

California SB 486 Needle Disposal Plan for SIMPONI

This describes the process in place for the end-of-life management of SIMPONI self-injection devices. SIMPONI (golimumab) - is a drug for treatment of adult patients with rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis. The drug is provided in a pre-filled syringe or a SmartJect™ autoinjector. It is self-injected monthly. SIMPONI is marketed nationwide by Centocor Ortho Biotech.

Centocor Ortho Biotech is a Johnson & Johnson (J&J) company. J&J is committed to the health & well-being of families everywhere. Our commitment is shown in various sustainability and environmental initiatives and projects. More information about J&J's environmental progress can be found at:

<http://www.jnj.com/connect/caring/environment-protection/>

I. Description of sharps disposal program:

When health care professionals prescribe SIMPONI, they provide the patients with education materials such as the Patient Starter Kit and the Patient Starter Brochure. Information about the end-of-life product management program called SimponiOneSM Safe ReturnsTM is mentioned throughout these patient education materials. Patients can also get information on SimponiOne Safe Returns by calling 1-877-MY-SIMPONI or going on the website: www.SimponiOne.com.

The SimponiOne Safe Returns program is available nationwide at no additional cost to the patients. Patients sign up for the program using either the toll-free number, completing a business reply card or the website (above). They will receive a Safe Returns pack in the mail, and will continue to receive a Safe Returns package each month until they request to opt-out of Safe Returns and/or stop shipping back their used prefilled syringes or used SmartJect™ Autoinjectors after 90 days. Include in this pack are: the Safe Returns instructions, a postage-paid shipping box with liner, sharps container tube, plastic bag, shipping documents and a SIMPONI package insert. By following the Safe Returns instructions and giving the box to the mail carrier, dropping it at a U.S. post office, or anywhere the U.S. Postal Service arranges pickup, the used SmartJect™ AutoInjector or used pre-filled syringe will be shipped to Stericycle, a licensed medical waste facility for disposal.

The SimponiOne Safe Returns instructions for patients are provided in Attachment 1.

The SimponiOne Safe Returns information sheet for healthcare professional is provided in Attachment 2.

II. Patient Education about sharps disposal:

Information about proper disposal of used SmartJect™ autoinjectors and pre-filled syringes are provided to the patients through literature, website, and toll-free phone number as described above. Also a DVD video that explains Safe Returns is provided in the Patient Starter Kit and is available on the SIMPONI website. (Patient Starter Brochure and DVD are included in this submission.)

III. Coordination with regional and state sharps management efforts:

The SimponiOne Safe Returns program is available free to SIMPONI patients nationwide. We believe that the program meets the intent and requirements of local, regional, and state-level sharps management efforts. We will consider other opportunities to engage with the state and regional authorities on sharps management patient education.

IV. Consumer Involvement:

The SimponiOne Safe Returns program was developed using Market Research and feedback data from patients and health care professionals. Feedback on returns is tracked weekly and reviewed monthly. We reach out to patients through surveys. We also involved stakeholders such as representatives from the medical waste disposal companies and the US postal service in the program development. Since the program was launched in late 2009, Centocor Ortho Biologics has continued to monitor the patient enrollment and participation to look for opportunities for improvement.

SAFE RETURNS™ INSTRUCTION GUIDE


SimponiOne™
SAFE RETURNS™
Simple Safe Disposal. Only From SimponiOne.™

SimponiOne™ Safe Returns™

Here's a unique monthly service exclusively for people being treated with once-a-month SIMPONI™ (golimumab) that lets you:

- Properly and easily dispose of your used SmartJect™ autoinjector or used prefilled syringe
- Get them out of your home and off your mind right after you use them
- Receive a new Safe Returns™ pack every month
- Sign up at no additional cost to you!



SIMPONI™ is the first monthly self-injected anti-TNF therapy for adults with moderate to severe rheumatoid arthritis (RA) with the medicine methotrexate, active psoriatic arthritis (PsA) alone or with the medicine methotrexate, or active ankylosing spondylitis (AS). Once you and your doctor are comfortable with the self-injection process, you will inject SIMPONI™ once a month under the skin. Just one dose monthly works to relieve the signs and symptoms of RA, PsA, and AS. Results may not be the same for everyone.

Selected Important Safety Information

SIMPONI™ is not for everyone; only your doctor can decide if SIMPONI™ is right for you. SIMPONI™, like other medicines that affect your immune system, is a strong medicine that can cause serious side effects. Please read the Important Safety Information and the Medication Guide for SIMPONI™ that follow, and discuss any questions or symptoms with your doctor.

monthly 
Simponi™
golimumab

To sign up for Safe Returns™, call 877-MY SIMPONI (877-697-4676) or visit www.SimponiOne.com

MAIL-BACK INSTRUCTIONS

Your SimponiOneSM Safe ReturnsTM pack has everything you need to properly and easily dispose of one SmartJectTM autoinjector or one prefilled syringe — at no additional cost — after you've used it for your once-a-month dose of SIMPONITM (golimumab). When these instructions are properly followed, the mail-back box will meet all U.S. Postal Service regulations for mailing to a disposal site through the U.S. mail.



- A Outer shipping box
 - B Postage-paid mail-back box with liner
 - C Container tube
 - D Plastic bag
 - E Shipping document
- Appearance may vary slightly

1 When you receive your shipment:

Remove the SimponiOneSM Safe ReturnsTM pack (B) from the outer shipping box (A). The outer shipping box can then be thrown away. **Don't discard your postage-paid mail-back box or anything inside it.** Store it in a dry area.



2 How to use your SimponiOneSM Safe ReturnsTM pack

- You're ready to dispose of a SmartJectTM autoinjector or prefilled syringe after your once-a-month dose of SIMPONITM. Open the mail-back box and take out the plastic container tube (C) and the plastic bag (D).
- Place the used SmartJectTM autoinjector or used prefilled syringe in the container tube, with the injection end pointed away from you, and close the tube by screwing the cap on firmly. Make sure it is tight and secure.



3 Now you're ready to send in your postage-paid mail-back box

- Place the filled container tube into the plastic bag and close the bag securely by zipping it closed. Put the plastic bag into the postage-paid mail-back box.
- Take out the 4-part shipping document (E) from the plastic pouch on the outside of the mail-back box. **Don't damage the pouch** — the completed forms must be reinserted.
- Seal the box by peeling off the strip covering the tape on the inside flap. Close the lid and press firmly to seal the adhesive.
- **Shipping Document:** Confirm the information in Section 1 and make changes as needed. Sign where it says Generator Certificate. Remove the last copy of the document and keep it for your records (NJ residents keep first copy only). Then put the three remaining copies back into the pouch and close it.
- Mail the properly sealed Safe Returns™ box at a U.S. post office, or anywhere the U.S. Postal Service arranges pickups. You may also give it to your mail carrier for pickup.



PLEASE NOTE

- Don't put anything in your SimponiOneSM Safe Returns™ mail-back box other than one used SmartJect™ autoinjector or one used prefilled syringe, following the instructions above.
- Centocor Ortho Biotech Inc., the manufacturer of SIMPONI™ (golimumab), is not liable for anything shipped via Safe Returns™.
 - The total residual fluid is limited to 50 mL.
 - Total weight of the container is limited to 1 lb.

When your SimponiOneSM Safe Returns™ mail-back boxes are received for disposal, new Safe Returns™ packs will be sent to you regularly every month.

If you need to change your mailing information, or if you damage or misplace your pack and need to order a new one — or to learn more about SimponiOneSM Support services,

call 877-MY SIMPONI (877-697-4676) or visit www.SimponiOne.com.

REGULATORY NOTICE TO PATIENT REGARDING MAILING OF PACK: All patients must be aware that they are responsible for preparing the pack for mailing in accordance with the directions provided. No other materials may be placed in the pack for mailing. All original packaging materials provided must be utilized. Improper packaging or mailing of any other materials is in violation of Federal Postal Service Regulations and could be subject to action up to and including full prosecution of the laws of the Federal U.S. Postal Service. Should you have any questions or have any problems with the pack call **877-MY SIMPONI (877-697-4676)**.



IMPORTANT SAFETY INFORMATION

SIMPONI™ (golimumab) is a prescription medicine. SIMPONI™ can lower your ability to fight infections. There are reports of serious infections caused by bacteria, fungi, or viruses that have spread throughout the body, including tuberculosis (TB) and histoplasmosis. Some of these infections have been fatal. Your doctor will test you for TB before starting SIMPONI™ and will monitor you for signs of TB during treatment. Tell your doctor if you have been in close contact with people with TB. Tell your doctor if you have been in a region (such as the Ohio and Mississippi River Valleys and the Southwest) where certain fungal infections like histoplasmosis or coccidioidomycosis are common.

You should not start SIMPONI™ if you have any kind of infection. Tell your doctor if you are prone to or have a history of infections or have diabetes, HIV or a weak immune system. You should also tell your doctor if you are currently being treated for an infection or if you have or develop any signs of an infection such as:

- fever, sweat, or chills
- muscle aches
- cough
- shortness of breath
- blood in phlegm
- weight loss
- warm, red, or painful skin or sores on your body
- diarrhea or stomach pain
- burning when you urinate or urinate more than normal
- feel very tired

Unusual cancers have been reported in children and teenage patients taking TNF-blocker medicines. For children and adults taking TNF blockers, including SIMPONI™, the chances for getting lymphoma or other cancers may increase. You should tell your doctor if you have had or develop lymphoma or other cancers.

Tell your doctor about all the medications you take including ORENCIA (abatacept), KINERET (anakinra), RITUXAN (rituximab) or another TNF blocker, or if you are scheduled to or recently received a vaccine. People taking SIMPONI™ should not receive live vaccines.

Reactivation of hepatitis B virus has been reported in patients who are carriers of this virus and are taking TNF-blocker medicines, such as SIMPONI™. Some of these cases have been fatal. Your doctor may do blood tests before and after you start treatment with SIMPONI™. Tell your doctor if you know or think you may be a carrier of hepatitis B virus or if you experience signs of hepatitis B infection, such as:

- feel very tired
- skin or eyes look yellow
- little or no appetite
- vomiting
- muscle aches
- dark urine
- clay-colored bowel movements
- fevers
- chills
- stomach discomfort
- skin rash

Heart failure can occur or get worse in people who use TNF blockers like SIMPONI™. Your doctor will closely monitor you if you have heart failure. Tell your doctor right away if you get new or worsening symptoms of heart failure like shortness of breath or swelling of your lower legs or feet.

Rarely, people using TNF blockers can have nervous system problems such as multiple sclerosis. Tell your doctor right away if you have symptoms like vision changes, weakness in your arms or legs, or numbness or tingling in any part of your body.

Liver problems can happen in people using TNF blockers. Contact your doctor immediately if you develop symptoms such as feeling very tired, skin or eyes look yellow, poor appetite or vomiting, or pain on the right side of your stomach.

Low blood counts have been seen with people using TNF blockers. If this occurs, your body may not make enough blood cells to help fight infections or help stop bleeding. Your doctor will check your blood counts before and during treatment. Tell your doctor if you have signs such as fever, bruising, bleeding easily, or paleness.

Rarely, people using TNF blockers have developed lupus-like symptoms. Tell your doctor if you have any symptoms such as a rash on your cheeks or other parts of the body, sensitivity to the sun, new joint or muscle pain, becoming very tired, chest pain or shortness of breath, swelling of the feet, ankles, and/or legs.

New or worse psoriasis symptoms may occur. Tell your doctor if you develop red scaly patches or raised bumps that are filled with pus.

Tell your doctor if you are allergic to rubber or latex. The needle cover contains dry natural rubber.

Tell your doctor if you have any symptoms of an allergic reaction while taking SIMPONI™ such as hives, swollen face, breathing trouble, chest pain.

Common side effects of SIMPONI™ include: upper respiratory tract infection, nausea, abnormal liver tests, redness at site of injection, high blood pressure, bronchitis, dizziness, sinus infection, flu, runny nose, fever, cold sores, numbness, or tingling.

Please read the Medication Guide for SIMPONI™ that follows and discuss any questions you have with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.



Medication Guide

MEDICATION GUIDE SIMPONI™ (SIM-po-nee) (golimumab)

Read the Medication Guide that comes with SIMPONI before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your doctor about your medical condition or treatment. It is important to remain under your doctor's care while using SIMPONI.

What is the most important information I should know about SIMPONI?

SIMPONI is a medicine that affects your immune system. SIMPONI can lower the ability of your immune system to fight infections. Some people have serious infections while taking SIMPONI, including tuberculosis (TB), and infections caused by bacteria, fungi, or viruses that spread throughout their body. Some people have died from these serious infections.

- Your doctor should test you for TB before starting SIMPONI.
- Your doctor should monitor you closely for signs and symptoms of TB during treatment with SIMPONI.

You should not start taking SIMPONI if you have any kind of infection unless your doctor says it is okay.

Before starting SIMPONI, tell your doctor if you:

- think you have an infection or have symptoms of an infection such as:
 - fever, sweat, or chills
 - muscle aches
 - cough
 - shortness of breath
 - blood in phlegm
 - weight loss
 - warm, red, or painful skin or sores on your body
 - diarrhea or stomach pain
 - burning when you urinate or urinate more often than normal
 - feel very tired
- are being treated for an infection
- get a lot of infections or have infections that keep coming back
- have diabetes, HIV, or a weak immune system. People with these conditions have a higher chance for infections.
- have TB, or have been in close contact with someone with TB
- live, have lived, or traveled to certain parts of the country (such as the Ohio and Mississippi River valleys and the Southwest) where there is an increased chance for getting certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis). These infections may happen or become more severe if you use SIMPONI. Ask your doctor, if you do not know if you have lived in an area where these infections are common.
- have or have had hepatitis B
- use the medicine Orenzia (abatacept), Kineret (anakinra), or Rituxan (rituximab)

After starting SIMPONI, call your doctor right away if you have any symptoms of an infection. SIMPONI can make you more likely to get infections or make worse any infection that you have.

Cancer

- There have been cases of unusual cancers in children and teenage patients taking TNF-blocking agents.
- For children and adults taking TNF-blocker medicines, including SIMPONI, the chances of getting lymphoma or other cancers may increase.
- People with inflammatory diseases including rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis, especially those with very active disease, may be more likely to get lymphoma.

What is SIMPONI?

SIMPONI is a prescription medicine called a tumor necrosis factor (TNF) blocker. SIMPONI is used in adults:

- with the medicine methotrexate to treat moderately to severely active rheumatoid arthritis (RA)
- to treat active psoriatic arthritis (PsA) alone or with methotrexate
- to treat active ankylosing spondylitis (AS)

You may continue to use other medicines that help treat your condition while taking SIMPONI, such as non-steroidal anti-inflammatory drugs (NSAIDs) and prescription steroids, as recommended by your doctor.

What should I tell my doctor before starting treatment with SIMPONI?

SIMPONI may not be right for you. Before starting SIMPONI, tell your doctor about all your medical conditions, including if you:

- have an infection (see “**What is the most important information I should know about SIMPONI?**”).
- have or have had lymphoma or any other type of cancer.
- have or had heart failure.
- have or have had a condition that affects your nervous system, such as multiple sclerosis.
- have recently received or are scheduled to receive a vaccine. People taking SIMPONI should not receive live vaccines. People taking SIMPONI can receive non-live vaccines.
- are allergic to rubber or latex. The needle cover on the prefilled syringe and SmartJect autoinjector contains dry natural rubber.
- are pregnant or planning to become pregnant. It is not known if SIMPONI will harm your unborn baby.
- are breastfeeding. You and your doctor should decide if you will take SIMPONI or breastfeed. You should not do both without talking to your doctor first.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Especially, tell your doctor if you use:

- ORENCIA (abatacept), KINERET (anakinra), or RITUXAN (rituximab). You should not take SIMPONI while you are also taking ORENCIA or KINERET. Your doctor may not want to give you SIMPONI if you have received RITUXAN recently.
- Another TNF-blocker medicine. You should not take SIMPONI while you are also taking REMICADE (infliximab), HUMIRA (adalimumab), ENBREL (etanercept), or CIMZIA (certolizumab pegol).

Ask your doctor if you are not sure if your medicine is one listed above.

Keep a list of all your medications with you to show your doctor and pharmacist each time you get a new medicine.

How should I use SIMPONI?

- SIMPONI is given as an injection under the skin (subcutaneous injection or SC).
- SIMPONI should be injected one time each month.
- If your doctor decides that you or a caregiver may be able to give your injections of SIMPONI at home, you should receive training on the right way to prepare and inject SIMPONI. Do not try to inject SIMPONI yourself until you have been shown the right way to give the injections by your doctor or nurse.
- Use SIMPONI exactly as prescribed by your doctor.
- SIMPONI comes in a prefilled syringe or SmartJect autoinjector. Your doctor will prescribe the type that is best for you.
- See the detailed **Patient Instructions for Use** at the end of this Medication Guide for instructions about the right way to prepare and give your SIMPONI injections at home.
- Do not miss any doses of SIMPONI. If you forget to use

SIMPONI, inject your dose as soon as you remember. Then, take your next dose at your regular scheduled time. In case you are not sure when to inject SIMPONI, call your doctor or pharmacist.

What are the possible side effects with SIMPONI?

SIMPONI can cause serious side effects, including:

See “What is the most important information I should know about SIMPONI?”

Serious Infections

Hepatitis B infection in people who carry the virus in their blood.

• If you are a carrier of the hepatitis B virus (a virus that affects the liver), the virus can become active while you use SIMPONI. Your doctor may do blood tests before you start treatment with SIMPONI and while you are using SIMPONI. Tell your doctor if you have any of the following symptoms of a possible hepatitis B infection:

- feel very tired
- skin or eyes look yellow
- little or no appetite
- vomiting
- muscle aches
- dark urine
- clay-colored bowel movements
- fevers
- chills
- stomach discomfort
- skin rash

Heart failure, including new heart failure or worsening of heart failure that you already have.

New or worse heart failure can happen in people who use TNF-blocker medicines like SIMPONI.

- If you have heart failure, your condition should be watched closely while you take SIMPONI.
- Call your doctor right away if you get new or worsening symptoms of heart failure while taking SIMPONI (such as shortness of breath or swelling of your lower legs or feet).

Nervous System Problems

Rarely, people using TNF-blocker medicine have nervous system problems such as multiple sclerosis.

- Tell your doctor right away if you get any of these symptoms:
 - vision changes
 - weakness in your arms or legs
 - numbness or tingling in any part of your body

Liver Problems

Liver problems can happen in people who use TNF blocker medicines, including SIMPONI. These problems can lead to liver failure and death. Call your doctor right away if you have any of these symptoms:

- feel very tired
- skin or eyes look yellow
- poor appetite or vomiting
- pain on the right side of your stomach (abdomen)

Blood Problems

Low blood counts have been seen with other TNF blockers. Your body may not make enough blood cells that help fight infections or help stop bleeding. Symptoms include fever, bruising or bleeding easily, or looking pale. Your doctor will check your blood counts before and during treatment with SIMPONI.

Common side effects with SIMPONI include:

- upper respiratory tract infection
- nausea
- abnormal liver tests
- redness at the site of injection
- high blood pressure
- bronchitis
- dizziness
- sinus infection (sinusitis)
- flu
- runny nose
- fever
- cold sores
- numbness or tingling

Other side effects with SIMPONI include:

- **Immune System Problems.** Rarely, people using TNF-blocker

medicines have developed symptoms that are like the symptoms of lupus. Tell your doctor if you have any of these symptoms:

- a rash on your cheeks or other parts of the body
- sensitivity to the sun
- new joint or muscle pains
- becoming very tired
- chest pain or shortness of breath
- swelling of the feet, ankles, and/or legs
- **Psoriasis.** Some people using SIMPONI had new psoriasis or worsening of psoriasis they already had. Tell your doctor if you develop red scaly patches or raised bumps that are filled with pus. Your doctor may decide to stop your treatment with SIMPONI.
- **Allergic Reactions.** Allergic reactions can happen in people who use TNF-blocker medicines. Call your doctor right away if you have any of these symptoms of an allergic reaction:
 - hives
 - swollen face
 - breathing trouble
 - chest pain

These are not all of the side effects with SIMPONI. Tell your doctor about any side effect that bothers you or does not go away. Call your doctor for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

How do I store SIMPONI?

- Refrigerate SIMPONI at 36°F to 46°F (2°C to 8°C).
- Do not freeze SIMPONI.
- Keep SIMPONI in the carton to protect it from light when not being used.
- Do not shake SIMPONI.

Keep SIMPONI and all medicines out of the reach of children.

General Information about SIMPONI

- Medicines are sometimes prescribed for purposes other than those listed in the Medication Guide. Do not use SIMPONI for a condition for which it was not prescribed.
- Do not give SIMPONI to other people, even if they have the same condition that you have. It may harm them.
- This Medication Guide summarizes the most important information about SIMPONI. If you would like more information, talk to your doctor. You can ask your doctor or pharmacist for information about SIMPONI that is written for health professionals. For more information go to www.simponi.com or call 1-800-457-6399.

What are the ingredients in SIMPONI?

Active ingredient: golimumab.

Inactive ingredients: L-histidine, L-histidine monohydrochloride monohydrate, sorbitol, polysorbate 80, and water for injection.

SIMPONI does not contain preservatives.

Manufactured by:

Centocor Ortho Biotech Inc.
Horsham, PA 19044
US License No. 1821

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25GL09421

This Medication Guide has been approved by the U.S. Food and Drug Administration.



Simpsoni[™]
golimumab

A HELPING HAND FOR SHARPS DISPOSAL



SimponiOneSM Safe ReturnsTM is a unique monthly service offered only to patients being treated with **SIMPONITM**.

SimponiOneSM Safe ReturnsTM allows your patients to properly and easily dispose of their used **SIMPONITM SmartJectTM** autoinjectors or used **SIMPONITM** prefilled syringes at no additional cost—right after they use them.

ONCE A MONTH



RECEIVE a Safe ReturnsTM pack.



FOLLOW instructions on how to return your used autoinjector or used prefilled syringe.



MAIL the box back to us. We'll take care of the rest.

Serious and sometimes fatal side effects have been reported with SIMPONITM (golimumab), including infections due to tuberculosis, invasive fungal infections (eg, histoplasmosis), bacterial, viral, or other opportunistic pathogens. Prior to initiating SIMPONITM and periodically during therapy, patients should be evaluated for active tuberculosis and tested for latent infection. Lymphoma and other malignancies, some fatal, can occur in adults and children. Other serious risks include hepatitis B reactivation, heart failure and demyelinating disorders. Please see related and other Important Safety Information on reverse side.

Healthcare provider benefits

- Assists your patients with a sharps disposal solution
- Helps you provide reassurance to patients who are concerned about disposing of their used SIMPONITM SmartJectTM autoinjectors or used SIMPONITM prefilled syringes
- Requires no additional involvement on your part

Patient benefits

- The service is provided at no additional cost as part of SimponiOneSM Support Services
- Patients enroll via www.SimponiOne.com or the SimponiOneSM support line at **877-MY-SIMPONI (877-697-4676)**
- Patients receive a monthly SimponiOneSM Safe ReturnsTM pack with a postage-paid mail-back box to return that month's used SIMPONITM SmartJectTM autoinjector or used SIMPONITM prefilled syringe
- A new Safe ReturnsTM pack will be shipped to patients in time for each month's dose of SIMPONITM, serving as an appropriate sharps disposal method

SIMPONITM is indicated for the treatment of¹:

- Moderately to severely active **RHEUMATOID ARTHRITIS** in adults, in combination with methotrexate
- Active **PSORIATIC ARTHRITIS** in adults, alone or in combination with methotrexate
- Active **ANKYLOSING SPONDYLITIS** in adults

SIMPONITM is administered by 50 mg subcutaneous injection once a month.¹

- SIMPONITM is intended for use under the guidance and supervision of a physician. Patients may self-inject with SIMPONITM after physician approval and proper training



Simple Safe Disposal. Only From SimponiOneSM.

IMPORTANT SAFETY INFORMATION FOR SIMPONI™ (GOLIMUMAB)

SERIOUS INFECTIONS

Patients treated with SIMPONI™ (golimumab) are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Discontinue SIMPONI™ if a patient develops a serious infection.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before SIMPONI™ use and during therapy. Treatment for latent infection should be initiated prior to SIMPONI™ use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens.**

The risks and benefits of treatment with SIMPONI™ should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Do not start SIMPONI™ in patients with clinically important active infections, including localized infections. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with SIMPONI™, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

Other serious infections observed in patients treated with SIMPONI™ included sepsis, pneumonia, cellulitis, abscess and hepatitis B infection.

MALIGNANCIES

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers of which SIMPONI™ is a member. Approximately half the cases were lymphomas, including Hodgkin's and non-Hodgkin's lymphoma. The other cases represented a variety of malignancies, including rare malignancies usually associated with immunosuppression and malignancies not usually observed in children or adolescents. Malignancies occurred after a median of 30 months after the first dose of therapy. Most of the patients were receiving concomitant immunosuppressants.

In the controlled portions of clinical trials of all TNF-blocking agents including SIMPONI™, more cases of lymphoma have been observed among patients receiving TNF-blocking treatment compared with control patients. In clinical trials, the incidence of lymphoma per 100 patient-years of follow-up was 0.21 (95% CI: 0.03, 0.77) in the combined SIMPONI™ group compared with an incidence of 0 (95% CI: 0, 0.96) in the placebo group. In clinical trials, the incidence of malignancies other than lymphoma was not increased with exposure to SIMPONI™ and was similar to what would be expected in the general population. Cases of acute and chronic leukemia have been reported with postmarketing TNF-blocker use. The risks and benefits of TNF-blocker therapy should be considered prior to initiating therapy in patients with a known malignancy or who develop a malignancy.

HEPATITIS B REACTIVATION

The use of TNF-blocking agents including SIMPONI™ has been associated with reactivation of hepatitis B virus (HBV) in patients who

are chronic hepatitis B carriers. In some instances, HBV reactivation occurring in conjunction with TNF-blocker therapy has been fatal. The majority of these reports have occurred in patients who received concomitant immunosuppressants.

Patients at risk for HBV infection should be evaluated for prior evidence of HBV infection before initiating SIMPONI™. Exercise caution when prescribing SIMPONI™ for patients identified as carriers of HBV and closely monitor for active HBV infection during and following termination of therapy with SIMPONI™. Discontinue SIMPONI™ in patients who develop HBV reactivation, and initiate antiviral therapy with appropriate supportive treatment. Exercise caution when considering resumption of SIMPONI™, and monitor patients closely.

HEART FAILURE

Cases of worsening congestive heart failure (CHF) and new-onset CHF have been reported with TNF blockers. Exercise caution and monitor patients with heart failure. Discontinue SIMPONI™ if new or worsening symptoms of heart failure appear.

DEMYELINATING DISORDERS

TNF-blocking agents have been associated with cases of new-onset or exacerbation of central nervous system demyelinating disorders, including multiple sclerosis. Exercise caution in considering the use of SIMPONI™ in patients with central nervous system demyelinating disorders.

HEMATOLOGIC CYTOPENIAS

There have been postmarketing reports of pancytopenia, leukopenia, neutropenia, aplastic anemia, and thrombocytopenia in patients receiving TNF blockers. Exercise caution when using SIMPONI™ in patients with significant cytopenias.

USE WITH OTHER DRUGS

The concomitant use of a TNF blocker and abatacept or anakinra was associated with a higher risk of serious infections, therefore the use of SIMPONI™ in combination with these products is not recommended. A higher rate of serious infections has also been observed in RA patients treated with rituximab who received subsequent treatment with a TNF blocker. People receiving SIMPONI™ can receive vaccinations, except for live vaccines.

ADVERSE REACTIONS

The most serious adverse reactions were serious infections and malignancies.

Upper respiratory tract infection and nasopharyngitis were the most common adverse reactions reported in the combined Phase 3 trials through Week 16, occurring in 7% and 6% of patients treated with SIMPONI™ as compared with 6% and 5% of patients in the control group, respectively. The rate of injection-site reactions was 6% with patients treated with SIMPONI™ compared with 2% of patients in the control group.

Cases of new-onset psoriasis, including pustular and palmoplantar, or exacerbation of pre-existing psoriasis have been reported with the use of TNF blockers, including SIMPONI™. Some of these patients required hospitalization. Most patients had improvement following discontinuation of the TNF blocker. Discontinuation of SIMPONI™ should be considered for severe cases and those that do not improve or that worsen despite topical treatments.

Please see accompanying full Prescribing Information and Medication Guide for SIMPONI™. Provide the Medication Guide to your patients and encourage discussion.

Reference: 1. SIMPONI™ (golimumab) Prescribing Information. Centocor Ortho Biotech Inc.

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