drug, you may not need to have another X-ray before receiving the study drug.
  - A picture of the joints in your lower back and buttock area will be used by your study doctor to see if there are any changes present that are visible on X-ray. If you have had an X-ray of these joints in your lower back (and it is of sufficient quality for the study), you may not need to have another X-ray of the joints for screening.
- **Perform a TB blood test:** There is a special blood test used to check for TB, called the **QuantiFERON-TB Gold test**. If the blood test is positive, you will need to take preventative tuberculosis medicine to be in this study. If you are already taking treatment for latent TB, this test is not required.
- **Joint motion and muscle testing (musculoskeletal assessment)**
  - Chest expansion:
    - You will be asked to sit with your hands above your head while someone from the study staff measures your chest when inhaling and exhaling.
  - Evaluation of inflammation at sites of ligament, tendon or joints (enthesitis):
    - For this purpose, the healthcare provider will use his/her fingers to apply local pressure on a few relevant bones, joints or tendons located either in your pelvis, spine, chest, or feet.
  - Evaluation of spinal mobility:
    - The healthcare provider will take measurements to assess mobility of your neck, spine, and hips.
- **Side effects:** At each visit the study doctor will ask about any side effects you may have. Side effects are any unexpected, unwanted or sometimes unpleasant events (that is, sign, symptom, or disease) occurring while having taken a drug or having a procedure.
- **Health questionnaires:** To help the study doctor assess your condition during the study, you will be asked to complete questionnaires about your overall health, your pain, and how your condition is affecting your health and quality of life. You will complete these questionnaires at the clinic using an electronic device to:
  - Rate your fatigue, pain, and stiffness
  - Rate your movement and your ability to cope with everyday life
  - Assess your disease
  - Assess your night back pain and total back pain
  - Assess flexibility
  - It may take you up to 40 minutes to complete these questionnaires.
- **Blood draw:** A needle will be used to draw blood from a vein in your arm. A total of about 17 tablespoons (250 mL or 1 cup) will be drawn during the entire study. Sometimes a blood test may need to be repeated. If this happens the total amount of blood drawn will be more than this.
  - Your blood will be used to check:
    - For TB, hepatitis B, and C, and human immunodeficiency virus (HIV-AIDS). If your test results show that you have hepatitis or HIV, you will be notified and given information on counseling services. The results of your hepatitis and HIV tests will be disclosed to local health agencies as required by law.

- Your general health
  - For signs of inflammation
  - To see how much study drug is in your blood
  - For an immune system response
  - For pregnancy (if you are a female who could get pregnant)
  - For scientific research (\*See the section below titled “Samples Collected for Scientific Research”).
- **TB evaluation:** You will be asked some questions which could help to find signs and symptoms of TB infection. Additional examinations may be done for further investigation when TB infection is suspected.
  - **Subcutaneous (SC) injection-site reaction:** You must stay at the study clinic for 30 minutes after each injection of study drug. You will be observed for any irritation or pain where the injection is given.
  - **Urine sample:** For pregnancy if you are female and able to get pregnant. If the test shows that you are pregnant, you will not be allowed to start or receive any more study drug.
  - **OPTIONAL Stool sample collection:** This is an optional procedure, part of the microbiome sub-study. If you agree to collect stool samples, you will be asked to use a provided kit to collect stool samples at Weeks 0, 4, 24, and 52 in the study. The stool samples can be collected within 48 hours before your scheduled study visit for Weeks 0, 4, 24, and 52, either at home or at the study site. The stool sample will be used for scientific research (see the section below titled “Samples Collected for Scientific Research.”)

You will be informed if testing on your samples for this study will change.

### **SAMPLES COLLECTED FOR SCIENTIFIC RESEARCH**

If you agree to be part of the sub-study, your blood and stool samples will be used for scientific research.

Different substances in your samples may be tested (for example, RNA, protein, etc.).

These samples may be used to help scientists understand how ustekinumab might work, or why it may cause side effects. These samples may also help scientists to understand Radiographic Axial Spondyloarthritis or develop new tests for it. They may also be used to study why people may respond differently to ustekinumab.

Your blood and stool samples will not be used for genetic research (genetic research is the study of DNA) unless you consent to the optional DNA analyses.

The results of tests done in these samples are only for research. They will not be used for your medical care. They will not be used to make a diagnosis about your health. Therefore, these results will not be given to you or your study doctor.

### **WHAT IS DONE AT EACH VISIT?**

First, your study doctor will do tests to see if you can join the study. This is called “Screening”.

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Below is a list of everything that is done during Screening.

<b>Screening</b>	
<b>Medical history</b>	✓
<b>Review of medications</b>	✓
<b>ECG</b>	✓
<b>Blood draw</b>	✓
<b>QuantiFERON-TB Gold test</b>	✓
<b>TB evaluation</b>	✓
<b>Pregnancy test</b>	✓
<b>Physical Exam</b>	✓
<b>Vital signs</b>	✓
<b>Height &amp; weight</b>	✓
<b>X-rays (Chest and SI joints)</b>	✓
<b>Health questionnaires/ Self assessments</b>	✓

The table below shows what tests and procedures will take place during the Study Drug and the Follow-Up visits.

	ON STUDY DRUG										SAFETY FOLLOW-UP VISIT
	0	4	8	12	16	20	24	28	40	52	64
Review of medications	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Injection (Study drug)*	✓	✓			✓		✓	✓	✓	✓	
Physical exam											✓
Blood draw	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Vital signs	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
TB evaluation	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Weight							✓			✓	✓
Urine pregnancy test	✓	✓			✓		✓	✓	✓	✓	✓
Health questionnaires/ Self-assessments	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Musculoskeletal evaluation	✓				✓		✓			✓	
Injection site reaction	✓	✓			✓		✓	✓	✓	✓	
Review of side effects	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Stool collection (Optional)	✓	✓					✓			✓	

\*Participants in all 3 study drug groups who are eligible for Early Escape may begin to take golimumab 50 mg home for self-administration. Participants unable to have injection administered away from study site will be required to return to the site for administration of golimumab 50 mg injection. For more details see section "How do I take the study drug?"

## HOW DO I TAKE THE STUDY DRUG?

If you decide to take part in the study, you also agree to take the study drug as directed by the study staff.

You will receive 2 shots subcutaneously (under the skin) 7 times in total, unless you meet early escape criteria determined at Week 16. The site of injections can be at different locations of

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your body each time. If you meet early escape criteria, then you will have received 2 shots subcutaneously at Weeks 0 and 4, then switch to golimumab as described below.

### **Early escape**

At Week 16, if you qualify for early escape, you will start to receive one golimumab 50 mg injection every 4 weeks. You have the possibility to do this at home, and, in this case, you will return less frequently to the study site (for Weeks 24, 28, 40, 52, and 64). The study staff will instruct you on how to give yourself a golimumab injection. After you have learned to self-inject golimumab, you will be allowed to take golimumab home where you will store it in your refrigerator. A friend or caregiver can also be taught to give you the injection at home. If you take golimumab at home, you will not need to come back to the study clinic for every injection. The study staff will instruct you on how to transport and store golimumab and will instruct you on how to bring the used golimumab back during a clinic visit. If you experience any issues or have any concerns with injections at home, you should contact the study staff.

If you experience any issue or have any concerns with injections at home, or if you cannot manage to do the golimumab injection at home, you will have to return every 4 weeks to the study clinic to receive it.

You will receive or self-inject 1 shot subcutaneously (under the skin) 10 times in total. The site of injection can be at a different location of your body each time.

### **WHAT OTHER THINGS WILL I HAVE TO DO OR AVOID DOING DURING THE STUDY?**

While you are in the study you must:

- Not take part in any other medical research or medical device study.
- Not receive a live virus or live bacterial vaccination during the study.
- Not receive a live vaccine for 3 months after receiving the last administration of study drug.
- Not receive a BCG vaccination during the study and for 12 months after the last administration of study drug.
- Not get pregnant or cause your partner to become pregnant.
- Give correct and accurate information about your medical history and current medical condition.
- Come to all study visit appointments.
- Tell the study doctor about any health problems you have during the study.
- Tell the study doctor about any new medicine or drug you take during the study.
- Not take any other drugs or remedies unless the study doctor has approved them beforehand. This includes prescription and over-the-counter drugs (including vitamins and herbs).
- Take golimumab as instructed, and if taking it home:
  - Do not give your study drug to anyone else
  - Return unused study drug and all empty packages to your study doctor at each visit
  - Store golimumab at temperatures ranging from 36°F to 46°F (2°C to 8°C)
  - Do not freeze

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- Protect it from light
- Avoid vigorous shaking

Keep study drug out of reach of children. The study drug packaging for ustekinumab is not child-resistant. Children may be able to open the package and get to the study drug if it is not kept out of their reach. If a child eats or plays with the study drug, it could be harmful (study drug is packaged in a syringe). By signing this consent, you are saying that you understand the study drug packaging is not child-resistant. You should not take part in this study, if you feel that you will not be able to keep your study drug(s) in a safe place where children cannot get to it.

You must not give your study drug to anyone else. Return all packaging and unused study drug to your doctor at each visit.

### **WILL THE STUDY DRUG BE AVAILABLE AFTER THE STUDY IS OVER?**

After the study is over, the sponsor will not continue to provide you with ustekinumab or golimumab.

Your study doctor will discuss your future medical care options with you.

### **WHAT ARE THE POSSIBLE SIDE EFFECTS, RISKS, AND INCONVENIENCES/DISCOMFORTS OF BEING IN THE STUDY?**

All medicines can cause side effects. The time it takes to recover from the effects of the drug are unknown.

Your participation in this study does not guarantee a specific outcome. There is a possibility that your condition may remain the same or get worse.

Tell your study doctor immediately if you have a side effect, an injury or any other symptom or complaint. You can contact your study doctor 24 hours a day by telephone.

- The telephone number is 510-585-3055 (after office hours).

### **Potential discomforts, side effects and risks associated with ustekinumab**

The possible discomforts, side effects and risks related to ustekinumab are not all known. Most side effects are not serious. Some may be serious and may require treatment or additional testing. This section describes how frequently side effects occurred in research participants who received ustekinumab. In this section, the following terms are used:

- Very common: Affects more than 1 user in 10
- Common: Affects 1 to 10 users in 100
- Uncommon: Affects 1 to 10 users in 1,000
- Rare: Affects 1 to 10 users in 10,000

Very Common:

- None

Common:

- Infection of the throat or airways
- Sore throat
- Feeling tired
- Redness and pain at drug injection site
- Back, joint or muscle pain
- Tooth infections
- Headache
- Dizziness
- Diarrhea
- Nausea
- Itchiness

Uncommon:

- Swelling, itching, hardness, bleeding, bruising and irritation where the injection is given
- Shingles (a painful rash)
- Depression
- Inflammation of tissue under the skin. Signs include warmth, swelling, redness and pain
- Nasal congestion
- A form of psoriasis with raised bumps on the skin that are filled with pus
- Allergic reactions including rash or raised, itchy bumps

Rare:

- Serious allergic reactions, which could be life-threatening (including low blood pressure, trouble breathing, swollen face, lips, mouth and/or throat)
- A form of psoriasis with redness and scaling of a much larger area of your skin or your entire body (erythrodermic psoriasis)

**Infections**

Ustekinumab is a drug that may change how your body fights infections.

Serious infections requiring hospitalization for medical observation and /or treatment have been seen in ustekinumab studies. Some of these infections have also been life threatening.

Tell your study doctor if you have a new infection, if an infection keeps coming back, or if you have any signs of infection such as:

- Fever
- Chills
- Headache
- Coughing
- Congestion

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- Chest tightness
- Shortness of breath
- Flu-like symptoms
- Nausea
- Vomiting
- Diarrhea
- Cold sores
- Weight loss
- Tiredness
- Night sweats
- New or worsening of pain in any location
- Frequency or burning while passing urine
- Redness, warmth, tenderness, or swelling of skin or joint

It is unknown if ustekinumab may stop you from developing a fever if you do have an infection, and therefore hide that you have one.

Fungal infections have been reported in participants who received ustekinumab. Some of these fungal infections can be serious and involve internal organs. You should find out from your study doctor which fungal infections are common where you live or travel and what symptoms they cause. Tell your study doctor and family physician right away if you develop symptoms of such illnesses.

Participants who receive ustekinumab may also be at a greater risk for certain serious infections such as tuberculosis. Tell your study doctor if you have ever had tuberculosis or anybody in your family has ever had tuberculosis or if you come in contact with someone who has tuberculosis. Tell your study doctor if you develop:

- A cough that does not go away
- Coughing up blood
- Shortness of breath
- Fever
- Night sweats
- Weight loss

## **Cancer**

Cancers have been reported in participants who have received ustekinumab, but it is unknown whether taking ustekinumab has increased their risk for developing cancer. Because ustekinumab may suppress your immune system, it is possible that it may increase your risk of developing cancer, including skin cancers. *Tell your study doctor if you have any new or changing skin lesions.*

It is known that people who have had inflammatory diseases (such as, Crohn's disease, Rheumatoid Arthritis, Ulcerative Colitis, etc.) for a long time and who use immunosuppressive

therapies (such as, azathioprine, methotrexate, etc.) for a long time have a higher risk of developing cancer. These people get cancer of the lymph nodes more often than other people.

### **Injection site reactions and allergic reactions**

Ustekinumab may cause an allergic reaction in some people. These reactions are usually mild to moderate. The following can be symptoms of an allergic reaction:

- Fever
- Chills
- Hives
- Rash
- Headache
- Nausea
- Flushing
- Light-headedness
- Shakiness
- Anaphylaxis (life-threatening allergic reaction)
- Irregular heartbeats
- Chest tightness
- Shortness of breath
- Wheezing
- Difficulty in swallowing or breathing
- Low blood pressure

Serious allergic reactions have been reported in participants who received ustekinumab and can be life threatening. Signs of a serious allergic reaction include skin rash, swollen face, mouth, lips, and/or throat, and trouble breathing. Tell your study doctor or get emergency medical help right away if you have an allergic reaction. If you experience a serious reaction to an injection, you will not receive any more study treatments.

If you have an allergic reaction at the doctor's office, additional necessary treatment will be provided immediately. Your study doctor may give you an antihistamine (medication used to treat allergic symptoms such as hay fever) or other medications used for treating an allergy. Antihistamines can make you sleepy, so please use caution when driving a car or operating machinery. **If you think you are having a severe allergic reaction after you leave the study site, dial 9-1-1 and seek medical attention immediately.**

Another type of allergic reaction has occurred in some participants 1 – 14 days after receiving similar medications. The symptoms of this type of allergic reaction may include fever, rash, muscle aches and joint pain.

### **Antibodies to ustekinumab**

Sometimes the body can make special antibodies that may increase the risk of an allergic reaction to either ustekinumab or other antibody medicines. If you have an allergic reaction, you

may not be able to have these types of medications in the future. You should always tell your doctors that you have been treated with human antibodies in this study.

### **Latex allergy**

The needle cover for the prefilled syringe that contains study drug contains dry natural rubber (a form of latex). This may cause allergic reactions in people who are sensitive to latex. Please tell your study doctor if you have ever had an allergic reaction to latex.

### **Cardiac and vascular**

Heart attacks and strokes have been reported in participants who have received ustekinumab. These events have rarely resulted in death. It is unknown whether taking ustekinumab increases your risk for developing these events.

People who have psoriasis, and certain other inflammatory diseases, have a higher risk of having heart attacks. These people have heart attacks more often than other people. Seek medical care immediately if you develop:

- Chest pain or discomfort
- Trouble breathing
- Irregular heartbeats
- Dizziness
- Loss of balance
- New numbness or weakness
- Visual or speech changes

### **Vaccination**

Vaccines are made to help protect people from certain illnesses. Some vaccines are made from live bacteria or live viruses. You cannot receive most kinds of live vaccines (for example, FluMist™, varicella) during the study or for 3 months after the last study injection. Another kind of live vaccine is BCG, which is a vaccine against tuberculosis. You cannot receive a BCG vaccine during this study or for 12 months after the last study injection. You could get sick from these kinds of vaccines while on ustekinumab. If you do get a live vaccination during this study, you must tell your study doctor immediately.

Tell your study doctor if anyone living in your home needs a live vaccine. Some viruses used in live vaccines can spread from a close contact (someone living in your home) to people with a weakened immune system.

Other kinds of vaccines, like tetanus and flu shots, are allowed. It is not known if ustekinumab may interfere with them from working. Tell your study doctor before getting any vaccine while you are in this study.

## **Other Therapies**

Tell your study doctor if you are receiving treatments that weaken the immune system while using ustekinumab (for example, immunosuppressant treatment for kidney disease or biologic treatment for osteoporosis or inflammatory bowel disease). These treatment combinations have not each been studied with ustekinumab, so it is unknown if they could possibly increase the risk of diseases related to a weakened immune system.

## **Allergy immunotherapy (Allergy injections)**

Tell your study doctor if you have ever had or are now getting allergy injections. Ustekinumab may affect your response to allergy injections.

## **Other risks**

A single case of a very rare disease of the brain, known as Reversible Posterior Leukoencephalopathy Syndrome (or RPLS), has been reported in a clinical study with ustekinumab. RPLS is generally reversible and is not caused by an infection. Symptoms of this condition are:

- Headache
- Seizures
- Confusion
- Loss of eyesight

## **Tell your study doctor if you experience any of these symptoms**

There may be other discomforts or risks to you from this study that are not yet known. Your study doctor and staff will ask you about any side effects you may have at every visit. If you have any problems, you should let your study doctor know right away.

Tell your doctors or dentist that you are or have been in a study where anti-IL-12 and anti-IL-23 is the study drug. This is important if you have any surgery, dental procedures, or receive treatment for any other medical condition.

## **Potential Discomforts, Side Effects, and Risks Associated with Golimumab**

The possible discomforts, side effects, and risks related to golimumab treatment are not all known. Most side effects are not serious. Some may be serious and may require treatment or additional testing. This section describes how frequently side effects occurred in adult patients who were treated with golimumab. The following terms are used:

- Very common: Affects 1 in 10 or more patients (10% or more)
- Common: Affects between 1 and 10 in 100 patients (between 1% and 10%)
- Uncommon: Affects between 1 and 10 in 1,000 patients (between 0.1% and 1%)
- Rare: Affects between 1 and 10 in 10,000 patients (between 0.01% and 0.1%)

- Very rare: Affects less than 1 in 10,000 patients (less than 0.01%)

You will be told of any new findings that may affect your decision to continue in this study.

Tell your doctors or dentist that you are or have been in a study where anti-TNF alpha is the study drug. This is important if you have any surgery, dental procedures, or receive treatment for any other medical condition.

## **Infections**

You could get more infections while taking golimumab or an existing infection could get worse. Golimumab may keep you from developing a fever if you have an infection and therefore hide that you may have one.

Upper respiratory tract infections, infections of the nose, and throat have been very commonly seen in patients treated with golimumab.

Infections in other locations of the body and throughout the body have also been reported. Infections could be caused by bacteria, viruses, or fungi.

There have been patients treated with golimumab who have reported serious infections, including pneumonia and sepsis. Some of these infections resulted in death. Pneumonia is an infection in the lungs and has occurred commonly in patients treated with golimumab. It can vary from mild and easy to treat to serious and difficult to treat. Sepsis is an infection of the blood and/or body tissue and has occurred uncommonly in patients treated with golimumab. Patients who have a weakened ability to fight infection are more likely to get pneumonia, sepsis, or other infections than other people.

In studies in patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis in which golimumab was given as injections under the skin, serious infections occurred more frequently in patients receiving 100 mg golimumab than in patients receiving 50 mg golimumab.

Fungal infections have been reported in patients taking golimumab. Some of these fungal infections occur rarely and can be serious and involve internal organs. You should find out from your study doctor which fungal infections are common where you live or travel, and what symptoms they cause. Tell your study doctor and family physician right away if you develop symptoms of such illnesses.

If you never had chickenpox, please tell your study doctor. If you come in contact with someone who has chickenpox or shingles, tell your study doctor right away. Your study doctor may offer you some measures to prevent these diseases or decrease the symptoms of these diseases.

Tell your study doctor if you have a new infection, if an infection keeps coming back, or if you have any signs of infection such as:

- Fever

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- Chills
- Headache
- Coughing
- Congestion
- Chest tightness
- Shortness of breath
- Flu-like symptoms
- Nausea
- Vomiting
- Diarrhea
- Cold sores
- Weight loss
- Tiredness
- Coughing up blood
- Night sweats
- New or worsening of pain in any location
- Change in urine frequency or burning feeling while passing urine
- Redness or swelling of limbs, skin, or joint

### **Tuberculosis**

Tuberculosis is a type of infection that usually develops in the lungs but can also develop in other areas of your body and throughout your body. Tuberculosis requires prolonged treatment with specific medication. Tuberculosis has been reported in patients who have received TNF-blockers, including patients receiving golimumab. Although a rare event, in studies in which golimumab was given as injections under the skin, tuberculosis occurred more frequently in patients receiving 100 mg golimumab than in patients receiving 50 mg golimumab or placebo. You may be more likely to get tuberculosis while being treated with golimumab. Tell your study doctor if you develop any of the symptoms noted above, if anybody in your family has ever had tuberculosis, or if you come in contact with anyone who has tuberculosis while you are participating in this study.

Your study doctor or qualified staff will do a blood test or/and skin test to see if you have come in contact with tuberculosis. A chest X-ray will be done to see if there is or has been tuberculosis in your lungs.

If you have a chest X-ray that shows signs of tuberculosis (or a positive blood test or/and positive skin test), you cannot be in this study.

### **Cancer**

Cancers have been reported in patients who have received golimumab and other TNF-blockers, and lymphoma (a cancer of lymph nodes) has been reported in these patients more frequently than expected for the general population. Cases of leukemia (a cancer of the blood) have also been reported in patients taking TNF-blockers, including golimumab. Leukemia has occurred rarely in patients treated with golimumab. There have been cases of unusual cancers in children

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and teenage patients taking TNF-blockers that sometimes resulted in death. It is known that patients who have had inflammatory diseases for a long time (such as rheumatoid arthritis, Crohn's disease or ulcerative colitis) and who use immunosuppressive therapies for a long time (such as methotrexate or azathioprine) may have a higher risk of developing cancer even if they never received a TNF-blocker. For children and adults taking TNF-blockers, the chances of getting lymphoma or other cancers may increase.

In larger clinical studies of golimumab, the frequency of patients developing cancer was similar in the golimumab and the placebo groups, with the exception of lymphoma in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis, which although a rare event, occurred more frequently in patients receiving 100 mg golimumab than in patients receiving 50 mg golimumab or placebo given as injections under the skin. Most of the patients with lymphoma in golimumab research studies had rheumatoid arthritis. In a smaller study in patients with severe asthma, there were more patients that developed cancer in the golimumab group than in the placebo group. A similar finding has been observed with another TNF blocker in patients with another lung disease that is often caused by smoking called COPD (Chronic Obstructive Pulmonary Disease). If you have asthma or COPD, discuss with your study doctor if taking part in this clinical study is right for you.

Rarely, patients who received golimumab in research studies developed skin cancers, including melanoma. Melanoma was observed more frequently in patients receiving golimumab than placebo. Another serious very rare skin cancer called "Merkel cell carcinoma" has been reported in patients treated with other TNF blockers. Merkel cell carcinoma and melanoma may result in death if not discovered early. If you notice an unusual or discolored skin bump or lesion, contact your study doctor.

If you take part in a clinical study with golimumab, your risk for developing lymphoma or other cancers may increase. You should tell your study doctor prior to participating in this study if you have a history of lymphoma or cancer, and if you develop lymphoma or cancer, including skin cancer, during or after you have participated in this study.

You should also regularly discuss cancer screenings, including skin examinations, with your study doctor, and the impact of life-style choices (for example, smoking) on the risk of developing cancer.

A very aggressive type of lymphoma, called "hepatosplenic T-cell lymphoma," has occurred rarely in patients who have been treated with TNF-blockers similar to golimumab. This type of cancer usually causes death. Nearly all of these cases have occurred in patients with Crohn's disease or ulcerative colitis. The majority were in adolescent and young adult males. Almost all these patients had received treatment with azathioprine or 6-mercaptopurine in combination with a TNF blocker at or prior to diagnosis. It is unclear what role golimumab may have in the development of the lymphoma. No patients treated with golimumab have developed this type of lymphoma.

It is not known if treatment with golimumab affects the risk for getting an abnormal growth of cells (dysplasia) in your colon or cancer in your colon. Your study doctor may want you to have

tests done regularly to check for colon dysplasia and colon cancer before you start and during treatment with golimumab. You should tell your study doctor if you have a history of colon dysplasia or colon cancer.

## **Liver**

It has been common for patients treated with golimumab to develop abnormal liver blood tests. Your study doctor will monitor the results of tests done on your blood during the study. If liver blood tests are abnormal, your study doctor may stop your treatment for a while or permanently, and may perform more tests to find the cause of abnormal liver blood tests. In most cases in studies with another TNF-blocker (REMICADE®), the liver blood tests return to normal after stopping the drug.

TNF-blockers, including golimumab, may reactivate the hepatitis B virus in patients who have been known to carry the virus. Reactivation of the hepatitis B virus has occurred rarely in patients treated with golimumab. If you now or anytime in the past, have had any liver problems, including hepatitis B and hepatitis C, you should tell your study doctor right away. You will have a blood test to see if you have hepatitis B and hepatitis C prior to treatment with golimumab.

There have been cases where patients taking TNF-blockers, including golimumab, have developed serious liver problems, sometimes fatal. Signs that you could be having a problem include:

- Skin and eyes turning yellow
- Dark brown urine
- Right-sided stomach pain
- Nausea
- Vomiting
- Loss of appetite
- Fever
- Extreme tiredness

**If you develop any of these symptoms, tell your study doctor right away.**

## **Injection Site Reactions and Allergic Reactions**

In patients treated with golimumab, when injected under the skin, common reactions seen at the injection site were:

- Hives
- Swelling
- Pain
- Bruising
- Skin irritation
- Tingling or burning
- Itching

- Redness

The majority of the injection site reactions have been mild or moderate.

Any drug may cause an allergic reaction in some people. The following can be signs of an allergic reaction:

- Fever
- Chills
- Hives
- Rash
- Headache
- Nausea
- Flushing
- Light-headedness
- Shakiness
- Irregular heartbeats
- Chest tightness
- Shortness of breath
- Wheezing
- Difficulty in swallowing or breathing
- Low blood pressure

These reactions are usually mild to moderate.

Serious allergic reactions called anaphylaxis have occurred during administration of golimumab and other drugs made from proteins and can be life threatening.

If you have an allergic reaction, your study doctor may give you a medication used to treat allergic symptoms (such as an antihistamine), or to reduce aches, pains, and fever (such as acetaminophen).

Another type of allergic reaction, called “serum sickness-like reaction,” has occurred in some patients 1 – 14 days after receiving TNF-blockers, including golimumab. The symptoms of this type of allergic reaction may include fever, rash, muscle aches and joint pain.

### **Latex Allergy**

The needle cover for the prefilled syringe that contains study drug may contain dry natural rubber (a form of latex). This may cause allergic reactions in people who are sensitive to latex. Please tell your study doctor if you have ever had an allergic reaction to latex.

### **Heart**

Congestive heart failure (CHF), a disease where the heart’s pumping action is weakened, has been reported in patients who have received TNF-blockers, including golimumab. In some

patients with known CHF, worsening of their CHF occurred. Rarely patients treated with golimumab have developed worsening CHF or developed CHF for the first time. Some of these patients died. If you have a history of CHF or have received treatment for CHF, you are not allowed to participate in this study. Signs of CHF may include shortness of breath or swelling in your ankles and/or feet; tell your study doctor right away if you have had these symptoms or if they develop.

## **Lung**

“Interstitial lung disease” is the name for diseases that inflame or scar the lungs. The inflammation and scarring may make it difficult to breathe and get enough oxygen in your blood. Patients treated with golimumab have uncommonly developed interstitial lung disease.

## **Nervous System**

Commonly, patients treated with golimumab experienced dizziness, numbness, or tingling.

Rarely, in studies with TNF-blockers, including golimumab, cases of multiple sclerosis and similar disorders have been observed. These events occurred more frequently in patients receiving higher golimumab doses. Multiple sclerosis is a serious disease of the central nervous system which may cause muscle weakness, difficulties in walking, visual problems and symptoms of pins and needles. If you have any personal or family history of nervous system disorders, tell your study doctor. Signs of nervous system disorders include:

- Changes in vision
- Weakness in arms and/or legs
- Numbness or tingling in any part of the body

Tell your study doctor right away if you experience any of these symptoms.

## **Blood**

In studies with TNF-blockers, including golimumab, sometimes the body fails to make enough white blood cells that help the body fight infection or fails to make enough red blood cells, resulting in anemia. In addition, sometimes the body fails to make enough blood cells that help you stop bleeding. Some patients have died from this failure to produce blood cells. Your study doctor will monitor the results of tests done on your blood during the study. If you develop a fever that does not go away, bruise or bleed very easily, look very pale or become tired easily tell your study doctor right away.

Patients treated with TNF-blockers including golimumab commonly developed abnormal blood tests called “ANA” (anti-nuclear antibodies); some of these patients rarely developed symptoms that look like a disease called lupus. Lupus-like symptoms may include:

- Muscle aches
- Joint pain

- Fever
- Rash on the cheeks or arms that gets worse in the sun
- Chest discomfort
- Shortness of breath

You should tell your study doctor if this happens.

## **Skin**

Rashes and hair loss have occurred commonly in patients treated with golimumab.

Some patients treated with golimumab may uncommonly develop fluid-filled blisters on the skin.

Uncommonly, patients treated with TNF-blockers, including golimumab, may develop worsening of psoriasis or new onset psoriasis, including a type called “pustular psoriasis.” Symptoms may include dry, red skin with yellow blisters, often on the palms of the hands or soles of the feet, although it can occur elsewhere.

Rarely, a type of rash called “vasculitis,” resulting from inflammation of blood vessels in the skin, can occur in patients treated with golimumab. You should tell your study doctor if you develop any of the symptoms above.

Rarely, scaly, peeling skin can occur in parts or all over your body.

## **Antibodies to Golimumab**

Sometimes the body can make special antibodies that may increase the risk of an allergic reaction to either golimumab or other antibody medicines. If you have an allergic reaction, you may not be able to have these types of medications in the future. You should always tell your doctors that you have been treated with human antibodies in this study.

## **Vaccinations/Therapeutic Infectious Agents**

Vaccines are made to help protect people from certain illnesses. Some vaccines are made from live bacteria or live viruses. You cannot receive this kind of live vaccine (for example, nasal flu vaccine, BCG) during this study or for 3 to 12 months after the last study drug administration. You could get sick from this kind of vaccine while on golimumab. Other kinds of vaccines, like tetanus and flu shots, are allowed but it is not known if golimumab may interfere with these vaccines and prevent them from working. Tell your study doctor before getting any vaccines while you are in this study. If you do get a live vaccination during this study, you should tell your study doctor, as you may no longer be allowed to receive any more study drug.

You could also get sick if you receive treatments that include live organisms (a therapeutic infectious agent) while on golimumab. An example of this type of treatment is BCG that is put into the bladder for the treatment of cancer. Tell your study doctor if you have received or are scheduled to receive treatment with a therapeutic infectious agent.

## **Other Medications**

Tell your study doctor about all the medicines you take, especially if you take any medications that affect your immune system. Taking those medications at the same time as golimumab may increase your chance of getting an infection; therefore golimumab should not be taken together with some medications that affect your immune system.

## **Other Risks**

It was common for patients treated with golimumab to have elevated blood pressure or fever. Uncommonly, patients treated with golimumab can have constipation.

Rarely, patients treated with golimumab develop an immune disorder called “sarcoidosis” which could affect the lungs, skin, and lymph nodes.

Rarely, a serious inflammation of the blood vessels called “systemic vasculitis” may occur and, in severe cases, may result in permanent damage of the affected internal body organs.

There may be other discomforts or risks to you from this study that are not yet known. Your study doctor and staff will ask you about any side effects you may have at every visit. **If you have any side effects or problems, you should let your study doctor know right away.**

## **Potential Discomforts, Side Effects, and Risks Associated with Placebo**

If you are assigned to the placebo study drug group, you will not be receiving any active drug for your condition. If your condition is not improving by Week 16 and you meet the criteria for early escape, your study doctor will provide you with active drug (golimumab). If you do not meet early escape criteria, you will be assigned to 1 of the 2 ustekimumab groups (45 mg or 90 mg).

## **Preventative Medicine for Tuberculosis Infection**

Sometimes these medicines have side effects. Side effects may include nausea, vomiting, abdominal pain, hepatitis and possibly other events. Your study doctor will provide you with more information on tuberculosis preventative treatment.

## **Side effects from tests**

- Blood draw: Taking blood may cause bruising at the place where the needle goes into the skin. Fainting, and in rare cases infection, may occur.
- X-Ray risks: The radiation dose that is in the X-ray(s) taken for this study is small. There is no significant risk from this amount of radiation.
- ECG risk: There is generally no risk with having an ECG. The sticky patches may pull your skin or cause redness or itching.
- Stool Risk: The stool samples can expose your skin to stool microorganisms; careful hand washing with warm water and soap can prevent any problems.

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## **Other**

During the study your condition may remain the same or get worse.

There may be risks with the use of ustekinumab and golimumab that are not yet known. We may learn new information that might change whether or not you want to continue in the study. If this happens, you will be told in a timely manner. You may decide to stop taking part in the study at the time. If you do, your study doctor will discuss the steps you should follow. If you decide to continue, you may be asked to read and sign a revised consent form containing the new information.

## **CAN THE STUDY DRUG CAUSE PROBLEMS TO OR DURING PREGNANCY OR WHEN BREAST FEEDING?**

### **Birth control and pregnancy precautions associated with ustekinumab**

The effect of ustekinumab on human sperm or unborn babies is not known.

Pregnant women and women who are making breast milk to feed infants cannot participate in this study. Female participants must have a blood test when beginning this study that shows they are not pregnant.

**It is very important that women taking part in this study do not become pregnant while taking part in this study. It is very important that men taking part in this study do not get a woman pregnant while taking part in this study.**

During this study and for 5 months after the last dose of study drug, women of childbearing potential must use proven birth control methods. Your study doctor will discuss effective birth control methods with you. Acceptable methods of birth control include: avoiding sex, birth control pills, intrauterine device (IUD), barrier method combined with gel or foam with spermicide, or proof of a woman having her tubes tied or a man having his sperm tubes cut or blocked. The type of birth control you use must be discussed with, and approved by, the study doctor before you begin the study.

If you think that you have become pregnant or may have fathered a child while taking part in the study, tell your study doctor immediately. You should also notify your childbirth doctor that the mother/father received an investigational drug (ustekinumab).

If you are a female participant and you become pregnant during your participation in this study, your study drug will be stopped and you may be withdrawn from some of the study procedures but not from follow-up by your study doctor. You will be removed from the study. The doctor will advise you regarding your medical care. The study doctor will ask for your permission to stay in contact with you throughout the length of the pregnancy.

If you are a female participant, you must not donate eggs during the study and for 5 months after your last dose of study drug.

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If you are a male participant and you father a child during your participation in this study, the study doctor will ask for your partner's permission to stay in contact with her throughout the length of the pregnancy.

If you are a male study participant who is sexually active with a woman of childbearing potential and has not had a vasectomy, you must agree to use a barrier method of birth control (for example, either condom with spermicidal foam/gel/film/cream/suppository or partner with occlusive cap [diaphragm or cervical/vault caps] with spermicidal foam/gel/film/cream/suppository).

You must also not donate sperm during the study and for 5 months after your last dose of study drug.

### **Birth control and pregnancy precautions associated with golimumab**

The effect of golimumab on human sperm, pregnant women, women making breast milk, unborn babies, or breast-feeding infants is not known. Pregnant women and women making breast milk to feed infants cannot participate in this study. Female participants must have a blood test when beginning this study that shows they are not pregnant.

**It is very important that women taking part in this study do not become pregnant while taking part in this study. It is very important that men taking part in this study do not get a woman pregnant while participating in this study.**

During this study and for 5 months after the last dose of study drug, women of childbearing potential must use proven birth control methods (such as avoiding sex, birth control pills, intrauterine device (IUD), barrier method combined with gel or foam with spermicide, or proof of a woman having her tubes tied or a man having his sperm tubes cut or blocked). Your study doctor will discuss effective birth control methods with you.

If you think that you have become pregnant or may have fathered a child while taking part in the study, you must tell your study doctor immediately. You should also notify your childbirth doctor that the mother/father received golimumab.

If you are a female participant, you must agree to not donate eggs (ova, oocytes) during the study and for 5 months after your last dose of study drug.

If you are a female participant and you become pregnant during your participation in this study, your treatment with study drug will be stopped and you may be withdrawn from some of the study procedures but not from follow-up by your study doctor. The study doctor will ask for your permission to stay in contact with you throughout the length of the pregnancy.

Golimumab crosses the placenta. You should tell the baby's doctor that you have received treatment with golimumab before the baby receives any vaccine and the baby should not receive any live vaccines for 6 months after your last study drug administration.

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If you are a male study participant who is sexually active with a woman of childbearing potential and has not had a vasectomy, you must agree to use a barrier method of birth control (for example, either condom with spermicidal foam/gel/film/cream/suppository or partner with occlusive cap [diaphragm or cervical/vault caps] with spermicidal foam/gel/film/cream/suppository).

You must also not donate sperm during the study and for 5 months after your last dose of study drug.

If you are a male participant and you father a child during your participation in this study, the study doctor will ask for your partner's permission to stay in contact with her throughout the length of pregnancy.

### **WHAT ARE THE BENEFITS OF BEING IN THE STUDY?**

Taking part in this study may improve your condition, although this cannot be guaranteed. There may be no benefit to you. While you are in this study, you may benefit from your study doctor closely following your condition. By taking part in this study, you may help patients in the future.

### **WHAT OTHER TREATMENTS ARE AVAILABLE?**

You do not have to take part in this study to receive treatment for your condition. You may choose not to take part in this study or to leave the study at any time. Instead of taking part in this study, you may choose to receive standard treatment with:

<b>Therapy Types</b>	<b>Some Examples</b>
<b>Biologic Agents</b>	adalimumab, etanercept, infliximab, golimumab, certolizumab pegol
<b>Corticosteroids (local or oral)</b>	Prednisone
<b>Disease Modifiers and Immunosuppressive Agents</b>	methotrexate, sulfasalazine, leflunomide, hydroxychloroquine, azathioprine, cyclosporine
<b>Non-Steroidal Anti-inflammatory Agents (NSAIDs)</b>	diclofenac, naproxen, ibuprofen

### **Can I take these during the study?**

Some therapies can be taken, some cannot.

If you want to be in the study, talk to your study doctor first about these therapies and any other therapies you want to take. The dose may need to be adjusted.

Your study doctor will explain the good and bad things that could happen with these other treatments before you take part in this study. He/she will answer any question you may have. You can also discuss these other options with your own health care provider.

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## **WHO PAYS FOR THE STUDY? WILL I BE PAID FOR TAKING PART IN THE STUDY?**

Janssen Research & Development, LLC will pay the study doctor (and/or the hospital) for doing this study.

You will receive the study drug and the medical testing needed for the study at no cost to you. There are no costs to you or your insurance for study drug and study procedures.

The sponsor will not pay for doctor visits or other treatments or tests that are not part of this study. This means that you, your insurance company or your government's health plan may have to pay for these.

The sponsor will not pay for co-medications. You are responsible to pay for co-medications if they are not covered by your personal or government's health plan. Co-payments and deductibles are your responsibility. You will be fully responsible for costs if payment is denied by your insurer.

Your expenses (such as travel and parking) for attending study visits will be reimbursed. You will receive \$50.00 per visit to help cover any of your expenses in taking part in this study. Payment will be made following each study visit.

## **WHAT HAPPENS IF I HAVE AN INJURY AS A RESULT OF THE STUDY AND NEED MEDICAL CARE?**

If you need medical care because of something that happened to you as a result of being in this study, medical care will be provided to you. Janssen Research & Development, LLC, as the Sponsor of the study, agrees to reimburse the reasonable and necessary medical expenses not routinely covered by insurance for tests and treatments required.

The Sponsor will not pay the costs to test or treat a condition or injury that is not related to the study drug or study procedure, or for expenses related to the normal progression of a pre-existing medical condition or an underlying disease. In no event will the Sponsor pay for treatment for injury or illness that is not a result of the study.

To help avoid injury, it is very important to follow all study directions.

Before or after paying for treatment, Janssen Research & Development, LLC may need to collect certain personal information about you such as your name, date of birth, gender, Social Security number, and Medicare identification number (if you have one) in order to comply with a Medicare reporting requirement. This information may be collected directly from you, or from researchers, physicians, or other health care providers who treated your problem or injury. This information and also information about your injury or other health problem may be shared with others, including the Centers for Medicare & Medicaid Services (the federal agency responsible for administering the Medicare program).

The above statements do not limit your legal rights.

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## **WHAT IF I CHANGE MY MIND AND DO NOT WANT TO BE IN THE STUDY ANYMORE?**

Your participation in this study is voluntary. You don't have to be in this research study. You can agree to be in the study now and change your mind later. You may stop your participation at any time. Your decision will not affect your regular care or the benefits to which you are otherwise entitled.

If you agree to participate in the study and later change your mind, call Dr. Shibuya at 510-791-1300.

Your study doctor has the right to take you out of the study at any time with or without your agreement. The sponsor has the right to direct your study doctor to take you out of the study at any time with or without your agreement. These decisions will be made if:

- it is not in your best medical interests to continue
- you need treatment not allowed in this study
- you fail to follow instructions
- the study is canceled

If you stop the study early or your participation is ended, you will be asked to return to the study site to have all of the final clinical evaluations and laboratory tests done.

## **WHAT HAPPENS AFTER THE STUDY IS OVER OR IF I STOP THE STUDY EARLY?**

If you stop the study early, you will be asked to return to the study doctor to have final tests done.

Tell the study doctor if you have any side effects after you stop taking the study drug. He/she may add that information to your study record.

If you stop the study early, your blood samples will continue to be analyzed as described in this form unless you specifically ask for your samples to be destroyed.

If you decide to stop the study early, you agree not to limit our use of your study information. The sponsor will not collect any new information from you.

## **WHAT HAPPENS TO THE SAMPLES COLLECTED FROM ME?**

Samples are any fluid (such as blood) or stools collected from you in this study.

The sponsor will use the samples collected from you for the purposes of the study and for scientific research (see the section titled "Samples Collected for Scientific Research").

Your samples will not be used for genetic research unless you consent to the optional DNA analyses.

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The results of any scientific research done on your samples will not be used for your medical care. They will not be used to make a diagnosis about your health. Therefore, results of scientific research will not be given to you or your study doctor.

To protect your privacy, your samples will be labeled with your study number. The scientists doing the research will not know your identity.

Your samples may be sent to other members of the Johnson & Johnson group of companies, to contractors working for them and to regulatory authorities.

Your samples may also be shared with research partners for scientific research purposes. Before sharing with research partners, your samples will be labeled with a code number that is different from your study number. Your samples will not contain any personal identifiers. Your samples will not be sold, loaned or given to any other independent groups for their own use. Research partners working with the sponsor are not allowed to share samples with anyone who is not authorized by the sponsor. The sponsor will control what is done with your samples.

You will not be paid for any use of your samples, results, or inventions made from research on them. You are providing your samples, for use by the sponsor. The sponsor (and research partners, where applicable) plan(s) to own the use of the results, treatments, or inventions that can be made from this research.

Some or all of your samples may also be kept and used for up to 15 years after this study ends. This will allow for the scientific research described above to be done in the future as new discoveries are made. The sponsor will ensure that your samples are kept securely. Your samples will be destroyed no later than 15 years. You will not be informed when they are destroyed.

You can withdraw your consent for your samples to be used for future research. In this case your samples will be destroyed only after they are no longer needed for the main study. You would need to tell your study doctor that you are withdrawing your consent for your samples to be used for future research. This can be done at any time, for any reason. This will not affect your access to the care, medicine, and equipment you would otherwise be getting. Your study doctor will then tell the sponsor to destroy all your samples when they are no longer needed for the main study.

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### **WHOM DO I CONTACT FOR INFORMATION?**

If you have questions, concerns or complaints about the research study or you experience a research-related injury, please contact Dr. Shibuya or the study staff at 510-791-1300 or 510-585-3055 (after office hours).

If you have questions regarding your rights as a research participant, or if you have questions, concerns, complaints about the research, would like information, or would like to offer input, you may contact the Sterling Institutional Review Board Regulatory Department, 6300 Powers Ferry Road, Suite 600-351, Atlanta, Georgia 30339 (mailing address) at telephone number 1-888-636-1062 (toll free).

The study doctor and his/her study team will answer any of your questions relating to this research study. You should report any injuries or side effects immediately to Dr. Shibuya. For answers to questions related to your rights as a study participant, or if you have any complaints about the study or about how you have been treated, you may contact Sterling Institutional Review Board (an impartial third party). You have been given a copy of the Research Subject's Bill of Rights and CA HIPAA.

### **WILL INFORMATION ABOUT THIS STUDY BE PUBLICLY AVAILABLE?**

A description of this clinical trial will be available on [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov), as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

## **SUMMARY REVIEW**

### **1. Will I get ustekinumab?**

You will not know if you get the study drug. Not everyone in the study will get ustekinumab for the entire study because placebo is a part of the study.

### **2. Will I know if I am taking ustekinumab, golimumab or placebo?**

If you are receiving ustekinumab or placebo, you won't know and the study team won't know either. They only find out once the study is over. In an emergency, the study doctor can find out which study drug you are receiving.

If you receive golimumab, you will know that you are taking this drug.

### **3. Can I ask to get either ustekinumab or placebo?**

No. You are given ustekinumab or placebo by chance.

### **4. Will I get side effects from being in the study?**

There is a chance you could get side effects. Please refer to the section "**What are the possible side effects, risks, and inconveniences/discomforts of being in the study?**" of this document for details.

### **5. How long will I be in the study?**

You may be in the study for up to 72 weeks. You should only join the study if you are willing and able to stay in the study until the end.

### **6. Can I quit the study?**

Yes. You can quit the study at any time. You do not have to give a reason. There is no charge or penalty for quitting. If you quit, you will be asked to come in for final safety and efficacy visits.

### **7. Can the study team remove me from the study?**

Yes. Your study doctor or the study team can remove you from the study at any time.

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## AGREEMENT TO TAKE PART IN THE RESEARCH STUDY

This consent form contains important information to help you decide if you wish to take part in this research study. If you still have questions, please ask the study doctor or a member of his/her staff, before signing this form.

I have read this information, which is printed in English. This is a language that I read and understand. This study has been explained to my satisfaction. My questions about the study procedures, possible risks, side effects and taking the study drug have been answered. Based on this information, I volunteer to take part in this study.

I have been informed that this study includes a sub-study for microbiome. I agree to be part of the sub-study. *(You may still be in this study even if you do not agree to be in the sub-study.)*

Yes      No  
     

*(Please check yes or no)*

We would like your permission to contact the doctors you see regularly to let them know that you are taking part in this study. It is important for all of your doctors to know that you may be taking an investigational drug. Your doctors will want to know and think about all the drugs you are taking before giving you any new ones. While you are in the study, the study doctor will ask about your symptoms. If you have symptoms after the study ends, your other doctors may want to contact the study personnel.

Do we have your permission to contact your doctors? Please **check** one.

- You have my permission to contact the doctors I see regularly to let them know that I am taking part in this study *(place a check mark in the box if you wish to give permission).*
- You **do not** have my permission to contact the doctors I see regularly to let them know that I am taking part in this study *(place a check mark in this box if you do not wish to give your permission).*
- NA, I have no other doctors.

You will receive a copy of this signed informed consent form, which has 38 pages.

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\_\_\_\_\_  
Printed Name of Participant, in full

\_\_\_\_\_  
Signature of Participant

\_\_\_\_\_  
Date: MMMDDYYYY

\_\_\_\_\_  
Printed Name of Person Obtaining Consent

\_\_\_\_\_  
Signature of Person Obtaining Consent

\_\_\_\_\_  
Date: MMMDDYYYY

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## **AUTHORIZATION TO USE AND DISCLOSE MEDICAL INFORMATION**

**STUDY TITLE:** A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study Evaluating the Efficacy and Safety of Ustekinumab in the Treatment of Anti-TNF $\alpha$  Refractory Subjects With Active Radiographic Axial Spondyloarthritis

**PROTOCOL NO:** CNTO1275AKS3002

### **WHAT HAPPENS TO THE INFORMATION COLLECTED ABOUT ME?**

The following information explains how your medical and health records and the research data collected about you for the study may be used and disclosed.

Regulatory authorities, such as the Food and Drug Administration, as well as members of Sterling Institutional Review Board (“IRB”), employees at the study site, and representatives of the Sponsor, **Janssen Research & Development, LLC**, may review your medical records to verify study procedures and/or data. The Sponsor may also use your information for registration of the drug in different countries.

Your study doctor will keep your personal medical records and a list that links each participant’s name to his or her code number for at least 15 years.

After your encoded Protected Health Information is disclosed to the study Sponsor, the results of the study may be reanalyzed at a later date and may be combined with the results of other studies. The study Sponsor and people who work with the study Sponsor may use the results of this study for other research purposes, including:

- reviewing the safety or effectiveness of the study drug and other products or therapies
- evaluating other products or therapies for patients

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- developing a better understanding of disease
- improving the design of future research studies

If you are participating in a multi-site research study, your information may also be shared, if necessary, with researchers at associated sites for purposes of data analysis.

Your records will be kept by the Sponsor for as long as necessary. During that time they will be kept confidential to the extent permitted by law.

The results of the study may be published in a medical book or journal, or presented at meetings for educational purposes. If the results of the study are published, you will not be personally identified and your identity will not be disclosed.

By signing this form, you are permitting direct access to and use of your medical records and information by the individuals and entities identified above for the purposes described.

By signing this document, you also give permission to the study doctor to disclose the study results to the Sponsor and representatives of the Sponsor. The study results will not contain information that directly identifies you. The Sponsor will prevent those that do not need to access the results from viewing the results. The Sponsor will not attempt to identify you.

### **Will my information be given to others?**

The information about you collected for the Sponsor will be stored on paper and computer records, without identifying you by name. The information collected by the study doctor or study staff as part of the study may be sent to other members of the Johnson & Johnson group of companies, to contractors and consultants working for the Sponsor and to regulatory authorities (Food and Drug Administration).

Some of this information, called Protected Health Information (“PHI”), is protected by federal privacy laws. By signing this consent form, you give your permission to have your PHI collected, used and disclosed for purposes of this study. After the study staff or the study doctor discloses your PHI to others, it could be re-disclosed and no longer protected by federal privacy laws.

You may decide not to give permission for the use or disclosure of your protected health information for the study. In that case, you will not be able to participate in the study. This is because the study staff and/or the study doctor would not be able to collect the information needed to evaluate the study drug.

### **Can I get a copy of my medical records?**

You have a right to see and make copies of your medical records. However, to ensure the reliability of the study, you agree that you will not be able to see or copy your records related to the study until the sponsor has completed all work related to the study. At that time, you may ask to see the study doctor’s files related to your participation in the study, and you may ask the study doctor to correct any study-related information about you that is wrong.

### **What if I change my mind and do not want my information used or disclosed?**

The permission to use or disclose your protected health information for this study will expire 50 years from the date of your signature. If you no longer want to share your protected health information, you may cancel your permission at any time by writing to the study staff and/or the study doctor at the address below:

Fremont Rheumatology  
3775 Beacon Ave., Ste. 100  
Fremont, CA 94538

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If you cancel your permission after you have started in the study, the study staff and the study doctor will stop collecting your health information. Although they will stop collecting new information about you, they will need to use the information they have already collected to evaluate the study results. If you start the study and then cancel your permission, you will not be able to continue to participate in the study or receive any treatment as part of the study. This is because the study staff and/or the study doctor would not be able to collect the information needed to evaluate the study drug.

If the study doctor or Sponsor ends your participation, or if you decide not to continue, you will be asked to return to the study doctor or study site to have all of the final clinical evaluations and laboratory tests done.

I give my permission to the study doctor to use and disclose my protected health information as described in this authorization form.

You will receive a copy of this signed authorization form.

\_\_\_\_\_  
Printed Name of Participant, in full

\_\_\_\_\_  
Signature of Participant

\_\_\_\_\_  
Date: MMMDDYYYY