

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**125289**

**LABELING**

4/24/09

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use SIMPONI (golimumab) safely and effectively. See full prescribing information for SIMPONI.

**SIMPONI (golimumab)**

Injection, solution for subcutaneous use

Initial U.S. Approval: 2009

**WARNING: RISK OF SERIOUS INFECTIONS**  
*See full prescribing information for complete boxed warning*

- Serious infections leading to hospitalization or death including tuberculosis (TB), bacterial sepsis, invasive fungal, and other opportunistic infections have occurred in patients receiving SIMPONI (5.1).
- SIMPONI should be discontinued if a patient develops a serious infection or sepsis (5.1).
- Perform test for latent TB; if positive, start treatment for TB prior to starting SIMPONI (5.1).
- Monitor all patients for active TB during treatment, even if initial latent TB test is negative (5.1)

-----**INDICATIONS AND USAGE**-----

SIMPONI is a tumor necrosis factor (TNF) blocker indicated for the treatment of:

- Moderately to severely active Rheumatoid Arthritis (RA) in adults, in combination with methotrexate (1.1)
- Active Psoriatic Arthritis (PsA) in adults, alone or in combination with methotrexate (1.2)
- Active Ankylosing Spondylitis in adults (AS) (1.3)

-----**DOSAGE AND ADMINISTRATION**-----

Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis (2.1)

- 50 mg administered by subcutaneous injection once a month.

-----**DOSAGE FORMS AND STRENGTHS**-----

- 50 mg/0.5 mL in a single dose prefilled SmartJect autoinjector (3)
- 50 mg/0.5 mL in a single dose prefilled syringe (3)

-----**CONTRAINDICATIONS**-----

- None (4)

-----**WARNINGS AND PRECAUTIONS**-----

- Serious Infections – Do not start SIMPONI during an active infection. If an infection develops, monitor carefully, and stop SIMPONI if infection becomes serious (5.1).
- Invasive fungal infections – For patients who develop a systemic illness on SIMPONI, consider empiric antifungal therapy for those who reside or travel to regions where mycoses are endemic (5.1).
- Hepatitis B reactivation – Monitor HBV carriers during and several months after therapy. If reactivation occurs, stop SIMPONI and begin anti-viral therapy (5.1).
- Malignancies – The incidence of lymphoma was seen more often than in the general U.S. population. Cases of other malignancies have been observed among patients receiving TNF-blockers (5.2).
- Heart failure – Worsening, or new onset, may occur. Stop SIMPONI if new or worsening symptoms occur (5.3).
- Demyelinating disease, exacerbation or new onset, may occur (5.4).

-----**ADVERSE REACTIONS**-----

Most common adverse reactions (incidence > 5%): upper respiratory tract infection, nasopharyngitis (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Centocor Ortho Biotech Inc. at 1-800-457-6399 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

-----**DRUG INTERACTIONS**-----

- Abatacept – increased risk of serious infection (5.1, 5.5, 7.2)
- Anakinra – increased risk of serious infection (5.1, 5.6, 7.2).
- Live vaccines – should not be given with SIMPONI (5.8, 7.3).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 4/2009

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## FULL PRESCRIBING INFORMATION

### WARNING RISK OF SERIOUS INFECTIONS

Patients treated with SIMPONI™ are at increased risk for developing serious infections that may lead to hospitalization or death [see *Warnings and Precautions (5.1)*]. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

SIMPONI should be discontinued if a patient develops a serious infection.

Reported infections include:

- Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis 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. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered 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.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with SIMPONI, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy [see *Warning and Precautions (5.1)*].

## 1.0 INDICATIONS AND USAGE

### 1.1 Rheumatoid Arthritis

SIMPONI, in combination with methotrexate, is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis.

## **1.2 Psoriatic Arthritis**

SIMPONI, alone or in combination with methotrexate, is indicated for the treatment of adult patients with active psoriatic arthritis.

## **1.3 Ankylosing Spondylitis**

SIMPONI is indicated for the treatment of adult patients with active ankylosing spondylitis.

## **2.0 DOSAGE AND ADMINISTRATION**

### **2.1 Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis**

The SIMPONI dose regimen is 50 mg administered by subcutaneous (SC) injection once a month.

For patients with rheumatoid arthritis (RA), SIMPONI should be given in combination with methotrexate and for patients with psoriatic arthritis (PsA) or ankylosing spondylitis (AS), SIMPONI may be given with or without methotrexate or other non-biologic DMARDs. For patients with RA, PsA, or AS, corticosteroids, non-biologic DMARDs, and/or NSAIDs may be continued during treatment with SIMPONI.

### **2.2 Monitoring to Assess Safety**

Prior to initiating SIMPONI and periodically during therapy, patients should be evaluated for active tuberculosis and tested for latent infection [*see Warnings and Precautions (5.1)*].

### **2.3 General Considerations for Administration**

SIMPONI is intended for use under the guidance and supervision of a physician. After proper training in subcutaneous injection technique, a patient may self inject with SIMPONI if a physician determines that it is appropriate. Patients should be instructed to follow the directions provided in the Medication Guide [*see Medication Guide (17.3)*]. To ensure proper use, allow the prefilled syringe or autoinjector to sit at room temperature outside the carton for 30 minutes prior to subcutaneous injection. Do not warm SIMPONI in any other way.

Prior to administration, visually inspect the solution for particles and discoloration through the viewing window. SIMPONI should be clear to slightly opalescent and colorless to light yellow. The solution should not be used if discolored, or cloudy, or if foreign particles are present. Any leftover product remaining in the prefilled syringe or prefilled autoinjector should not be used. NOTE: The needle cover on the prefilled syringe as well as the prefilled syringe in the autoinjector contains dry natural rubber (a derivative of latex), which should not be handled by persons sensitive to latex.

Injection sites should be rotated and injections should never be given into areas where the skin is tender, bruised, red, or hard.

### 3.0 DOSAGE FORMS AND STRENGTHS

#### SmartJect™ Autoinjector

Each single dose SmartJect autoinjector contains a prefilled glass syringe (27 gauge ½ inch) providing 50 mg of SIMPONI per 0.5 mL of solution.

#### Prefilled Syringe

Each single dose prefilled glass syringe (27 gauge ½ inch) contains 50 mg of SIMPONI per 0.5 mL of solution.

### 4.0 CONTRAINDICATIONS

None.

### 5.0 WARNINGS AND PRECAUTIONS (see Boxed WARNINGS)

#### 5.1 Serious Infections

Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, protozoal, or other opportunistic pathogens have been reported in patients receiving TNF-blockers including SIMPONI. Among opportunistic infections, tuberculosis, histoplasmosis, aspergillosis, candidiasis, coccidioidomycosis, listeriosis, and pneumocystosis were the most commonly reported with TNF-blockers. Patients have frequently presented with disseminated rather than localized disease, and were often taking concomitant immunosuppressants such as methotrexate or corticosteroids. The concomitant use of a TNF-blocker and abatacept or anakinra was associated with a higher risk of serious infections; therefore, the concomitant use of SIMPONI and these biologic products is not recommended [*see Warning and Precautions (5.5, 5.6) and Drug Interactions (7.2)*].

Treatment with SIMPONI should not be initiated in patients with an active infection, including clinically important localized infections. The risks and benefits of treatment should be considered prior to initiating SIMPONI in patients:

- with chronic or recurrent infection;
- who have been exposed to tuberculosis;
- with a history of an opportunistic infection;
- who have resided or traveled in areas of endemic tuberculosis or endemic mycoses, such as histoplasmosis, coccidioidomycosis, or blastomycosis; or
- with underlying conditions that may predispose them to infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with SIMPONI. SIMPONI should be discontinued if a patient develops a serious infection, an opportunistic infection, or sepsis. A patient who develops a new infection during treatment with SIMPONI should undergo a prompt and complete diagnostic workup appropriate for an immunocompromised patient, appropriate antimicrobial therapy should be initiated, and the patient should be closely monitored.

In controlled Phase 3 trials through Week 16 in patients with RA, PsA, and AS, serious infections were observed in 1.4% of SIMPONI-treated patients and 1.3% of control-treated patients. In the

controlled Phase 3 trials through Week 16 in patients with RA, PsA, and AS, the incidence of serious infections per 100 patient-years of follow-up was 5.4 (95% CI: 4.0, 7.2) for the SIMPONI group and 5.3 (95% CI: 3.1, 8.7) for the placebo group. Serious infections observed in SIMPONI-treated patients included sepsis, pneumonia, cellulitis, abscess, tuberculosis, invasive fungal infections, and hepatitis B infection.

### **Tuberculosis**

Cases of reactivation of tuberculosis or new tuberculosis infections have been observed in patients receiving TNF-blockers, including patients who have previously received treatment for latent or active tuberculosis. Patients should be evaluated for tuberculosis risk factors and tested for latent infection prior to initiating SIMPONI and periodically during therapy.

Treatment of latent tuberculosis infection prior to therapy with TNF-blockers has been shown to reduce the risk of tuberculosis reactivation during therapy. Induration of 5 mm or greater with tuberculin skin testing should be considered a positive test result when assessing if treatment for latent tuberculosis is needed prior to initiating SIMPONI, even for patients previously vaccinated with Bacille Calmette-Guerin (BCG).

Anti-tuberculosis therapy should also be considered prior to initiation of SIMPONI in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent tuberculosis but having risk factors for tuberculosis infection. Consultation with a physician with expertise in the treatment of tuberculosis is recommended to aid in the decision whether initiating anti-tuberculosis therapy is appropriate for an individual patient.

Patients should be closely monitored for the development of signs and symptoms of tuberculosis including patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Tuberculosis should be strongly considered in patients who develop a new infection during SIMPONI treatment, especially in patients who have previously or recently traveled to countries with a high prevalence of tuberculosis, or who have had close contact with a person with active tuberculosis.

In the controlled and uncontrolled portions of the Phase 2 RA and Phase 3 RA, PsA, and AS trials, the incidence of active TB was 0.23 and 0 per 100 patient-years in 2347 SIMPONI-treated patients and 674 placebo-treated patients, respectively. Cases of TB included pulmonary and extra pulmonary TB. The overwhelming majority of the TB cases occurred in countries with a high incidence rate of TB.

### **Invasive Fungal Infections**

For SIMPONI-treated patients who reside or travel in regions where mycoses are endemic, invasive fungal infection should be suspected if they develop a serious systemic illness. Appropriate empiric antifungal therapy should be considered while a diagnostic workup is being performed. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. When feasible, the decision to administer empiric antifungal therapy in these patients should be made in consultation with a physician with expertise in the diagnosis and treatment of invasive fungal infections and should take into account both the risk for severe fungal infection and the risks of antifungal therapy.

### **Hepatitis B Virus Reactivation**

The use of TNF-blockers including SIMPONI has been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic hepatitis B carriers (i.e., surface antigen positive). 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 TNF-blocker therapy. The risks and benefits of treatment should be considered prior to prescribing TNF-blockers, including SIMPONI, to patients who are carriers of HBV. Adequate data are not available on whether anti-viral therapy can reduce the risk of HBV reactivation in HBV carriers who are treated with TNF-blockers. Patients who are carriers of HBV and require treatment with TNF-blockers should be closely monitored for clinical and laboratory signs of active HBV infection throughout therapy and for several months following termination of therapy.

In patients who develop HBV reactivation, TNF-blockers should be stopped and antiviral therapy with appropriate supportive treatment should be initiated. The safety of resuming TNF-blockers after HBV reactivation has been controlled is not known. Therefore, prescribers should exercise caution when considering resumption of TNF-blockers in this situation and monitor patients closely.

### **5.2 Malignancies**

The risks and benefits of TNF-blocker treatment including SIMPONI should be considered prior to initiating therapy in patients with a known malignancy other than a successfully treated non-melanoma skin cancer (NMSC) or when considering continuing a TNF-blocker in patients who develop a malignancy.

In the controlled portions of clinical trials of TNF-blockers including SIMPONI, more cases of lymphoma have been observed among patients receiving anti-TNF treatment compared with patients in the control groups. During the controlled portions of the Phase 2 trials in RA, and the Phase 3 trials in RA, PsA and AS, 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 the controlled and uncontrolled portions of these clinical trials in 2347 SIMPONI-treated patients with a median follow-up of 1.4 years, the incidence of lymphoma was 3.8-fold higher than expected in the general U.S. population according to the SEER database (adjusted for age, gender, and race).<sup>1</sup> Patients with RA and other chronic inflammatory diseases, particularly patients with highly active disease and/or chronic exposure to immunosuppressant therapies, may be at higher risk (up to several fold) than the general population for the development of lymphoma, even in the absence of TNF-blocking therapy.

During the controlled portions of the Phase 2 trial in RA, and the Phase 3 trials in RA, PsA and AS, the incidence of malignancies other than lymphoma per 100 patient-years of follow-up was not elevated in the combined SIMPONI group compared with the placebo group. In the controlled and uncontrolled portions of these trials, the incidence of malignancies, other than lymphoma, in SIMPONI-treated patients was similar to that expected in the general U.S. population according to the SEER database (adjusted for age, gender, and race).<sup>1</sup>

In controlled trials of other TNF-blockers in patients at higher risk for malignancies (e.g., patients with COPD, patients with Wegener's granulomatosis treated with concomitant cyclophosphamide) a greater portion of malignancies occurred in the TNF-blocker group compared to the controlled group. In an exploratory 1-year clinical trial evaluating the use of 50, 100 and 200 mg of SIMPONI in 309 patients with severe persistent asthma, 6 patients developed malignancies other than NMSC in the SIMPONI groups compared to none in the control group. Three of the 6 patients were in the 200 mg SIMPONI group.

### **5.3 Congestive Heart Failure**

Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF-blockers. In several exploratory trials of other TNF-blockers in the treatment of CHF, there were greater proportions of TNF-blocker treated patients who had CHF exacerbations requiring hospitalization or increased mortality. SIMPONI has not been studied in patients with a history of CHF and SIMPONI should be used with caution in patients with CHF. If a decision is made to administer SIMPONI to patients with CHF, these patients should be closely monitored during therapy, and SIMPONI should be discontinued if new or worsening symptoms of CHF appear.

### **5.4 Demyelinating Disorders**

Use of TNF-blockers has been associated with cases of new onset or exacerbation of central nervous system (CNS) demyelinating disorders, including multiple sclerosis (MS). While no trials have been performed evaluating SIMPONI in the treatment of patients with MS, another TNF-blocker was associated with increased disease activity in patients with MS. Therefore, prescribers should exercise caution in considering the use of TNF-blockers including SIMPONI in patients with CNS demyelinating disorders including MS.

### **5.5 Use with Abatacept**

In controlled trials, the concurrent administration of another TNF-blocker and abatacept was associated with a greater proportion of serious infections than the use of a TNF-blocker alone; and the combination therapy, compared to the use of a TNF-blocker alone, has not demonstrated improved clinical benefit in the treatment of RA. Therefore, the combination of TNF-blockers including SIMPONI and abatacept is not recommended [*see Drug Interactions (7.2)*].

### **5.6 Use with Anakinra**

Concurrent administration of anakinra (an interleukin-1 antagonist) and another TNF-blocker, was associated with a greater portion of serious infections and neutropenia and no additional benefits compared with the TNF-blocker alone. Therefore, the combination of anakinra with TNF-blockers, including SIMPONI, is not recommended [*see Drug Interactions 7.2*].

### **5.7 Hematologic Cytopenias**

There have been post-marketing reports of pancytopenia, leukopenia, neutropenia, aplastic anemia, and thrombocytopenia in patients receiving TNF-blockers. Although, there were no cases of severe cytopenias seen in the SIMPONI clinical trials, caution should be exercised when using TNF-blockers, including SIMPONI, in patients who have significant cytopenias.

## 5.8 Vaccinations

Patients treated with SIMPONI may receive vaccinations, except for live vaccines. No data are available on the response to live vaccination or the risk of infection, or transmission of infection after the administration of live vaccines to patients receiving SIMPONI. In the Phase 3 PsA study, after pneumococcal vaccination, a similar proportion of SIMPONI-treated and placebo-treated patients were able to mount an adequate immune response of at least a 2-fold increase in antibody titers to pneumococcal polysaccharide vaccine. In both SIMPONI-treated and placebo-treated patients, the proportions of patients with response to pneumococcal vaccine were lower among patients receiving MTX compared with patients not receiving MTX. The data suggest that SIMPONI does not suppress the humoral immune response to the pneumococcal vaccine.

## 6.0 ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

### 6.1 Clinical Studies Experience

The safety data described below are based on 5 pooled, randomized, double-blind, controlled Phase 3 trials in patients with RA, PsA, and AS (Studies RA-1, RA-2, RA-3, PsA, and AS) [*see Clinical Studies (14.1, 14.2 and 14.3)*]. These 5 trials included 639 control-treated patients and 1659 SIMPONI-treated patients including 1089 with RA, 292 with PsA, and 278 with AS. The proportion of patients who discontinued treatment due to adverse reactions in the controlled Phase 3 trials through Week 16 in RA, PsA and AS was 2% for SIMPONI-treated patients and 3% for placebo-treated patients. The most common adverse reactions leading to discontinuation of SIMPONI in the controlled Phase 3 trials through Week 16 were sepsis (0.2%), alanine aminotransferase increased (0.2%), and aspartate aminotransferase increased (0.2%).

The most serious adverse reactions were:

- Serious Infections [*see Warnings and Precautions (5.1)*]
- Malignancies [*see Warnings and Precautions (5.2)*]

Upper respiratory tract infection and nasopharyngitis were the most common adverse reactions reported in the combined Phase 3 RA, PsA and AS trials through Week 16, occurring in 7% and 6% of SIMPONI-treated patients as compared with 6% and 5% of control-treated patients, respectively.

### Infections

In controlled Phase 3 trials through Week 16 in RA, PsA, and AS, infections were observed in 28% of SIMPONI-treated patients compared to 25% of control-treated patients [*for Serious Infections, see Warnings and Precautions (5.1)*].

### Liver Enzyme Elevations

There have been reports of severe hepatic reactions including acute liver failure in patients receiving TNF-blockers. In controlled Phase 3 trials of SIMPONI in patients with RA, PsA, and AS through Week 16, ALT elevations  $\geq 5 \times$  ULN occurred in 0.2% of control-treated patients and 0.7% of SIMPONI-treated patients and ALT elevations  $\geq 3 \times$  ULN occurred in 2% of control-treated patients and 2% of SIMPONI-treated patients. Since many of the patients in the Phase 3 trials were also taking

medications that cause liver enzyme elevations (e.g., NSAIDs, MTX), the relationship between golimumab and liver elevation is not clear.

#### **Autoimmune Disorders and Autoantibodies**

The use of TNF-blockers has been associated with the formation of autoantibodies and, rarely, with the development of a lupus-like syndrome. In the controlled Phase 3 trials in patients with RA, PsA, and AS through Week 14, there was no association of SIMPONI treatment and the development of newly positive anti-dsDNA antibodies.

#### **Injection Site Reactions**

In controlled Phase 3 trials through Week 16 in RA, PsA and AS, 6% of SIMPONI-treated patients had injection site reactions compared with 2% of control-treated patients. The majority of the injection site reactions were mild and the most frequent manifestation was injection site erythema. In controlled Phase 2 and 3 trials in RA, PsA, and AS, no patients treated with SIMPONI developed anaphylactic reactions.

#### **Psoriasis: New-Onset and Exacerbations**

Cases of new onset psoriasis, including pustular psoriasis and palmoplantar psoriasis, have been reported with the use of TNF-blockers, including SIMPONI. Cases of exacerbation of pre-existing psoriasis have also been reported with the use of TNF-blockers. Many of these patients were taking concomitant immunosuppressants (e.g., MTX, corticosteroids). Some of these patients required hospitalization. Most patients had improvement of their psoriasis following discontinuation of their TNF-blocker. Some patients have had recurrences of the psoriasis when they were re-challenged with a different TNF-blocker. Discontinuation of SIMPONI should be considered for severe cases and those that do not improve or that worsen despite topical treatments.

#### **Immunogenicity**

Antibodies to SIMPONI were detected in 57 (4%) of SIMPONI-treated patients across the Phase 3 RA, PsA and AS trials through Week 24. Similar rates were observed in each of the three indications. Patients who received SIMPONI with concomitant MTX had a lower proportion of antibodies to SIMPONI than patients who received SIMPONI without MTX (approximately 2% versus 7%, respectively). Of the patients with a positive antibody response to SIMPONI in the Phase 2 and 3 trials, most were determined to have neutralizing antibodies to golimumab as measured by a cell-based functional assay. The small number of patients positive for antibodies to SIMPONI limits the ability to draw definitive conclusions regarding the relationship between antibodies to golimumab and clinical efficacy or safety measures.

The data above reflect the percentage of patients whose test results were considered positive for antibodies to SIMPONI in an ELISA assay, and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors including sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to SIMPONI with the incidence of antibodies to other products may be misleading.

### Other Adverse Reactions

Table 1 summarizes the adverse drug reactions that occurred at a rate of at least 1% in the combined SIMPONI groups during the controlled period of the 5 pooled Phase 3 trials through Week 16 in patients with RA, PsA, and AS.

**Table 1. Adverse Drug Reactions Reported by  $\geq 1\%$  of Patients in the Phase 3 Trials of RA, PsA, and AS through Week 16<sup>a</sup>**

	Placebo $\pm$ DMARDs	SIMPONI $\pm$ DMARDs
Patients treated	639	1659
Adverse Reaction (Preferred Term)		
Upper respiratory tract infection	37 (6%)	120 (7%)
Nasopharyngitis	31 (5%)	91 (6%)
Alanine aminotransferase increased	18 (3%)	58 (4%)
Injection site erythema	6 (1%)	56 (3%)
Hypertension	9 (1%)	48 (3%)
Aspartate aminotransferase increased	10 (2%)	44 (3%)
Bronchitis	9 (1%)	31 (2%)
Dizziness	7 (1%)	32 (2%)
Sinusitis	7 (1%)	27 (2%)
Influenza	7 (1%)	25 (2%)
Pharyngitis	8 (1%)	22 (1%)
Rhinitis	4 (< 1%)	20 (1%)
Pyrexia	4 (< 1%)	20 (1%)
Oral herpes	2 (< 1%)	16 (1%)
Paraesthesia	2 (< 1%)	16 (1%)

a Patients may have taken concomitant MTX, sulfasalazine, hydroxychloroquine, low dose corticosteroids ( $\leq 10$  mg of prednisone/day or equivalent), and/or NSAIDs during the trials).

## 7.0 DRUG INTERACTIONS

### 7.1 Methotrexate

For the treatment of RA, SIMPONI should be used with methotrexate (MTX) [see *Clinical Studies (14.1)*]. Since the presence or absence of concomitant MTX did not appear to influence the efficacy or safety of SIMPONI in the treatment of PsA or AS, SIMPONI can be used with or without MTX in the treatment of PsA and AS [see *Clinical Studies (14.1)* and *Clinical Pharmacology (12.3)*].

## **7.2 Biologic Products for RA, PsA, and/or AS**

An increased risk of serious infections has been seen in clinical RA studies of other TNF-blockers used in combination with anakinra or abatacept, with no added benefit; therefore, use of SIMPONI with abatacept or anakinra is not recommended [see *Warnings and Precautions (5.5 and 5.6)*]. A higher rate of serious infections has also been observed in RA patients treated with rituximab who received subsequent treatment with a TNF-blocker. There is insufficient information to provide recommendations regarding the concomitant use of SIMPONI and other biologic products approved to treat RA, PsA, or AS.

## **7.3 Live Vaccines**

Live vaccines should not be given concurrently with SIMPONI [see *Warnings and Precautions (5.8)*].

## **7.4 Cytochrome P450 Substrates**

The formation of CYP450 enzymes may be suppressed by increased levels of cytokines (e.g., TNF $\alpha$ ) during chronic inflammation. Therefore, it is expected that for a molecule that antagonizes cytokine activity, such as golimumab, the formation of CYP450 enzymes could be normalized. Upon initiation or discontinuation of SIMPONI in patients being treated with CYP450 substrates with a narrow therapeutic index, monitoring of the effect (e.g., warfarin) or drug concentration (e.g., cyclosporine or theophylline) is recommended and the individual dose of the drug product may be adjusted as needed.

## **8.0 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

Pregnancy Category B – There are no adequate and well-controlled studies of SIMPONI in pregnant women. Because animal reproduction and developmental studies are not always predictive of human response, it is not known whether SIMPONI can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. SIMPONI should be used during pregnancy only if clearly needed.

An embryofetal developmental toxicology study was performed in which pregnant cynomolgus monkeys were treated subcutaneously with golimumab during the first trimester with doses up to 50 mg/kg twice weekly (360 times greater than the maximum recommended human dose-MHRD) and has revealed no evidence of harm to maternal animals or fetuses. Umbilical cord blood samples collected at the end of the second trimester showed that fetuses were exposed to golimumab during gestation. In this study, *in utero* exposure to golimumab produced no developmental defects to the fetus.

A pre- and post-natal developmental study was performed in which pregnant cynomolgus monkeys were treated with golimumab during the second and third trimesters, and during lactation at doses up to 50 mg/kg twice weekly (860 times and 310 times greater than the maximal steady state human blood levels for maternal animals and neonates, respectively) and has revealed no evidence of harm to maternal animals or neonates. Golimumab was present in the neonatal serum from the time of birth and for up to six months postpartum. Exposure to golimumab during gestation and during the postnatal period caused no developmental defects in the infants.

### **8.3 Nursing Mothers**

It is not known whether SIMPONI is excreted in human milk or absorbed systemically after ingestion. Because many drugs and immunoglobulins are excreted in human milk, and because of the potential for adverse reactions in nursing infants from SIMPONI, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

In the pre- and post-natal development study in cynomolgus monkeys in which golimumab was administered subcutaneously during pregnancy and lactation, golimumab was detected in the breast milk at concentrations that were approximately 400-fold lower than the maternal serum concentrations.

### **8.4 Pediatric Use**

Safety and effectiveness of SIMPONI in pediatric patients less than 18 years of age have not been established.

### **8.5 Geriatric Use**

In the Phase 3 trials in RA, PsA, and AS, there were no overall differences in SAEs, serious infections, and AEs in SIMPONI-treated patients ages 65 or older (N = 155) compared with younger SIMPONI-treated patients. Because there is a higher incidence of infections in the geriatric population in general, caution should be used in treating geriatric patients with SIMPONI.

## **10.0 OVERDOSAGE**

In a clinical study, 5 patients received protocol-directed single infusions of 10 mg/kg of intravenous SIMPONI without serious adverse reactions or other significant reactions. The highest weight patient was 100 kg, and therefore received a single intravenous infusion of 1000 mg of SIMPONI. There were no SIMPONI overdoses in the clinical studies.

## **11.0 DESCRIPTION**

SIMPONI (golimumab) is a human IgG1 $\kappa$  monoclonal antibody specific for human tumor necrosis factor alpha (TNF $\alpha$ ) that exhibits multiple glycoforms with molecular masses of approximately 150 to 151 kilodaltons. SIMPONI was created using genetically engineered mice immunized with human TNF, resulting in an antibody with human-derived antibody variable and constant regions. SIMPONI is produced by a recombinant cell line cultured by continuous perfusion and is purified by a series of steps that includes measures to inactivate and remove viruses.

The SIMPONI drug product is a sterile solution of the golimumab antibody supplied as either a single dose prefilled syringe (with a passive needle safety guard) or a single dose prefilled autoinjector. The Type 1 glass syringe has a coated stopper. The fixed stainless steel needle (5 bevel, 27G, half-inch) is covered with a needle shield to prevent leakage of the solution through the needle and to protect the needle during handling prior to administration. The needle shield is made of a dry natural rubber containing latex.

SIMPONI does not contain preservatives. The solution is clear to slightly opalescent, colorless to light yellow with a pH of approximately 5.5. SIMPONI is provided in one strength: 50 mg of the golimumab antibody in 0.5 mL of solution. Each 0.5 mL of SIMPONI contains 50 mg of the

golimumab antibody, 0.44 mg of L-histidine and L-histidine monohydrochloride monohydrate, 20.5 mg of sorbitol, 0.08 mg of polysorbate 80, and Water for Injection.

## 12.0 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Golimumab is a human monoclonal antibody that binds to both the soluble and transmembrane bioactive forms of human TNF $\alpha$ . This interaction prevents the binding of TNF $\alpha$  to its receptors, thereby inhibiting the biological activity of TNF $\alpha$  (a cytokine protein). There was no evidence of the golimumab antibody binding to other TNF superfamily ligands; in particular, the golimumab antibody did not bind or neutralize human lymphotoxin. Golimumab did not lyse human monocytes expressing transmembrane TNF in the presence of complement or effector cells.

Elevated TNF $\alpha$  levels in the blood, synovium, and joints have been implicated in the pathophysiology of several chronic inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. TNF $\alpha$  is an important mediator of the articular inflammation that is characteristic of these diseases. Golimumab modulated the *in vitro* biological effects mediated by TNF in several bioassays, including the expression of adhesion proteins responsible for leukocyte infiltration (E-selectin, ICAM-1 and VCAM-1) and the secretion of proinflammatory cytokines (IL-6, IL-8, G-CSF and GM-CSF).

### 12.2 Pharmacodynamics

In clinical studies, decreases in C-reactive protein (CRP), interleukin (IL)-6, matrix metalloproteinase 3 (MMP-3), intercellular adhesion molecule (ICAM)-1 and vascular endothelial growth factor (VEGF) were observed following SIMPONI administration in patients with RA, PsA, and AS.

### 12.3 Pharmacokinetics

Following subcutaneous (SC) administration of SIMPONI to healthy subjects and patients with active RA, the median time to reach maximum serum concentrations ( $T_{max}$ ) ranged from 2 to 6 days. A SC injection of 50 mg SIMPONI to healthy subjects produced a mean maximum serum concentration ( $C_{max}$ ) of approximately 2.5  $\mu\text{g/mL}$ . SIMPONI exhibited dose-proportional pharmacokinetics (PK) in patients with active RA over the dose range of 0.1 to 10.0 mg/kg following a single intravenous (IV) dose. Following a single IV administration over the same dose range in patients with active RA, mean systemic clearance of SIMPONI was estimated to be 4.9 to 6.7 mL/day/kg, and mean volume of distribution ranged from 58 to 126 mL/kg. The volume of distribution for SIMPONI indicates that SIMPONI is distributed primarily in the circulatory system with limited extravascular distribution. Median terminal half-life values were estimated to be approximately 2 weeks in healthy subjects and patients with active RA, PsA or AS. By cross-study comparisons of mean  $AUC_{inf}$  values following an IV or SC administration of SIMPONI, the absolute bioavailability of SC SIMPONI was estimated to be approximately 53%.

When 50 mg SIMPONI was administered SC to patients with RA, PsA or AS every 4 weeks, serum concentrations appeared to reach steady state by Week 12. With concomitant use of methotrexate (MTX), treatment with 50 mg SIMPONI SC every 4 weeks resulted in a mean steady-state trough serum concentration of approximately 0.4-0.6  $\mu\text{g/mL}$  in patients with active RA, approximately 0.5  $\mu\text{g/mL}$  in patients with active PsA, and approximately 0.8  $\mu\text{g/mL}$  in patients with active AS.

Patients with RA, PsA and AS treated with SIMPONI 50 mg and MTX had approximately 52%, 36% and 21% higher mean steady-state trough concentrations of golimumab, respectively compared with those treated with SIMPONI 50 mg without MTX. The presence of MTX also decreased anti-golimumab antibody incidence from 7% to 2% [see *Adverse Reactions (6.1)*]. For RA, SIMPONI should be used with MTX. In the PsA and AS trials, the presence or absence of concomitant MTX did not appear to influence clinical efficacy and safety parameters [see *Drug Interactions (7.1)* and *Clinical Studies (14.1)*].

Population PK analyses indicated that concomitant use of NSAIDs, oral corticosteroids, or sulfasalazine did not influence the apparent clearance of SIMPONI.

Population PK analyses showed there was a trend toward higher apparent clearance of SIMPONI with increasing weight. However, across the PsA and AS populations, no meaningful differences in clinical efficacy were observed among the subgroups by weight quartile. The RA trial in MTX-experienced and TNF-blocker-naïve patients (Study RA-2) did show evidence of a reduction in clinical efficacy with increasing body weight, but this effect was observed for both tested doses of SIMPONI (50 mg and 100 mg). Therefore, there is no need to adjust the dosage of SIMPONI based on a patient's weight.

Population PK analyses suggested no PK differences between male and female patients after body weight adjustment in the RA and PsA trials. In the AS trial, female patients showed 13% higher apparent clearance than male patients after body weight adjustment. Subgroup analysis based on gender showed that both female and male patients achieved clinically significant response at the proposed clinical dose. Dosage adjustment based on gender is not needed.

Population PK analyses indicated that PK parameters of SIMPONI were not influenced by age in adult patients. Patients with age  $\geq$  65 years had apparent clearance of SIMPONI similar to patients with age  $<$  65 years. No ethnicity-related PK differences were observed between Caucasians and Asians, and there were too few patients of other races to assess for PK differences.

Patients who developed anti-SIMPONI antibodies generally had lower steady-state serum trough concentrations of SIMPONI.

No formal study of the effect of renal or hepatic impairment on the PK of golimumab was conducted.

## **13.0 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Long-term animal studies of golimumab have not been conducted to evaluate its carcinogenic potential. Mutagenicity studies have not been conducted with golimumab. A fertility study conducted in mice using an analogous anti-mouse TNF $\alpha$  antibody showed no impairment of fertility.

## 14.0 CLINICAL STUDIES

### 14.1 Rheumatoid Arthritis

The efficacy and safety of SIMPONI were evaluated in 3 multicenter, randomized, double-blind, controlled trials (Studies RA-1, RA-2, and RA-3) in 1542 patients  $\geq$  18 years of age with moderately to severely active RA, diagnosed according to the American College of Rheumatology (ACR) criteria, for at least 3 months prior to administration of study agent. Patients were required to have at least 4 swollen and 4 tender joints. SIMPONI was administered subcutaneously at doses of 50 mg or 100 mg every 4 weeks. Double-blinded controlled efficacy data were collected and analyzed through Week 24. Patients were allowed to continue stable doses of concomitant low dose corticosteroids (equivalent to  $\leq$  10 mg of prednisone a day) and/or NSAIDs and patients may have received oral MTX during the trials.

Study RA-1 evaluated 461 patients who were previously treated (at least 8 to 12 weeks prior to administration of study agent) with one or more doses of a biologic TNF-blocker without a serious adverse reaction. Patients may have discontinued the biologic TNF-blocker for a variety of reasons. Patients were randomized to receive placebo (n = 155), SIMPONI 50 mg (n = 153), or SIMPONI 100 mg (n = 153). Patients were allowed to continue stable doses of concomitant MTX, sulfasalazine (SSZ), and/or hydroxychloroquine (HCQ) during the trial. The use of other DMARDs including cytotoxic agents or other biologics was prohibited.

Study RA-2 evaluated 444 patients who had active RA despite a stable dose of at least 15 mg/week of MTX and who had not been previously treated with a biologic TNF-blocker. Patients were randomized to receive background MTX (n = 133), SIMPONI 50 mg + background MTX (n = 89), SIMPONI 100 mg + background MTX (n = 89), or SIMPONI 100 mg monotherapy (n = 133). The use of other DMARDs including SSZ, HCQ, cytotoxic agents, or other biologics was prohibited.

Study RA-3 evaluated 637 patients with active RA who were MTX-naïve and had not previously been treated with a biologic TNF-blocker. Patients were randomized to receive MTX (n = 160), SIMPONI 50 mg + MTX (n = 159), SIMPONI 100 mg + MTX (n = 159), or SIMPONI 100 mg monotherapy (n = 159). For patients receiving MTX, MTX was administered at a dose of 10 mg/week beginning at Week 0 and increased to 20 mg/week by Week 8. The use of other DMARDs including SSZ, HCQ, cytotoxic agents, or other biologics was prohibited.

The primary endpoint in Study RA-1 and Study RA-2 was the percentage of patients achieving an ACR 20 response at Week 14 and the primary endpoint in Study RA-3 was the percentage of patients achieving an ACR 50 response at Week 24.

In Studies RA-1, RA-2, and RA-3, the median duration of RA disease was 9.4, 5.7, and 1.2 years; and 99%, 75%, and 54% of the patients used at least one DMARD in the past, respectively. Approximately 77% and 57% of patients received concomitant NSAIDs and low dose corticosteroids, respectively, in the 3 pooled RA trials.

#### Clinical Response

In the 3 RA trials, a greater percentage of patients treated with the combination of SIMPONI and MTX achieved ACR responses at Week 14 (Studies RA-1 and RA-2) and Week 24 (Studies RA-1,

RA-2, and RA-3) versus patients treated with the MTX alone. There was no clear evidence of improved ACR response with the higher SIMPONI dose group (100 mg) compared to the lower SIMPONI dose group (50 mg). In Studies RA-2 and RA-3, the SIMPONI monotherapy groups were not statistically different from the MTX monotherapy groups in ACR responses. Table 2 shows the proportion of patients with the ACR response for the SIMPONI 50 mg and control groups in Studies RA-1, RA-2, and RA-3. In the subset of patients who received SIMPONI in combination with MTX in Study RA-1, the proportion of patients achieving ACR 20, 50 and 70 responses at wWeek 14 were 40%, 18%, and 13%, respectively, in the SIMPONI 50 mg + MTX group (N = 103) compared with 17%, 6%, and 2%, respectively, in the placebo + MTX group (N = 107). Table 3 shows the percent improvement in the components of the ACR response criteria for the SIMPONI 50 mg + MTX and MTX groups in Study RA-2. The percent of patients achieving ACR 20 responses by visit for Study RA-2 is shown in Figure 1. ACR 20 responses were observed in 38% of patients in the SIMPONI 50 mg + MTX group at the first assessment (Week 4) after the initial SIMPONI administration.

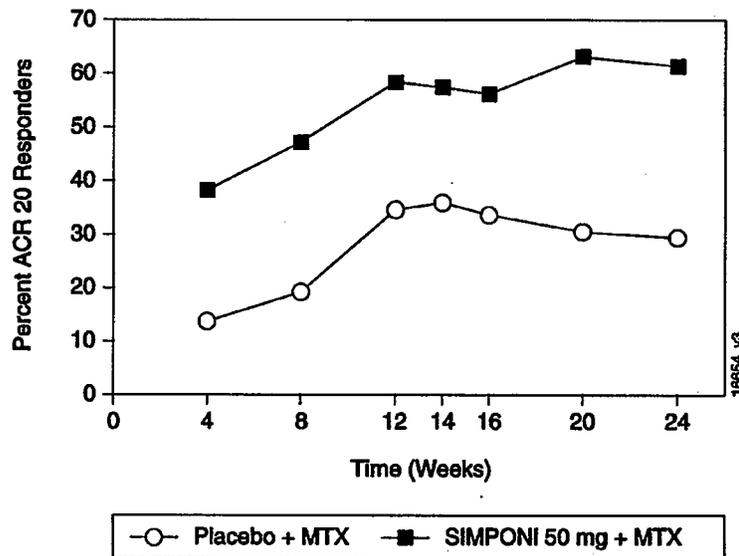
**Table 2. Studies RA-1, RA-2, and RA-3 Proportion of Patients with an ACR Response<sup>a</sup>**

	Study RA-1 Active RA previously treated with one or more doses of TNF-blockers		Study RA-2 Active RA, despite MTX		Study RA-3 Active RA, MTX Naïve	
	Placebo ± DMARDs <sup>b</sup>	SIMPONI 50 mg ± DMARDs <sup>b</sup>	Background MTX	SIMPONI 50 mg + Background MTX	MTX	SIMPONI 50 mg + MTX
N <sup>c</sup>	155	153	133	89	160	159
<b>ACR 20</b>						
Week 14	18%	35%	33%	55%	NA	NA
Week 24	17%	34%	28%	60%	49%	62%
<b>ACR 50</b>						
Week 14	6%	16%	10%	35%	NA	NA
Week 24	5%	18%	14%	37%	29%	40%
<b>ACR 70</b>						
Week 14	2%	10%	4%	13%	NA	NA
Week 24	3%	12%	5%	20%	16%	24% <sup>d</sup>
a	Approximately 78% and 58% of the patients received concomitant low dose corticosteroids (equivalent to ≤ 10 mg of prednisone a day) and NSAIDs, respectively, during the 3 pooled RA trials.					
b	DMARDs in Study RA-1 included MTX, HCQ, and/or SSZ (about 68%, 8%, and 5% of patients received MTX, HCQ, and SSZ, respectively).					
c	N reflects randomized patients.					
d	Not significantly different from MTX monotherapy.					
NA Not applicable, as data was not collected at Week 14 in Study RA-3.						

**Table 3. Study RA-2 – Median Percent Improvement from Baseline in the Individual ACR Components at Weeks 14<sup>a</sup>**

	<b>Background MTX</b>	<b>SIMPONI 50 mg + Background MTX</b>
N <sup>b</sup>	133	89
<b>Number of swollen joints (0-66)</b>		
Baseline	12	13
Week 14	38%	62%
<b>Number of tender joints (0-68)</b>		
Baseline	21	26
Week 14	30%	60%
<b>Patient's assessment of pain (0-10)</b>		
Baseline	5.7	6.1
Week 14	18%	55%
<b>Patient's global assessment of disease activity (0-10)</b>		
Baseline	5.3	6.0
Week 14	15%	45%
<b>Physician's global assessment of disease activity (0-10)</b>		
Baseline	5.7	6.1
Week 14	35%	55%
<b>HAQ score (0-3)</b>		
Baseline	1.25	1.38
Week 14	10%	29%
<b>CRP (mg/dl)</b>		
Baseline	0.8	1.0
Week 14	2%	44%
<p>Note: Baseline values are medians.</p> <p>a In Study RA-2, about 70% and 85% of patients received concomitant low dose corticosteroids (equivalent to ≤ 10 mg of prednisone a day) and/or NSAIDs during the trials, respectively.</p> <p>b N reflects randomized patients; actual number of patients evaluable for each endpoint may vary.</p>		

**Figure 1. RA Study RA-2 — Percent of Patients Achieving ACR 20 Response by Visit; Randomized Patients\***



\* The same patients may not have responded at each timepoint.

**Physical Function Response in Patients with RA**

In Studies RA-1 and RA-2, the SIMPONI 50 mg groups demonstrated a greater improvement compared to the control groups in the change in mean Health Assessment Questionnaire Disability Index (HAQ-DI) score from baseline to Week 24: 0.25 vs. 0.05 in RA-1, 0.47 vs. 0.13 in RA-2, respectively. Also in Studies RA-1 and RA-2, the SIMPONI 50 mg groups compared to the control groups had a greater proportion of HAQ responders (change from baseline > 0.22) at Week 24: 44% vs. 28%, 65% vs. 35%, respectively.

**14.2 Psoriatic Arthritis**

The safety and efficacy of SIMPONI were evaluated in a multi-center, randomized, double-blind, placebo-controlled trial in 405 adult patients with moderately to severely active PsA (≥ 3 swollen joints and ≥ 3 tender joints) despite NSAID or DMARD therapy (Study PsA). Patients in this study had a diagnosis of PsA for at least 6 months with a qualifying psoriatic skin lesion of at least 2 cm in diameter. Previous treatment with a biologic TNF-blocker was not allowed. Patients were randomly assigned to placebo (n = 113), SIMPONI 50 mg (n = 146), or SIMPONI 100 mg (n = 146) given subcutaneously every 4 weeks. Patients were allowed to receive stable doses of concomitant MTX (≤ 25 mg/week), low dose oral corticosteroids (equivalent to ≤ 10 mg of prednisone a day), and/or NSAIDs during the trial. The use of other DMARDs including SSZ, HCQ, cytotoxic agents, or other biologics was prohibited. The primary endpoint was the percentage of patients achieving ACR 20 response at Week 14. Placebo-controlled efficacy data were collected and analyzed through Week 24.

Patients with each subtype of PsA were enrolled, including polyarticular arthritis with no rheumatoid nodules (43%), asymmetric peripheral arthritis (30%), distal interphalangeal (DIP) joint arthritis (15%), spondylitis with peripheral arthritis (11%), and arthritis mutilans (1%). The median duration of

PsA disease was 5.1 years, 78% of patients received at least one DMARD in the past, and approximately 48% of patients received MTX, and 16% received low dose oral steroids.

**Clinical Response in Patients with PsA**

SIMPONI ± MTX, compared with placebo ± MTX, resulted in significant improvement in signs and symptoms as demonstrated by the proportion of patients with an ACR 20 response at Week 14 in Study PsA (see Table 4). There was no clear evidence of improved ACR response with the higher SIMPONI dose group (100 mg) compared to the lower SIMPONI dose group (50 mg). ACR responses observed in the SIMPONI-treated groups were similar in patients receiving and not receiving concomitant MTX. Similar ACR 20 responses at Week 14 were observed in patients with different PsA subtypes. However, the number of patients with arthritis mutilans was too small to allow meaningful assessment. SIMPONI 50 mg treatment also resulted in significantly greater improvement compared with placebo for each ACR component in Study PsA (Table 5). Treatment with SIMPONI resulted in improvement in enthesitis and skin manifestations in patients with PsA. However, the safety and efficacy of SIMPONI in the treatment of patients with plaque psoriasis has not been established.

The percent of patients achieving ACR 20 responses by visit for Study PsA is shown in Figure 2. ACR 20 responses were observed in 31% of patients in the SIMPONI 50 mg + MTX group at the first assessment (Week 4) after the initial SIMPONI administration.

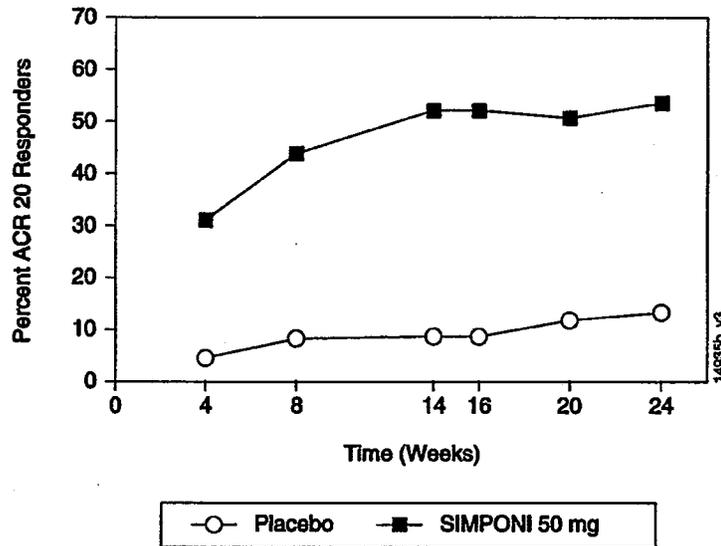
**Table 4. Study PsA - Proportion of Patients with ACR Responses**

	Placebo ± MTX <sup>a</sup>	SIMPONI 50 mg ± MTX <sup>a</sup>
N <sup>b</sup>	113	146
<b>ACR 20</b>		
Week 14	9 %	51 %
Week 24	12 %	52 %
<b>ACR 50</b>		
Week 14	2 %	30 %
Week 24	4 %	32 %
<b>ACR 70</b>		
Week 14	1 %	12 %
Week 24	1 %	19 %
<p>a In Study PsA, about 48%, 16%, and 72% of the patients received stable doses of MTX (≤ 25 mg/day), low dose corticosteroids (equivalent to ≤ 10 mg of prednisone a day), and NSAIDs, respectively.</p> <p>b N reflects randomized patients.</p> <p><b>Bold text indicates primary endpoint</b></p>		

**Table 5. Study PsA - Percent Improvement in ACR Components at Week 14**

	Placebo± MTX <sup>a</sup>	SIMPONI 50 mg ± MTX <sup>a</sup>
<b>N<sup>b</sup></b>	113	146
<b>Number of swollen joints (0-66)</b>		
Baseline	10.0	11.0
Week 14	8 %	60 %
<b>Number of tender joints (0-68)</b>		
Baseline	18.0	19.0
Week 14	0 %	54 %
<b>Patient's assessment of pain (0-10)</b>		
Baseline	5.4	5.8
Week 14	-1 %	48 %
<b>Patient's global assessment of disease activity (0-10)</b>		
Baseline	5.2	5.2
Week 14	2 %	49 %
<b>Physician's global assessment of disease activity (0-10)</b>		
Baseline	5.2	5.4
Week 14	7 %	59 %
<b>HAQ score (0-10)</b>		
Baseline	1.0	1.0
Week 14	0 %	28 %
<b>CRP (mg/dL) (0-10)</b>		
Baseline	0.6	0.6
Week 14	0 %	40 %
<p>Note: Baseline are median values</p> <p>a In Study PsA, about 48%, 16%, and 78% of the patients received stable doses of MTX (≤ 25 mg/day), low dose corticosteroids (equivalent to ≤ 10 mg of prednisone a day), and NSAIDs, respectively.</p> <p>b N reflects randomized patients; actual number of patients evaluable for each endpoint may vary by timepoint</p>		

**Figure 2. Study PsA – Percent of ACR 20 PsA Responders by Visit; Randomized Patients \***



\* The same patients may not have responded at each timepoint.

**Physical Function Response in Patients with PsA**

In Study PsA, SIMPONI 50 mg demonstrated a greater improvement compared to placebo in the change in mean Health Assessment Questionnaire Disability Index (HAQ-DI) score from baseline to Week 24 (0.33 and -0.01, respectively). In addition, the SIMPONI 50 mg group compared to the placebo group had a greater proportion of HAQ responders ( $\geq 0.3$  change from baseline) at Week 24: 43% vs. 22%, respectively.

**14.3 Ankylosing Spondylitis**

The safety and efficacy of SIMPONI were evaluated in a multi-center, randomized, double-blind, placebo-controlled trial in 356 adult patients with active ankylosing spondylitis according to modified New York criteria for at least 3 months (Study AS). Patients had symptoms of active disease [defined as a Bath AS Disease Activity Index (BASDAI)  $\geq 4$  and VAS for total back pain of  $\geq 4$ , on scales of 0 to 10 cm] despite current or previous NSAID therapy. Patients were excluded if they were previously treated with a biologic TNF-blocker or if they had complete ankylosis of the spine. Patients were randomly assigned to placebo (n = 78), SIMPONI 50 mg (n = 138), or SIMPONI 100 mg (n = 140) administered subcutaneously every 4 weeks. Patients were allowed to continue stable doses of concomitant MTX, sulfasalazine (SSZ), hydroxychloroquine (HCQ), low dose corticosteroids (equivalent to < 10 mg of prednisone a day), and/or NSAIDs during the trial. The use of other DMARDs including cytotoxic agents or other biologics was prohibited.

The primary endpoint was the percentage of patients achieving an ASsessment in Ankylosing Spondylitis (ASAS) 20 response at Week 14. Placebo-controlled efficacy data were collected and analyzed through Week 24.

In Study AS, the median duration of AS disease was 5.6 years, median duration of inflammatory back pain was 12 years, 83% were HLA-B27 positive, 24% had prior joint surgery or procedure, and 55% received at least one DMARD in the past. During the trial, the use of concomitant DMARDs and/or NSAIDs was as follows: MTX (20%), SSZ (26%), HCQ (1%), low dose oral steroids (16%), and NSAIDs (90%).

#### Clinical Response in Patients with AS

In Study AS, SIMPONI ± DMARDs treatment, compared with placebo ± DMARDs, resulted in a significant improvement in signs and symptoms as demonstrated by the proportion of patients with an ASAS 20 response at Week 14 (see Table 6). There was no clear evidence of improved ASAS response with the higher SIMPONI dose group (100 mg) compared to the lower SIMPONI dose group (50 mg). Table 7 shows the percent improvement in the components of the ASAS response criteria for the SIMPONI 50 mg ± DMARDs and placebo ± DMARDs groups in Study AS.

The percent of patients achieving ASAS 20 responses by visit for Study AS is shown in Figure 3. ASAS 20 responses were observed in 48% of patients in the SIMPONI 50 mg + MTX group at the first assessment (Week 4) after the initial SIMPONI administration.

**Table 6. Study AS – Proportion of ASAS Responders at Weeks 14 and 24**

	Placebo ± DMARDs <sup>a</sup>	SIMPONI 50 mg ± DMARDs <sup>a</sup>
N <sup>b</sup>	78	138
<b>Responders, % of patients</b>		
<b>ASAS 20</b>		
Week 14	<b>22%</b>	<b>59%</b>
Week 24	23%	56%
<b>ASAS 40</b>		
Week 14	15%	45%
Week 24	15%	44%
<sup>a</sup> During the trial, the concomitant use of stable doses of DMARDs was as follows: MTX (21%), SSZ (25%), and HCQ (1%). About 16% and 89% of patients received stable doses of low dose oral steroids and NSAIDs during the trial, respectively.		
<sup>b</sup> N reflects randomized patients.		
<b>Bold text indicates primary endpoint</b>		

**Table 7. Study AS – Median Percent Improvement in ASAS Components at Week 14**

	Placebo ± DMARDs <sup>a</sup>	SIMPONI 50 mg ± DMARDs <sup>a</sup>
N <sup>b</sup>	78	138
<b>ASAS components</b>		
<b>Patient global assessment (0-10)</b>		
Baseline	7.2	7.0
Week 14	13%	47%
<b>Total back pain (0-10)</b>		
Baseline	7.6	7.5
Week 14	9%	50%
<b>BASFI (0-10)<sup>c</sup></b>		
Baseline	4.9	5.0
Week 14	-3%	37%
<b>Inflammation (0-10)<sup>d</sup></b>		
Baseline	7.1	7.1
Week 14	6%	59%

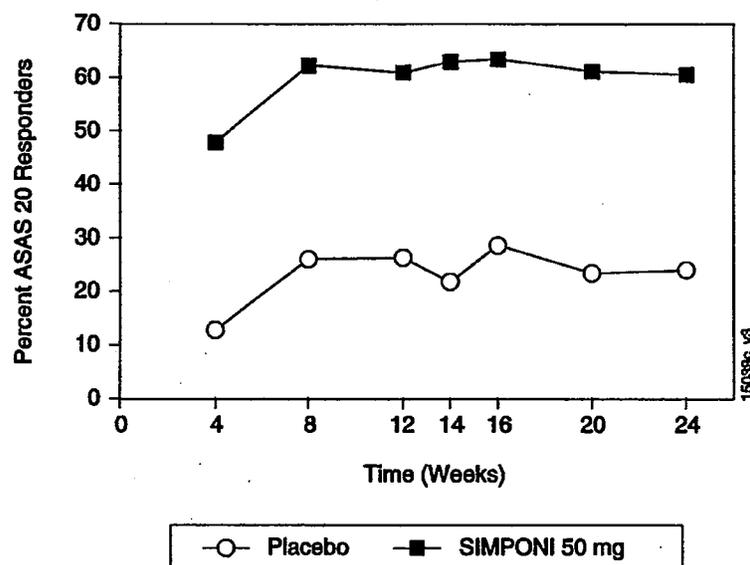
a During the trial, the concomitant use of stable doses of DMARDs was as follows: MTX (21%), SSZ (25%), and HCQ (1%). About 16% and 89% of patients received stable doses of low dose oral steroids and NSAIDs during the trial, respectively.

b N reflects randomized patients

c BASFI is Bath Ankylosing Spondylitis Functional Index

d Inflammation is the mean of two patient-reported stiffness self-assessments in the Bath AS Disease Activity Index (BASDAI)

**Figure 3. Study AS – Percent of AS Patients Achieving ASAS 20 Response by Visit; Randomized Patients\***



\* The same patients may not have responded at each timepoint.

## **15.0 REFERENCES**

1. SEER [database online]. US Population Data – 1969-2004. Bethesda, MD: National Cancer Institute. Release date: January 3, 2007. Available at: <http://seer.cancer.gov/popdata/>.

## **16.0 HOW SUPPLIED/STORAGE AND HANDLING**

Each SIMPONI prefilled autoinjector or prefilled syringe is packaged in a light-blocking, cardboard outer carton. SIMPONI is available in packs of 1 prefilled syringe NDC 57894-070-01 or 1 prefilled SmartJect autoinjector NDC 57894-070-02.

### **Prefilled SmartJect Autoinjector**

Each single dose SmartJect autoinjector contains a prefilled glass syringe (27 gauge ½ inch) providing 50 mg of SIMPONI per 0.5 mL of solution.

### **Prefilled Syringe**

Each single dose prefilled glass syringe (27 gauge ½ inch) contains 50 mg of SIMPONI per 0.5 mL of solution.

### **Storage and Stability**

SIMPONI must be refrigerated at 2°C to 8°C (36°F to 46°F) and protected from light. Keep the product in the original carton to protect from light until the time of use. Do not freeze. Do not shake. Do not use SIMPONI beyond the expiration date (EXP) on the carton or the expiration date on the prefilled syringe (observed through the viewing window) or the prefilled SmartJect autoinjector.

## **17.0 PATIENT COUNSELING INFORMATION**

See Medication Guide (17.3)

### **17.1 Patient Counseling**

Patients should be advised of the potential benefits and risks of SIMPONI. Physicians should instruct their patients to read the Medication Guide before starting SIMPONI therapy and to read it each time the prescription is renewed.

### **Infections**

Inform patients that SIMPONI may lower the ability of their immune system to fight infections. Instruct the patient of the importance of contacting their doctor if they develop any symptoms of infection, including tuberculosis, invasive fungal infections, and hepatitis B reactivation.

### **Malignancies**

Patients should be counseled about the risk of lymphoma and other malignancies while receiving SIMPONI.

### **Allergic Reactions**

Advise latex-sensitive patients that the needle cover on the prefilled syringe as well as the prefilled syringe in the prefilled SmartJect autoinjector contains dry natural rubber (a derivative of latex).

**Other Medical Conditions**

Advise patients to report any signs of new or worsening medical conditions such as congestive heart failure, demyelinating disorders, autoimmune diseases, liver disease, cytopenias, or psoriasis.

**17.2 Instruction on Injection Technique**

The first self-injection should be performed under the supervision of a qualified healthcare professional. If a patient or caregiver is to administer SIMPONI, he/she should be instructed in injection techniques and their ability to inject subcutaneously should be assessed to ensure the proper administration of SIMPONI [*see Medication Guide (17.3)*].

Prior to use, remove the prefilled syringe or the prefilled SmartJect autoinjector from the refrigerator and allow SIMPONI to sit at room temperature outside of the carton for 30 minutes and out of the reach of children.

Do not warm SIMPONI in any other way. For example, do not warm SIMPONI in a microwave or in hot water.

Do not remove the prefilled syringe needle cover or SmartJect autoinjector cap while allowing SIMPONI to reach room temperature. Remove these immediately before injection.

Do not pull the autoinjector away from the skin until you hear a first “click” sound and then a second “click” sound (the injection is finished and the needle is pulled back). It usually takes about 3 to 6 seconds but may take up to 15 seconds for you to hear the second “click” after the first “click.” If the autoinjector is pulled away from the skin before the injection is completed, a full dose of SIMPONI may not be administered.

A puncture-resistant container for disposal of needles and syringes should be used. Patients or caregivers should be instructed in the technique of proper syringe and needle disposal, and be advised not to reuse these items.

### 17.3 Medication Guide

#### Rx Only

### 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.

#### **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:

**Serious Infections**

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

**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

**Cancer**

- 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.
- If you use SIMPONI or other TNF-blockers, your risk of getting lymphoma or other cancers may increase.

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

### **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 TNF-blocker medicines including SIMPONI had new psoriasis or worsening of psoriasis that they already had. Symptoms of psoriasis include: red scaly patches or raised bumps that are filled with pus on the skin. Psoriasis may go away or get better after stopping SIMPONI in some people.
- **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](http://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.

**Patient Instructions for Use  
SIMPONI™ (SIM-po-nee)  
(golimumab)  
SmartJect™ autoinjector**

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.

It is important to read, understand, and follow these instructions so that you inject SIMPONI the right way. Call your doctor if you or your caregiver has any questions about the right way to inject SIMPONI.

Important information about your SmartJect autoinjector:

- When the button on the SmartJect autoinjector is pressed to give the dose of SIMPONI you will hear a loud 'click' sound. It is very important that you practice injecting SIMPONI with your doctor or nurse so that you are not startled by this click when you start giving the injections to yourself at home.
- If you pull the SmartJect autoinjector away from the skin before the injection is completed, you may not get your full dose of medicine and may lose some of the medicine.

**Do not:**

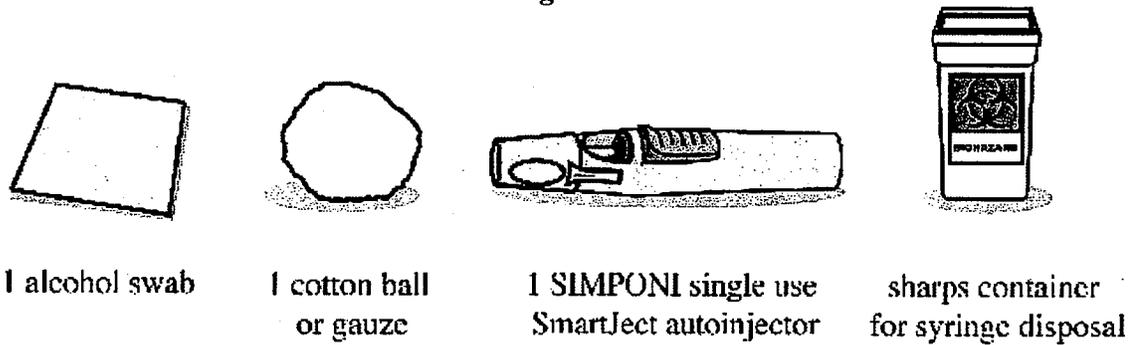
- shake the SmartJect autoinjector at any time
- remove the SmartJect autoinjector cap until you get to that step

**Step 1: Gather and inspect the supplies for your injection**

You will need these supplies for an injection of SIMPONI. See Figure 1.

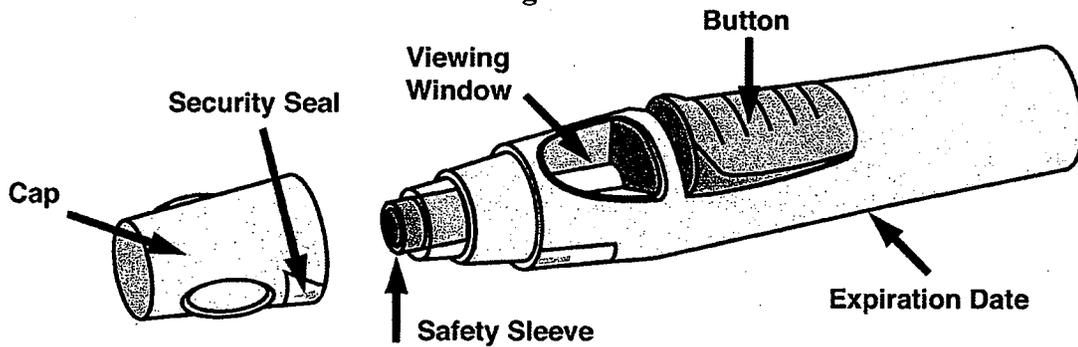
- 1 alcohol swab
- 1 cotton ball or gauze
- 1 SIMPONI prefilled SmartJect autoinjector
- sharps container for autoinjector disposal

Figure 1



The figure below shows what the SmartJect autoinjector looks like. See Figure 2.

Figure 2



### 1.1 Check Expiration Date

- Check the expiration date (“EXP”) on the SmartJect autoinjector.
- You can also check the expiration date printed on the carton.
- If the expiration date has passed, do not use the SmartJect autoinjector. Call your doctor or pharmacist, or call 1-800-457-6399 for help.

### 1.2 Check Security Seal

- Check the security seal around the cap of the SmartJect autoinjector. If the security seal is broken, do not use the SmartJect autoinjector.

### 1.3 Wait 30 minutes

- To ensure proper injection, allow the autoinjector to sit at room temperature outside the carton for 30 minutes and out of the reach of children.



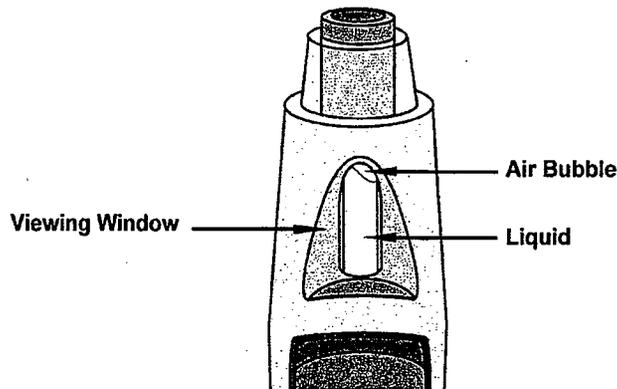
**Do not** warm the SmartJect autoinjector in any other way (For example, **do not** warm it in a microwave or in hot water).

**Do not** remove the SmartJect autoinjector cap while allowing it to reach room temperature.

#### 1.4 Check the Liquid in the SmartJect autoinjector

- Look through the viewing window of the SmartJect autoinjector. See Figure 3. Make sure that the liquid in the prefilled syringe is clear and colorless to slightly yellow in color. You may see a small amount of tiny particles that are white, or that you can see through. Do not inject the liquid if it is cloudy or discolored, or has large particles in it.
- You may also notice an air bubble. This is normal. See Figure 3.

Figure 3

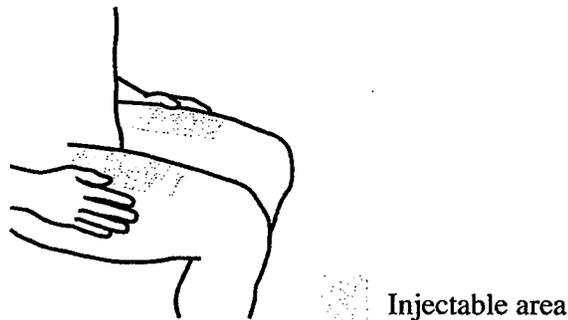


#### Step 2: Choose and prepare the injection site

##### 2.1 Choose the Injection Site

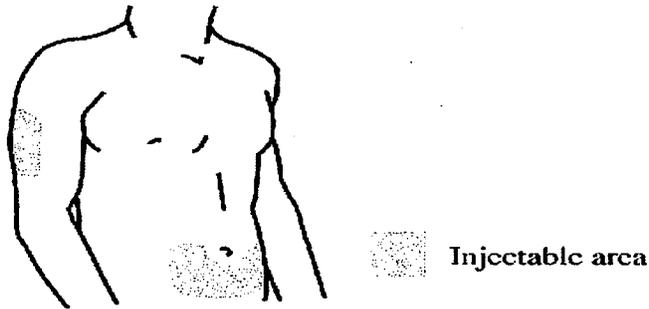
- The recommended injection site is the front of your middle thighs. See Figure 4.

Figure 4



- You can also use the lower part of the abdomen below the navel (belly button), except for the two-inch area directly around the navel. See Figure 5.
- If a caregiver is giving you the injection, the outer area of the upper arms may also be used. See Figure 5.

**Figure 5**



- **Do not** inject into areas where the skin is tender, bruised, red, scaly, or hard. Avoid areas with scars or stretch marks.

### **2.2 Prepare the Injection Site**

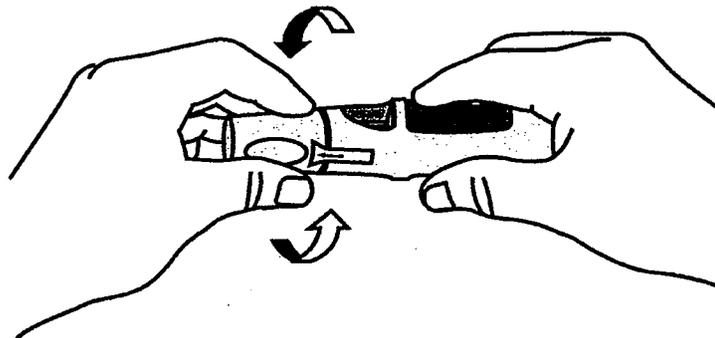
- Wash your hands well with soap and warm water.
- Wipe the injection site with an alcohol swab.
- **Do not** touch this area again before giving the injection. Allow the skin to dry before injecting.
- **Do not** fan or blow on the clean area.

### **Step 3: Injecting SIMPONI using the single dose SmartJect autoinjector**

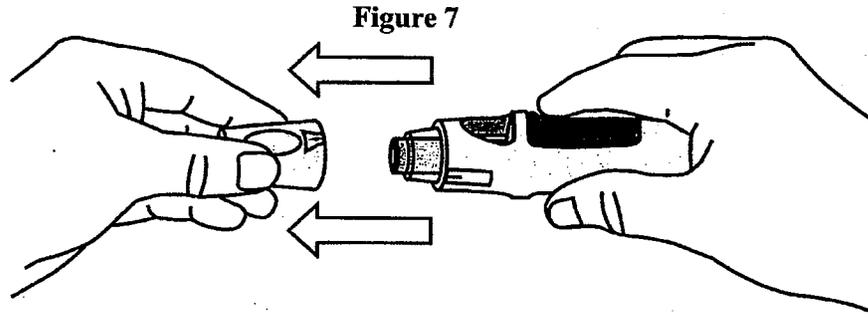
#### **3.1 Remove the Cap**

- Do not remove the cap until you are ready to inject SIMPONI. Inject SIMPONI within 5 minutes after the cap has been removed.
- When you are ready to inject, twist the cap slightly to break the security seal. See Figure 6.

**Figure 6**



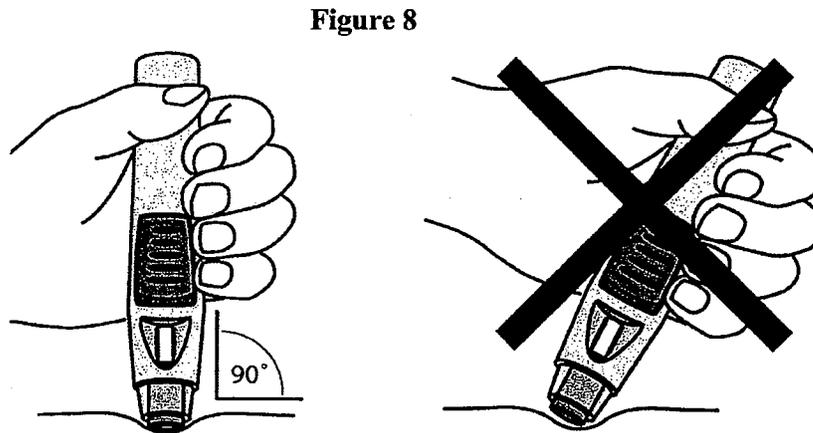
- Pull the cap off and throw it in the trash right away. See Figure 7.



- **Do not** put the cap back on because it may damage the needle inside the SmartJect autoinjector.
- **Do not** use your SmartJect autoinjector if it is dropped without the cap in place.

### 3.2 Push the SmartJect autoinjector against the skin

- Hold the SmartJect autoinjector comfortably in your hand.
- Do not press the button. Push the open end of the SmartJect autoinjector firmly against the skin at **90-degree angle**. See Figure 8.

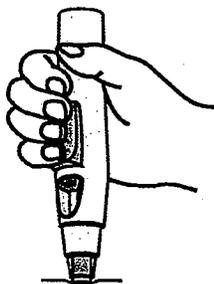


- Use **your** free hand to pinch and hold the skin at the injection site. This may make injecting easier.

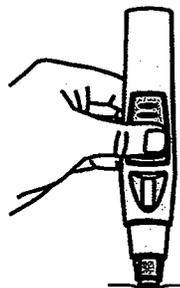
### 3.3 Press button to inject

- Continue to hold the SmartJect autoinjector firmly against the skin, and press the button with your fingers (see Figure 9) or thumb (see Figure 10). You will not be able to push in the button unless the SmartJect autoinjector is pushed firmly against your skin.

**Figure 9**

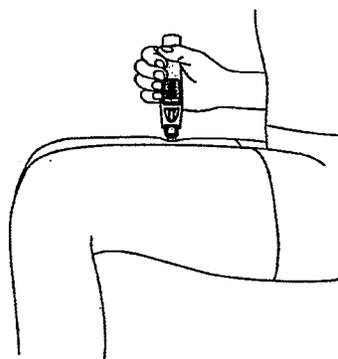


**Figure 10**



- After the button is pressed, it will stay pressed in so you do not need to keep pressure on it. See Figure 11.

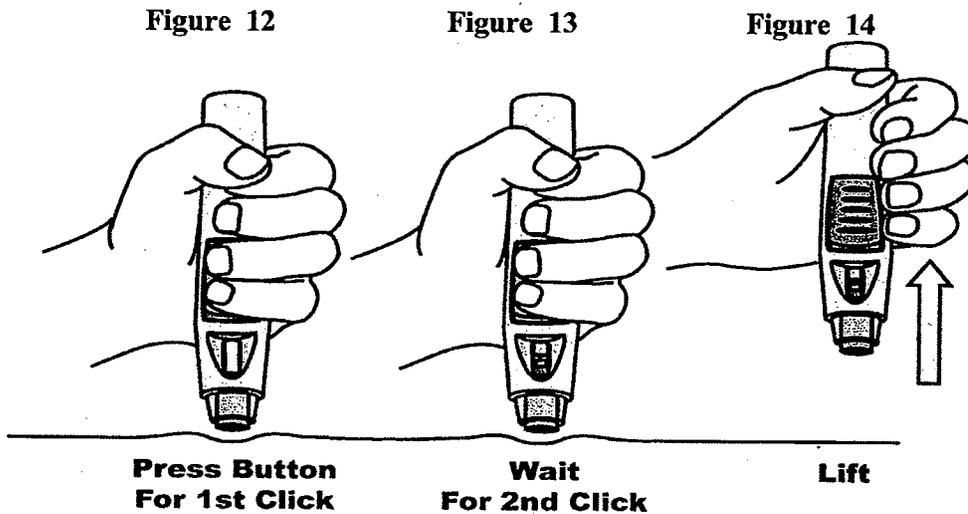
**Figure 11**



- You will hear a loud 'click' sound. This means that the injection has started. Do not pull the SmartJect autoinjector away from your skin. If you pull the SmartJect autoinjector away from the skin, you may not get your full dose of medicine. See Figure 12.
- **Do not** lift the SmartJect autoinjector yet.

### **3.4 Wait for Second "Click"**

- Keep holding the SmartJect autoinjector against your skin until you hear the second 'click' sound. It usually takes about 3 to 6 seconds, but may take up to 15 seconds for you to hear the second 'click' sound. See Figure 13.
- The second 'click' sound means that the injection is finished and the needle has pulled back (retracted) into the SmartJect autoinjector.
- Lift the SmartJect autoinjector from the injection site. See Figure 14.
- If you have hearing problems, count for 15 seconds from the time you pressed the button and then lift the SmartJect autoinjector from the injection site.

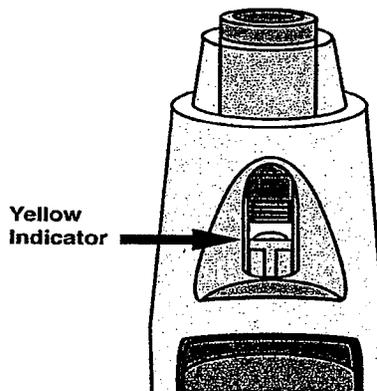


**Step 4: After the injection**

**4.1 Check the Viewing Window**

- After you finish injecting, check the viewing window to see the yellow indicator. See Figure 15. This means the SmartJect autoinjector has worked the right way.

**Figure 15**

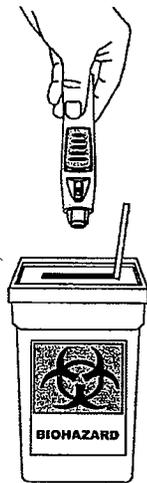


- If you do not see the yellow indicator in the viewing window, call 1-800-457-6399 for help.

**4.2 Dispose of the used SmartJect autoinjector**

- Place the used SmartJect autoinjector into a closable puncture-resistant container. You may use a sharps container (such as a red biohazard container), a hard plastic container (such as a detergent bottle), or a metal container (such as an empty coffee can). See Figure 16.

**Figure 16**



- Ask your doctor for instructions on the right way to throw away (dispose of) the container. There may be local or state laws about how you should throw away used needles and syringes.
- Do not throw away your used SmartJect autoinjector in household trash. Do not recycle.

#### **4.3 Use Cotton Ball or Gauze**

- There may be a small amount of blood or liquid at the injection site, which is normal.
- You can press a cotton ball or gauze over the injection site for 10 seconds. Do not rub the injection site.
- You may cover the injection site with a small adhesive bandage, if needed.

**Patient Instructions for Use**  
**SIMPONI™**  
**Prefilled Syringe**

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.

It is important to read, understand, and follow these instructions so that you inject SIMPONI the right way. Call your doctor if you or your caregiver has any questions about the right way to inject SIMPONI.

Important information about your prefilled syringe:

- Always hold the prefilled syringe by the body of the syringe.

**Do not:**

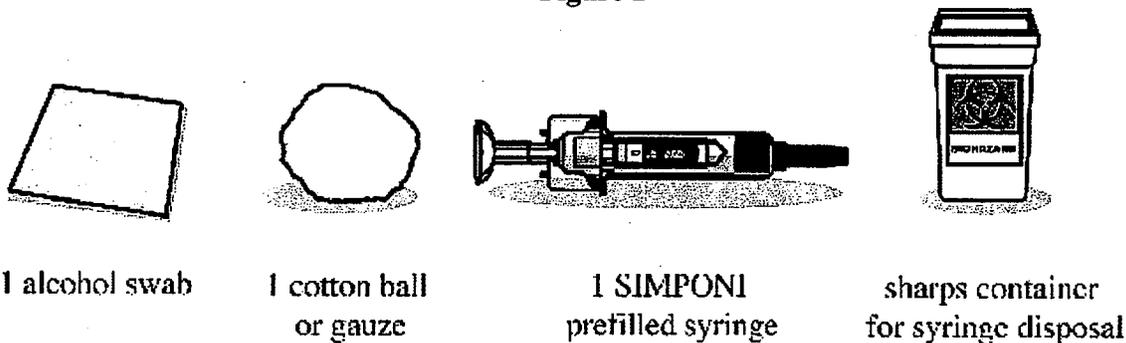
- pull back on the plunger at any time.
- shake the SIMPONI prefilled syringe. This may damage the medicine.
- remove the needle cover from the prefilled syringe until you get to that step.
- touch the needle guard activation clips to prevent covering the needle with the needle guard too soon (See Figure 2).
- use SIMPONI if it has been frozen or if it has been kept at a room temperature that is too warm. See the Medication Guide section: “How should I store SIMPONI?”
- use your SIMPONI prefilled syringe if it looks damaged.

**Step 1: Gather the supplies for your injection**

You will need these supplies for an injection of SIMPONI. See Figure 1.

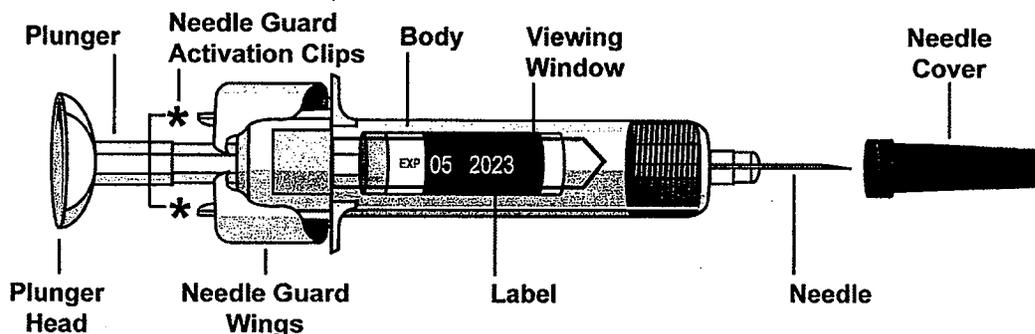
- 1 alcohol swab
- 1 cotton ball or gauze
- 1 SIMPONI prefilled syringe
- sharps container for syringe disposal

Figure 1



The diagram below shows what the prefilled syringe looks like. See Figure 2.

Figure 2



## Step 2: Get ready to use your prefilled syringe

### 2.1 Check the Expiration Date

- Look for the expiration date printed on the back panel of the SIMPONI carton.
- **If the expiration date has passed, do not use the prefilled syringe. Call your doctor or pharmacist or call 1-800-457-6399 for help.**

### 2.2 Wait 30 minutes

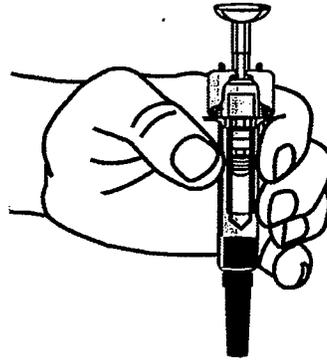
- To ensure proper injection, allow the prefilled syringe to sit at room temperature outside of the carton for 30 minutes and out of the reach of children.
- **Do not** warm the prefilled syringe in any other way (For example, **Do not** warm it in a microwave or in hot water).
- **Do not** remove the prefilled syringe needle cover while allowing it to reach room temperature.



### 2.3 Check the Liquid in the Prefilled Syringe

- Hold your SIMPONI prefilled syringe by the body with the covered needle pointing down. See Figure 3.

**Figure 3**



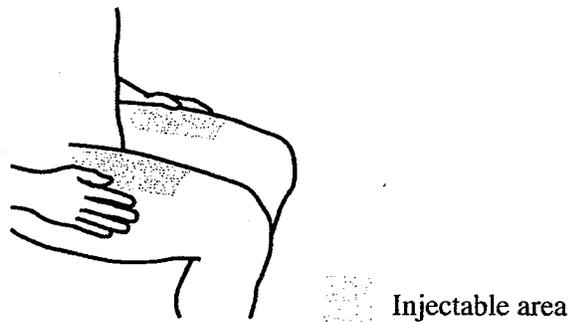
- Look at the liquid through the viewing window of the prefilled syringe. Make sure that the liquid in the prefilled syringe is clear and colorless to slightly yellow in color. You may see a small amount of tiny particles that are white, or that you can see through. Do not inject the liquid if it is cloudy or discolored, or has large particles in it.
- You may also see an air bubble. This is normal.

**Step 3: Choose and prepare the injection site**

**3.1 Choose the Injection Site**

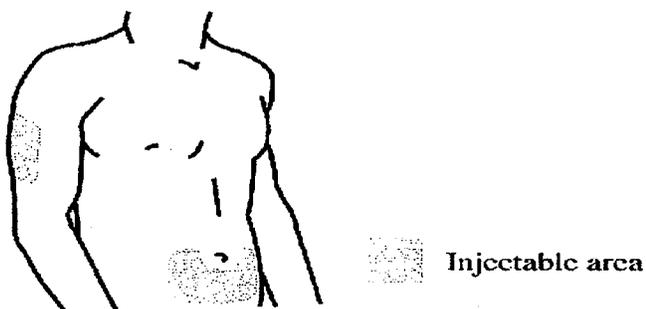
- The recommended injection site is the front of your middle thighs. See Figure 4.

**Figure 4**



- You can also use the lower part of the abdomen below the navel (belly button), except for the two-inch area directly around the navel. See Figure 5.
- If a caregiver is giving you the injection, the outer area of the upper arms may also be used. See Figure 5.

**Figure 5**



**Do not** inject into areas where the skin is tender, bruised, red, scaly, or hard. Avoid areas with scars or stretch marks.

### **3.2 Prepare the Injection Site**

- Wash your hands well with soap and warm water.
- Wipe the injection site with an alcohol swab.
- **Do not** touch this area again before giving the injection. Let your skin dry before injecting.
- **Do not** fan or blow on the clean area.

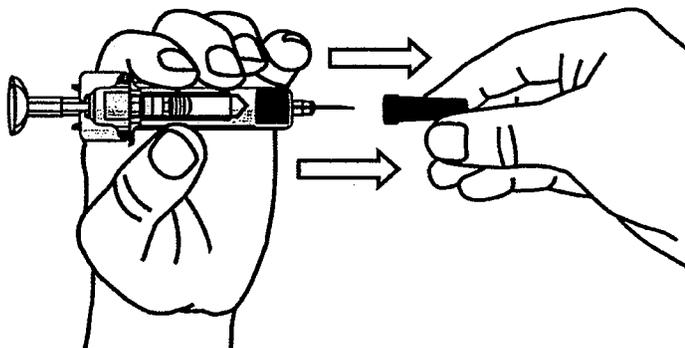
### **Step 4: Inject SIMPONI**

Do not remove the needle cover until you are ready to inject SIMPONI. Inject SIMPONI within 5 minutes after you remove the needle cover.

### **4.1 Remove the Needle Cover**

- **Do not** touch the plunger while removing the needle cover.
- Hold the body of the prefilled syringe with one hand, and pull the needle cover straight off. See Figure 6.

**Figure 6**



- Put the needle cover in the trash.
- You may see an air bubble in the prefilled syringe. This is normal.
- You may also see a drop of liquid at the end of the needle. This is normal.
- **Do not** touch the needle or let it touch any surface.
- **Do not** use the prefilled syringe if it is dropped without the needle cover in place.

#### 4.2 Position the prefilled syringe and inject SIMPONI

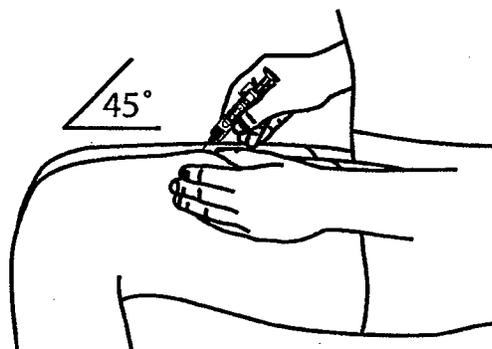
- Hold the body of the prefilled syringe in one hand between the thumb and index fingers. See Figure 7.

Figure 7



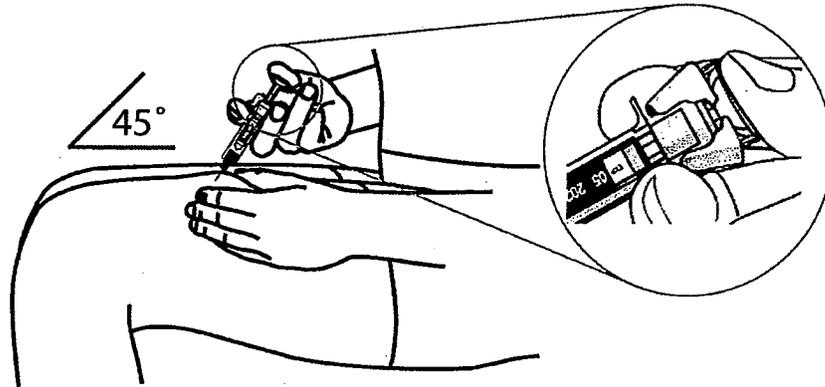
- **Do not** pull back on the plunger at any time.
- Use the other hand to gently pinch the area of skin that you previously cleaned. Hold firmly.
- Use a quick, dart-like motion to insert the needle into the pinched skin at about a **45-degree angle**. See Figure 8.

Figure 8



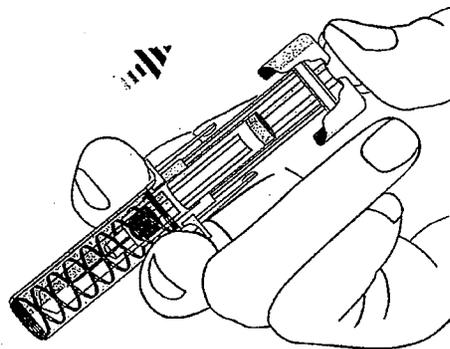
- Inject all of the medicine by using your thumb to push in the plunger until the plunger head is completely between the needle guard wings. See Figure 9.

**Figure 9**



- When the plunger is pushed as far as it will go, keep pressure on the plunger head. Take the needle out of the skin and let go of the skin.
- Slowly take your thumb off the plunger head. This will let the empty syringe move up until the entire needle is covered by the needle guard. See Figure 10.

**Figure 10**

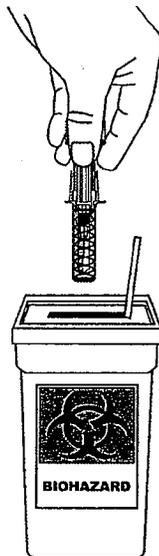


## Step 5: After the injection

### 5.1 Dispose of the used prefilled syringe

- Place the used prefilled syringe in a closable puncture-resistant container. You may use a sharps container (such as a red biohazard container), a hard plastic container (such as a detergent bottle), or a metal container (such as an empty coffee can). For the safety and health of you and others, needles and used syringes **must never** be re-used. See Figure 11.

Figure 11



- Ask your doctor for instructions on the right way to throw away (dispose of) the container. There may be local or state laws about how you should throw away used needles and syringes.
- Do not throw away your used prefilled syringe in household trash. Do not recycle.

### 5.2 Use Cotton Ball or Gauze

- There may be a small amount of blood or liquid at the injection site, which is normal.
- You can press a cotton ball or gauze over the injection site and hold for 10 seconds. Do not rub the injection site.
- You may cover the injection site with a small adhesive bandage, if needed.

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

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

SIMPONI (golimumab)

712 **17.3 Medication Guide**

713 **Rx Only**

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**MEDICATION GUIDE  
SIMPONI (SIM-POH-NEE)  
(golimumab)**

719

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.

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

725

SIMPONI is a medicine that affects your immune system. SIMPONI can lower the ability of your immune system to fight infections. Some patients have had serious infections while receiving SIMPONI, including tuberculosis (TB), and systemic bacterial and fungal infections. Some patients have died from these serious infections.

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729

- 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.

730

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733

**Before starting SIMPONI, tell your doctor if you:**

734

- think you have an infection. You should not start taking SIMPONI if you have any kind of infection.
- are being treated for an infection
- have signs of an infection, such as a fever, cough, flu-like symptoms
- have any open cuts or sores on your body
- get a lot of infections or have infections that keep coming back
- have diabetes or an immune system problem. People with these conditions have a higher chance for infections.
- have TB, or if you have been in close contact with someone with TB
- live or have lived or traveled to certain parts of the country (such as the Ohio and Mississippi River valleys) where there is an increased risk for getting certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis). These infections may develop or become more severe if you take SIMPONI. If you don't know if you have lived in an area where histoplasmosis, coccidioidomycosis, or blastomycosis is common, ask your doctor.
- have or have had hepatitis B
- use the medicine Kineret (anakinra)

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**After starting SIMPONI**, if you have an infection, any sign of an infection including a fever, cough, flu-like symptoms, or have open cuts or sores on your body, call your doctor right away. SIMPONI can make you more likely to get infections or make any infection that you have worse.

752

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755

**What is SIMPONI?**

756

SIMPONI is a prescription medicine that is approved for the treatment of adult patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. In these diseases, the body

757

SIMPONI (golimumab)

758 produces too much of a substance called tumor necrosis factor alpha (TNF-alpha). Too much of this  
759 substance causes your body's immune system to attack healthy tissue and results in inflammation.  
760 Blocking TNF-alpha with SIMPONI can reduce inflammation associated with these diseases, but can  
761 also reduce your immune system's ability to fight off infections.

762

763 **Rheumatoid arthritis:**

764 Rheumatoid arthritis is an inflammatory disease of the joints. If you have active rheumatoid arthritis,  
765 you will be given SIMPONI, which you will take in combination with methotrexate to:

- 766 • Reduce the signs and symptoms of your disease

767

768 **Psoriatic arthritis:**

769 Psoriatic Arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis. If you  
770 have active psoriatic arthritis, you will be given SIMPONI, alone or in combination with methotrexate  
771 to:

- 772 • Reduce signs and symptoms of your arthritis

773

774 **Ankylosing spondylitis:**

775 Ankylosing spondylitis is an inflammatory disease of the spine. If you have active ankylosing  
776 spondylitis, you will be given SIMPONI to:

- 777 • Reduce the signs and symptoms of your disease

778

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

780 Before receiving treatment with SIMPONI, tell your doctor if you:

- 781 • have an infection (see "What is the most important information I should know about  
782 SIMPONI).
- 783 • have heart failure, or if you previously had or currently have any heart condition. If you  
784 develop new or worsening symptoms of heart failure, such as shortness of breath or swelling of  
785 your feet, you must notify your doctor.
- 786 • have or have had a condition that affects your nervous system, like multiple sclerosis. You  
787 should tell your doctor if you experience weakness in the arms or legs, numbness, tingling, or  
788 visual disturbances.
- 789 • have or have had any type of cancer.
- 790 • have recently received or are scheduled to receive a vaccine.
- 791 • have a latex allergy
- 792 • are pregnant, planning to become pregnant, or breastfeeding. SIMPONI should only be used  
793 during pregnancy if clearly needed. Women who are breastfeeding should talk to their doctor  
794 about whether or not to use SIMPONI.

795

796 **Tell your doctor about all the medicines you take**, including prescription and non-prescription  
797 medicines, vitamins, and herbal supplements. Especially, tell your doctor if you take KINERET  
798 (anakinra). SIMPONI and KINERET should not be taken together. Also, tell your doctor if you are  
799 taking other medications that affect your immune system.

800

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

803

804 **How should I take SIMPONI?**

- 805 • SIMPONI 50 mg is given by injection under the skin with a pre-filled syringe or autoinjector  
806 once a month, on the same date each month.
- 807 • SIMPONI is intended for use under the guidance and supervision of your doctor. Your doctor  
808 will tell you how often to take SIMPONI. **Do not take SIMPONI more often than**  
809 **prescribed.** If your doctor determines that it is appropriate, you may be able to administer  
810 SIMPONI to yourself, after proper training in injection technique (see the "Instructions for  
811 **Injecting SIMPONI under the skin yourself**").
- 812 • If you take more SIMPONI than you were told to take, call your doctor.  
813 • Do not miss any doses of SIMPONI. If you forget to take SIMPONI, inject a dose as soon as  
814 you remember. Then, take your next dose at your regular scheduled time. This will put you  
815 back on schedule. In case you are not sure when to inject SIMPONI, contact your doctor or  
816 pharmacist.

817

818 **What are the possible side effects with SIMPONI?**

819 Serious side effects that may require treatment can occur during SIMPONI therapy. Possible serious  
820 side effects of SIMPONI include:

821

822 **Serious infections**

823 (see "What is the most important information I should know about SIMPONI?"). Some patients  
824 have had serious infections while receiving SIMPONI, including TB, and systemic bacterial and  
825 fungal infections. Some patients have died from these serious infections.

826

827 If you develop a fever, chills, headache, flu-like symptoms, feel tired, have a cough, blood in your  
828 sputum, shortness of breath, night sweats, weight loss, nausea, vomiting, diarrhea, frequency or  
829 burning while passing urine, redness or swelling of skin or joint, cold sores, tooth pain or new or  
830 worsening of pain in any location while or after receiving SIMPONI, you should tell your doctor right  
831 away because these could be signs that you are getting an infection.

832

833 Your doctor will examine you for TB and perform a test to see if you have TB. If your doctor feels  
834 that you are at risk for TB, you may be treated with medicine for TB before you begin treatment with  
835 SIMPONI and during treatment with SIMPONI. Even if your TB test is negative your doctor should  
836 carefully monitor you for TB infections while you are taking SIMPONI. Patients who had a **negative**  
837 TB skin test before receiving SIMPONI have developed active TB.

838

839 If you are a chronic carrier of the hepatitis B virus, the virus can become active while you are being  
840 treated with SIMPONI. Your doctor may do a blood test before you start treatment with SIMPONI and  
841 occasionally while you are being treated. Tell your doctor if you have any of the following symptoms:  
842 feel unwell, poor appetite, tiredness (fatigue), fever, skin rash and/or joint pain.

843

844 **Allergic reactions**

845 Some patients may get allergic reactions to SIMPONI. Symptoms of an allergic reaction may include  
846 hives, rash, difficulty breathing, chest pain, and high or low blood pressure. You should contact your  
847 doctor if you experience any of these symptoms.

848

849 **Needle Cover with Dry Natural Rubber (a form of latex)**

850 The needle cover on the pre-filled syringe as well as the pre-filled syringe in the autoinjector contains  
851 dry natural rubber (a form of latex). This may cause allergic reactions in people who are sensitive to  
852 latex. Tell your doctor if you have ever had an allergic reaction to latex and developed any allergic  
853 reaction to SIMPONI injection.

854

855 **Injection site reactions**

856 Some patients develop reactions at the injection site on their skin after SIMPONI injections. These  
857 reactions may include mild rash, swelling bruising, hives, pain and irritation. You should contact your  
858 doctor if you experience severe symptoms at injection site.

859

860 **Cancer**

861 In clinical studies, reports of blood cancer called lymphoma were more frequent in patients on  
862 SIMPONI than expected for people in general. People who have been treated for rheumatoid arthritis,  
863 psoriatic arthritis or ankylosing spondylitis for a long time, particularly those with highly active  
864 disease may be more prone to develop lymphoma. Cancers, other than lymphoma, have also been  
865 reported in patients treated with SIMPONI or other TNF blockers. In a study of SIMPONI in patients  
866 with severe persistent asthma, cancers occurred in SIMPONI treated patients but not in control treated  
867 patients. If you have severe persistent asthma you should discuss with your doctor whether SIMPONI  
868 is appropriate for you.

869

870 If you take SIMPONI or other TNF blockers, your risk of developing lymphoma or other cancers may  
871 increase. You should also tell your doctor if you have had or develop lymphoma or other cancers  
872 while you are taking SIMPONI. Whether you decide to use SIMPONI or not, you should discuss with  
873 your doctor the cancer screening measures and impact of the life style choices on the risk of  
874 developing cancer.

875

876 **Congestive heart failure**

877 Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF-  
878 blocking agents. SIMPONI has not been studied in patients with CHF. Tell your doctor if you have  
879 heart failure. If you have heart failure and doctor decides to administer SIMPONI, your condition  
880 should be closely monitored during treatment. If you develop new or worsening symptoms of heart  
881 failure (such as shortness of breath or swelling of your feet), you should contact your doctor right  
882 away.

883

884 **Neurological Events**

885 In rare instances patients treated with TNF blocking agents may develop diseases such as multiple  
886 sclerosis. Tell your doctor if you have a history of a neurological disease. If you develop symptoms  
887 of neurological disease such as changes in your vision, weakness in your arms or legs, numbness or  
888 tingling in any part of your body, you should contact your doctor right away.

889

890 **Vaccinations**

891 You should not receive certain vaccines while using SIMPONI. If you have recently received or are  
892 scheduled to receive a vaccine, please inform your doctor.  
893

894 **Liver Problems**

895 There have been cases where patients taking SIMPONI developed liver problems. Signs that you  
896 could be having a problem include: skin and eyes turning yellow, dark brown-colored urine, right-  
897 sided abdominal pain, fever, nausea, vomiting, and severe fatigue. You should contact your doctor  
898 right away if you experience these symptoms.  
899

900 **Common side effects with SIMPONI include:**

901 Flu, bronchitis, infection of soft tissues, sore throat, upper respiratory infection, sinus infection, runny  
902 nose, cold sores, abnormal liver tests, dizziness, numbness or tingling, high blood pressure, fever and  
903 redness at the site of injection.  
904

905 Any medicine may have side effects. These are not all of the side effects with SIMPONI. Tell your  
906 doctor about any side effect that bothers you or does not go away. Ask your doctor or pharmacist for  
907 more information.  
908

909 **How do I store SIMPONI?**

910 If you are using SIMPONI at home, it is important that it is stored in your refrigerator although not in  
911 the freezer compartment. SIMPONI should not be frozen. Keep the product in the original carton to  
912 protect from light until the time of use. Do not shake.  
913

914 **General Information about SIMPONI**

915 Medicines are sometimes prescribed for purposes other than those listed in the Medication Guide. Do  
916 not use SIMPONI for a condition for which it was not prescribed. Do not give SIMPONI to other  
917 people, even if they have the same condition. It may harm them and it is against the law.  
918

919 This Medication Guide summarizes the most important information about SIMPONI. If you would  
920 like more information, talk to your doctor. You can ask your doctor or pharmacist for information  
921 about SIMPONI that is written for health professionals. For more information go to *<insert website>*  
922 or call 1-XXX-XXX-XXXX.  
923

924 Call your doctor for medical advice about side effects. You may report side effects to the FDA at  
925 1-800-FDA-1088.  
926

927 **What are the ingredients in SIMPONI?**

928 The active ingredient is golimumab. The inactive ingredients in SIMPONI are: sorbitol, L-histidine,  
929 L-histidine monohydrochloride monohydrate, polysorbate 80 and water for injection. No preservatives  
930 are present.  
931

932 **Other important points**

933 SIMPONI is a clear to slightly clear, colorless to light yellow solution. This appearance is not unusual  
934 for solutions containing protein.

935 SIMPONI should not be used:

SIMPONI (golimumab)

- 936 - after the expiration date on the label;
- 937 - if the product is damaged;
- 938 - if the liquid is discolored, cloudy or you can see other particulate matter floating in it;
- 939 - if you know, or think that it may have been exposed to extreme temperatures (such as accidentally
- 940 frozen or heated);
- 941 Always keep medicine out of the reach of children.

942

**943 Instructions for Injecting SIMPONI under the skin yourself**

944 At the start of your therapy, SIMPONI may be injected by medical or nursing staff. However, your  
945 doctor may decide that it is right for you or your caregiver to learn how to inject SIMPONI under the  
946 skin (subcutaneously) yourself. Make sure you (or your caregiver) have been trained how to inject  
947 SIMPONI before you do it yourself. Call your doctor if you have any questions about giving yourself  
948 an injection.

949

949 **INSTRUCTIONS FOR INJECTING SIMPONI USING A PRE-FILLED SYRINGE**

950

951 **If you would like to self-inject SIMPONI, you must be trained by a healthcare professional to**  
 952 **prepare an injection and give it to yourself. If you have not been trained, please contact your**  
 953 **healthcare professional to schedule a training session.**

954

955 **STEP 1: PREPARING TO USE THE PRE-FILLED SYRINGE**

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957 The diagram below shows what the pre-filled syringe looks like:

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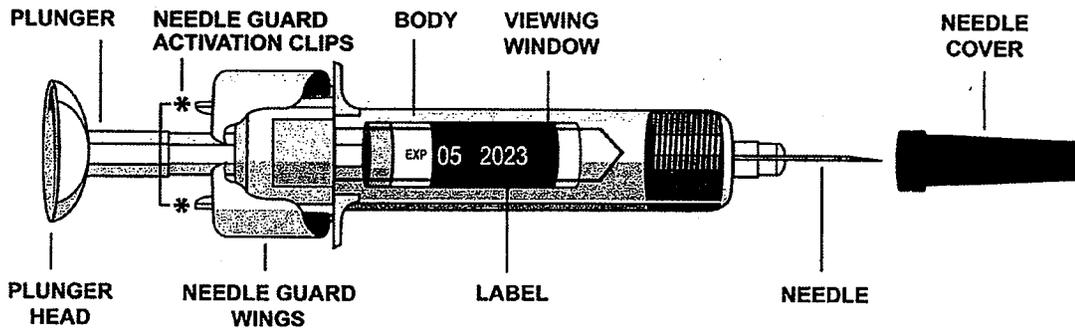
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969



970 **Hold the pre-filled syringe by the body of the syringe**

971

972 **DO NOT** hold the pre-filled syringe by the plunger head, plunger, needle guard wings, or needle cover

973

974 **DO NOT** pull back on the plunger at any time

975

976 **DO NOT** shake the pre-filled syringe at any time

977

978 **DO NOT** remove the needle cover from the pre-filled syringe until instructed to do so

979

980 **DO NOT** touch the needle guard activation clips (as indicated by asterisks \* in the first illustration) to  
 981 prevent prematurely covering the needle with the needle guard

982

983 **Check the Expiration Date**

- 984 • Check the expiration date (as indicated by “EXP”) on the label by looking through the viewing window located within the body of the pre-filled syringe

985

- 986 • If you cannot see the expiration date through the viewing window, hold the pre-filled syringe by its body and rotate the needle cover to line up the expiration date to the viewing window

987

- 988 • You can also check the expiration date printed on the carton

989

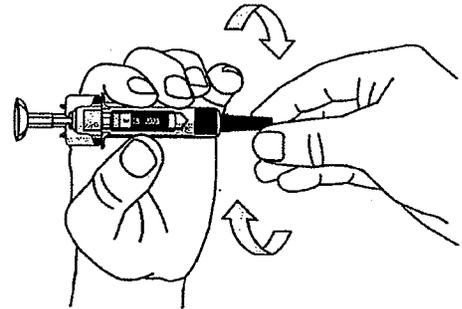
- 990 • If the expiration date has passed, **DO NOT** use the pre-filled syringe and please contact your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for assistance

991

992 **Wait 30 minutes**

993

- 994 • To ensure proper injection, allow the pre-filled syringe to sit at room temperature outside of the carton for 30 minutes out of the reach of children



995

996

**DO NOT** warm the pre-filled syringe in any other way (For example, **DO NOT** warm it in a microwave or in hot water)

997

998

**DO NOT** remove the pre-filled syringe needle cover while allowing it to reach room temperature.

999

1000

### **Assemble Additional Supplies**

1001

- Assemble additional supplies you will need for your injection. These include an alcohol swab, a cotton ball or gauze, and a sharps container for syringe disposal

1002

1003

1004

### **Check the Liquid in the Pre-filled Syringe**

1005

- Hold the pre-filled syringe by its body with the covered needle pointing downward

1006

- Look at the liquid through the viewing window of the pre-filled syringe to make sure that it is clear to slightly opalescent and colorless to slightly yellow

1007

1008

- If you cannot see the liquid through the viewing window, hold the pre-filled syringe by its body and rotate the needle cover to line up the liquid to the viewing window

1009

1010

- You may also notice an air bubble – this is normal

1011

1012

**DO NOT** use if the liquid is discolored, cloudy or contains particles. If this is the case, please contact your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for assistance.

1013

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1015

## **STEP 2: CHOOSING AND PREPARING THE INJECTION SITE**

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1017

### **Choose the Injection Site**

1018

- The recommended injection site is the front of the middle thighs

1019

1020

- You can also use the lower abdomen below the belly button, except for the two-inch area directly underneath the belly button

1021

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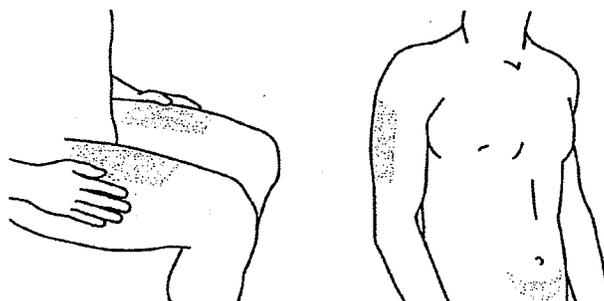
1023

- If a caregiver is giving you the injection, the caregiver can also use the outer area of the upper arms

1024

1025

1026



1027

**DO NOT** inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks

1028

1029

1030

### **Preparing the Injection Site**

1031

- Thoroughly wash your hands with soap and warm water

1032

- Wipe the injection site with an alcohol swab

1033

1034

**DO NOT** touch this area again before giving the injection. Allow the skin to dry before injecting

1035

**DO NOT** fan or blow on the clean area

1036

1037

## **STEP 3: INJECTING THE MEDICATION**

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The needle cover should **NOT** be removed until you are ready to inject the medication. The medication should be injected within 5 minutes after the needle cover has been removed.

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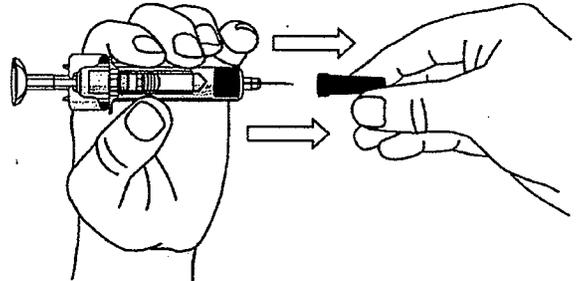
1042 **Remove the Needle Cover**

1043

1044 **DO NOT** touch the plunger during needle cover removal

1045

- 1046 • When you are ready to inject, hold the body of the pre-filled syringe with one hand, and pull the needle cover straight off
- 1047
- 1048
- 1049 • Place the needle cover into the trash
- 1050 • You may notice an air bubble in the pre-filled syringe. You **DO NOT** need to remove the air bubble
- 1051
- 1052 • You may also see a drop of liquid at the end of the needle – this is normal
- 1053
- 1054



1055

1056 **DO NOT** touch the needle or allow it to touch any surface

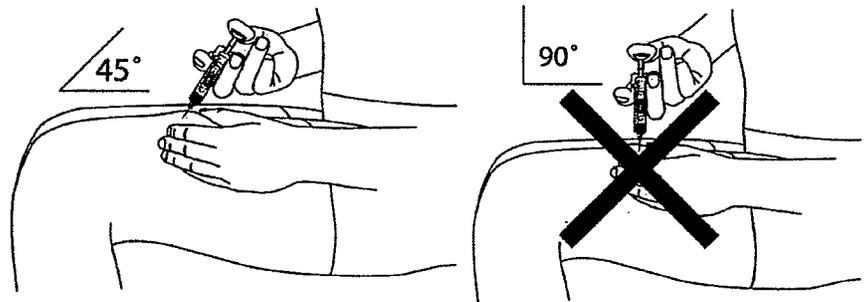
1057 **DO NOT** use the pre-filled syringe if it is dropped without the needle cover in place. If you drop the pre-filled syringe without the needle cover in place, please contact your doctor, pharmacist or call 1-888-xxx-xxxx (US only) for assistance

1058

1059 **Position the Syringe and Inject the Medication**

1060

- 1061 • Hold the body of the pre-filled syringe in one hand between the middle and index fingers and place the thumb on top of the plunger head
- 1062
- 1063
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1069 **DO NOT** pull back on the plunger at any time

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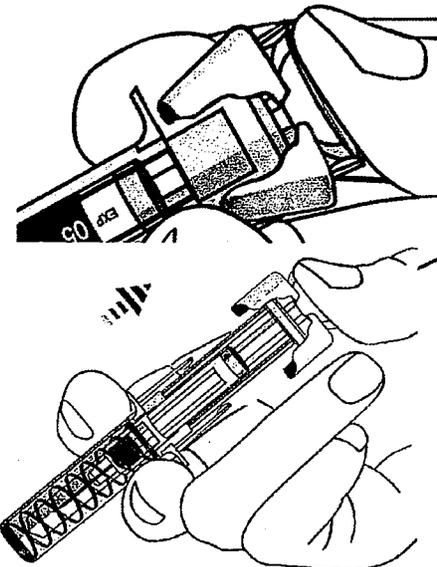
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- 1096 • Use the other hand to gently pinch the area of skin that you previously cleaned. Hold firmly
- 1097 • Place the needle at approximately a 45-degree angle to the pinched skin. In a single and swift motion, insert the needle through the skin as far as it will go
- 1098 • Inject all of the medication by pushing in the plunger until the plunger head is completely between the needle guard wings
- 1099 • When the plunger is pushed as far as it will go, continue to keep the pressure on the plunger head, take out the needle and let go of the skin
- 1100 • Slowly take your thumb off the plunger head to allow the empty syringe to move up until the entire needle is covered by the needle guard, as shown by the illustration



SIMPONI (golimumab)

1097 **STEP 4: AFTER THE INJECTION**

1098

1099 **Disposing of the Empty Syringe**

- 1100 • Immediately dispose of the empty syringe into the sharps container. For your safety and health and for the safety of others, needles and empty syringes **must NEVER** be re-used
- 1101
- 1102
- 1103 • Dispose of sharps container according to your local regulations
- 1104

1105 **Use Cotton Ball or Gauze**

- 1106 • There may be a small amount of blood or liquid at the injection site, which is normal
- 1107 • You can press a cotton ball or gauze over the injection site and hold for 10 seconds
- 1108

1109 **DO NOT** rub the injection site

1110

- 1111 • You may cover the injection site with a small adhesive bandage, if necessary
- 1112
- 1113
- 1114



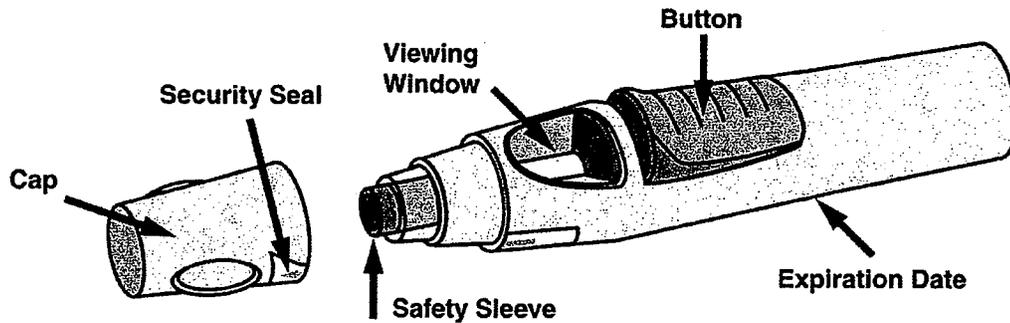
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**INSTRUCTIONS FOR INJECTING SIMPONI USING A SINGLE-USE SmartJect™ AUTOINJECTOR**

If you would like to self-inject SIMPONI, you must be trained by a healthcare professional to prepare an injection and give it to yourself. If you have not been trained, please contact your healthcare professional to schedule a training session.

**STEP 1: PREPARING TO USE THE SmartJect™ AUTOINJECTOR**

The diagram below shows what the autoinjector looks like:



**DO NOT** shake the autoinjector at any time  
**DO NOT** remove the autoinjector cap until instructed to do so

**Check Expiration Date**

- Check the expiration date (as indicated as “EXP”) on the autoinjector
- You can also check the expiration date printed on the carton
- If the expiration date has passed, do not use the autoinjector and please contact your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for assistance

**Check Security Seal**

- Check the security seal around the cap of the autoinjector. If the security seal is broken, do not use the autoinjector and please contact your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for assistance

**Wait 30 minutes**

- To ensure proper injection, allow the autoinjector to sit at room temperature outside the carton for 30 minutes out of the reach of children



**DO NOT** warm the autoinjector in any other way (For example, **DO NOT** warm it in a microwave or in hot water)

**DO NOT** remove the autoinjector cap while allowing it to reach room temperature

1159 **Assemble Additional Supplies**

- 1160 • Assemble additional supplies you will need for your injection. These include an alcohol swab, a  
1161 cotton ball or gauze, and a sharps container  
1162

1163 **Check the Liquid in the SmartJect™ Autoinjector**

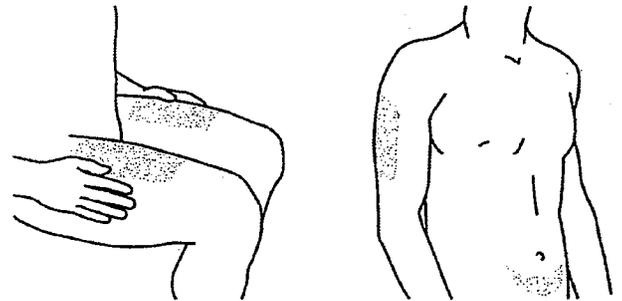
- 1164 • Look through the viewing window to make sure that the liquid in the autoinjector is clear to slightly  
1165 opalescent and colorless to slightly yellow  
1166 • You may also notice an air bubble – this is normal  
1167

1168 **DO NOT** use if the liquid is discolored, cloudy or contains particles. If this is the case, please contact  
1169 your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for assistance.  
1170

1171 **STEP 2: CHOOSING AND PREPARING THE INJECTION SITE**

1172 **Choose the Injection Site**

- 1173 • The recommended injection site is the front of the  
1174 middle thighs  
1175 • You can also use the lower abdomen below the belly  
1176 button, except for the two-inch area directly  
1177 underneath the belly button  
1178 • If a caregiver is giving you the injection, the  
1179 caregiver can also use the outer area of the upper  
1180 arms  
1181



1182 **DO NOT** inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars  
1183 or stretch marks  
1184

1185 **Preparing Injection Site**

- 1186 • Thoroughly wash your hands with soap and warm water  
1187 • Wipe the injection site with an alcohol swab  
1188

1189 **DO NOT** touch this area again before giving the injection. Allow the skin to dry before injecting

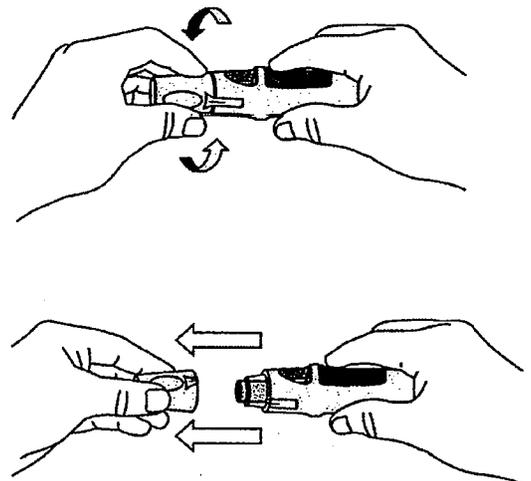
1190 **DO NOT** fan or blow on the clean area  
1191

1192 **STEP 3: INJECTING SIMPONI USING THE**  
1193 **SINGLE-USE SmartJect™ AUTOINJECTOR**  
1194

1195 **Remove the Cap**

1196  
1197 The cap should **NOT** be removed until you are ready to  
1198 inject the medication. The medication should be injected  
1199 within 5 minutes after the cap has been removed.

- 1200 • When you are ready to inject, twist the cap slightly to  
1201 break the security seal  
1202 • Pull the cap off and immediately place the cap into  
1203 the trash  
1204

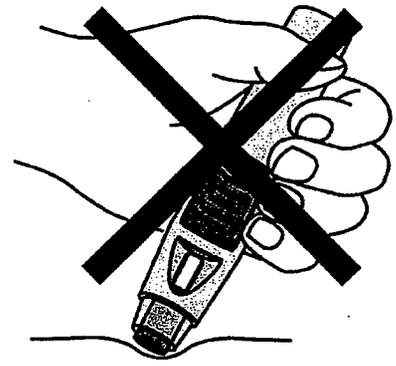
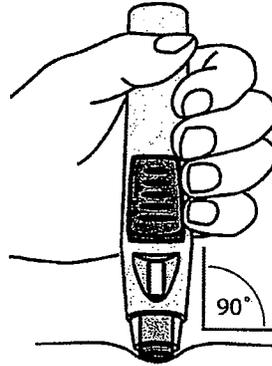


1205 **DO NOT** put the cap back on because it may damage the needle inside the autoinjector  
1206 **Note:** Do not use autoinjector if it is dropped without the cap in place. If you drop the autoinjector  
1207 without the cap in place, please contact your doctor, pharmacist or call 1 888-xxx-xxxx (US only) for  
1208 assistance.

1209  
1210 **Push the SmartJect™ Autoinjector**  
1211 **Against the Skin**

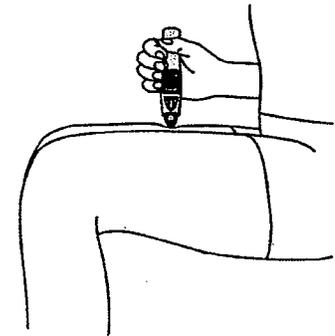
- 1212 • Hold the autoinjector comfortably in your hand
- 1213
- 1214 • Without pressing the button, push the
- 1215 open end of the autoinjector firmly
- 1216 against the skin at a 90-degree angle

1217 **Note:** Some people find that using their  
1218 free hand to pinch and hold the skin at the  
1219 injection site during administration makes  
1220 injecting easier.



1221  
1222 **Press Button to Inject**

- 1223 • Continue to hold the autoinjector firmly against the skin, and press the
- 1224 button. Once the button is pressed, it will remain pressed in so you do
- 1225 not need to keep pressure on it
- 1226 • The first loud 'click' indicates the start of the injection



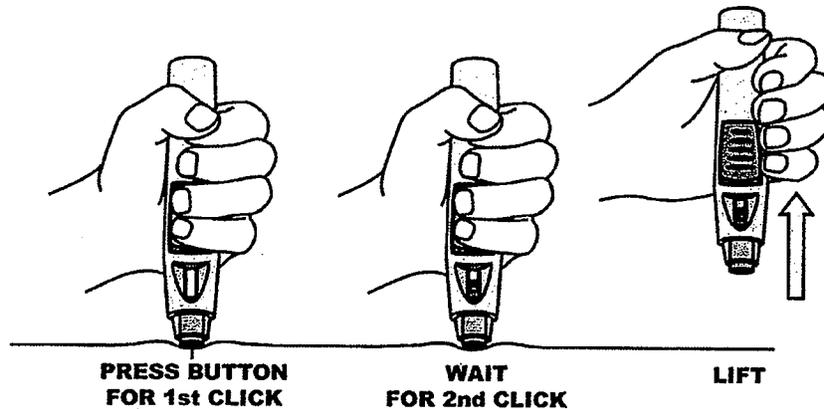
1227  
1228 **DO NOT** lift the autoinjector yet

1229 **Note:** You will not be able to push in the button unless the autoinjector is  
1230 pushed firmly against the skin

1231  
1232 **Wait for Second "Click"**

- 1233 • Continue to hold the autoinjector against the skin until you hear the second 'click' (may take up to
- 1234 15 seconds)
- 1235 • The second click indicates that the injection is finished and the needle has retracted into the
- 1236 autoinjector
- 1237 • Lift the autoinjector from the injection site

1238 **Note:** If you have hearing impairment, count 15 seconds from the time you press the button and then  
1239 lift the autoinjector from the injection site.



1240  
1241  
1242  
1243  
1244  
1245  
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1248  
1249

SIMPONI (golimumab)

1250 **STEP 4: AFTER THE INJECTION**

1251

1252 **Check the Viewing Window**

- 1253 • After injecting, check the viewing window to make sure that the
- 1254 yellow indicator is visible
- 1255 • This indicates that the autoinjector has worked properly
- 1256 • If the yellow indicator is not visible in the viewing window, call
- 1257 1-888-xxx-xxxx for assistance

1258

1259 **Disposing of the SmartJect™ Autoinjector**

- 1260 • Immediately dispose of the autoinjector in the sharps container
- 1261 • Dispose of the sharps container according to your local regulations

1262

1263 **Use Cotton Ball or Gauze**

- 1264 • There may be a small amount of blood or liquid at the injection site, which is
- 1265 normal
- 1266 • You can press a cotton ball or gauze over the injection site for 10 seconds

1267

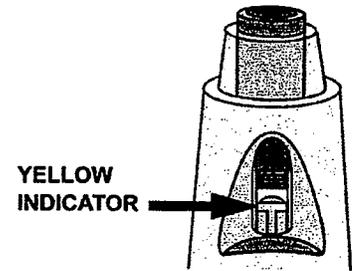
1268 **DO NOT** rub the injection site.

1269

- 1270 • You may cover the injection site with a small adhesive bandage, if necessary

1271

1272



**SIMPONI (golimumab)**

- 1272**    **Manufactured for:**
- 1273**    **Centocor Inc.**
- 1274**    **Horsham, PA 19044**
- 1275**    **US License No. 1242**
- 1276**
- 1277**    **Revised: Month/Year**
- 1278**
- 1279**    **This Medication Guide has been approved by the U.S. Food and Drug Administration.**

## SIMPONI (golimumab)

684 **17.3 FDA-Approved Patient Labeling**685 **Rx Only**

686

687

**SIMPONI (SIM-POH-NEE)**

688

**(golimumab)**

689

690 Review this patient information each time before you use SIMPONI. There may be new information.  
 691 This information does not take the place of talking with your doctor about your medical condition or  
 692 treatment. It is important to remain under your doctor's care while using SIMPONI.

693

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

695 SIMPONI is a medicine that affects your immune system. SIMPONI can lower the ability of your  
 696 immune system to fight infections. Some patients have had serious infections while receiving  
 697 SIMPONI, including tuberculosis, and systemic bacterial and fungal infections. Some patients have  
 698 died from these serious infections.

699

700 **What is SIMPONI?**

701 SIMPONI is a prescription medicine that is approved for the treatment of adult patients with  
 702 rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. In these diseases, the body  
 703 produces too much of a substance called tumor necrosis factor alpha (TNF-alpha). Too much of this  
 704 substance causes your body's immune system to attack healthy tissue and results in inflammation.  
 705 Blocking TNF-alpha with SIMPONI can reduce inflammation associated with these diseases, but can  
 706 also reduce your immune system's ability to fight off infections.

707

708 **Rheumatoid arthritis:**

709 Rheumatoid arthritis is an inflammatory disease of the joints. If you have active rheumatoid arthritis,  
 710 you will be given SIMPONI, which you will take in combination with methotrexate to:

- 711 • Reduce the signs and symptoms of your disease

712

713 **Psoriatic arthritis:**

714 Psoriatic Arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis. If you  
 715 have active psoriatic arthritis, you will be given SIMPONI, alone or in combination with methotrexate  
 716 to:

- 717 • Reduce signs and symptoms of your arthritis

718

719 **Ankylosing spondylitis:**

720 Ankylosing spondylitis is an inflammatory disease of the spine. If you have active ankylosing  
 721 spondylitis, you will be given SIMPONI to:

- 722 • Reduce the signs and symptoms of your disease

723

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

725 Before receiving treatment with SIMPONI, tell your doctor if you:

- 726 • have any kind of infection even if it is very minor.
- 727 • have an infection that won't go away or a history of infection that keeps coming back.

## SIMPONI (golimumab)

- 728 • have had TB (tuberculosis), or if you have recently been near anyone who might have TB.  
729 Your doctor will evaluate you for TB and perform a skin or a blood test. If your doctor feels that  
730 you are at risk for TB, he or she may start treating you for TB before you begin SIMPONI therapy.
- 731 • have a history of Hepatitis B infection
- 732 • have heart failure, or if you previously had or currently have any heart condition. If you  
733 develop new or worsening symptoms of heart failure, such as shortness of breath or swelling of  
734 your feet, you must notify your doctor.
- 735 • have or have had a condition that affects your nervous system, like multiple sclerosis. You  
736 should tell your doctor if you experience weakness in the arms or legs, numbness, tingling, or visual  
737 disturbances.
- 738 • have or have had any type of cancer.
- 739 • have recently received or are scheduled to receive a vaccine.
- 740 • have a latex allergy
- 741 • are pregnant, planning to become pregnant, or breastfeeding. SIMPONI should only be used  
742 during pregnancy if clearly needed. Women who are breastfeeding should talk to their doctor about  
743 whether or not to use SIMPONI.

744

745 **Tell your doctor about all the medicines you take**, including prescription and non-prescription  
746 medicines, vitamins, and herbal supplements. Especially, tell your doctor if you take KINERET  
747 (anakinra). SIMPONI and KINERET should not be taken together. Also, tell your doctor if you are  
748 taking other medications that affect your immune system.

749

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

752

### 753 **How should I take SIMPONI?**

- 754 • SIMPONI 50 mg is given by injection under the skin with a pre-filled syringe or autoinjector  
755 once a month, on the same date each month.
- 756 • SIMPONI is intended for use under the guidance and supervision of your doctor. Your doctor  
757 will tell you how often to take SIMPONI. **Do not take SIMPONI more often than prescribed.** If  
758 your doctor determines that it is appropriate, you may be able to administer SIMPONI to yourself,  
759 after proper training in injection technique (see the "**Instructions for Injecting SIMPONI under  
760 the skin yourself**").

- 761 • If you take more SIMPONI than you were told to take, call your doctor.

- 762 • Do not miss any doses of SIMPONI. If you forget to take SIMPONI, inject a dose as soon as  
763 you remember. Then, take your next dose at your regular scheduled time. This will put you back  
764 on schedule. In case you are not sure when to inject SIMPONI, contact your doctor or pharmacist.

765

### 766 **What are the possible side effects with SIMPONI?**

767 Serious side effects that may require treatment can occur during SIMPONI therapy. Possible serious  
768 side effects of SIMPONI include:

769

770 **Serious infections**

771 (see **"What is the most important information I should know about SIMPONI?"**). If you develop  
772 a fever, chills, headache, flu-like symptoms, feel tired, have a cough, blood in your sputum, shortness  
773 of breath, night sweats, weight loss, nausea, vomiting, diarrhea, frequency or burning while passing  
774 urine, redness or swelling of skin or joint, cold sores, tooth pain or new or worsening of pain in any  
775 location while or after receiving SIMPONI, you should tell your doctor right away because these could  
776 be signs that you are getting an infection.

777

778 Treatment with TNF-blocking agents such as SIMPONI may result in reactivation of the hepatitis B  
779 virus in patients who carry this virus. If you know or suspect you may be a carrier of hepatitis B virus,  
780 be sure to tell your doctor about this as this may impact the decision to start or continue treatment with  
781 SIMPONI.

782

783 **Allergic reactions**

784 Some patients may get allergic reactions to SIMPONI. Symptoms of an allergic reaction may include  
785 hives, rash, difficulty breathing, chest pain, and high or low blood pressure. You should contact your  
786 doctor if you experience any of these symptoms.

787

788 **Needle Cover with Dry Natural Rubber (a form of latex)**

789 The needle cover on the pre-filled syringe as well as the pre-filled syringe in the autoinjector contains  
790 dry natural rubber (a form of latex). This may cause allergic reactions in people who are sensitive to  
791 latex. Tell your doctor if you have ever had an allergic reaction to latex and developed any allergic  
792 reaction to SIMPONI injection.

793

794 **Injection site reactions**

795 Some patients develop reactions at the injection site on their skin after SIMPONI injections. These  
796 reactions may include mild rash, swelling bruising, hives, pain and irritation. You should contact your  
797 doctor if you experience severe symptoms at injection site.

798

799 **Cancer**

800 In clinical studies, reports of blood cancer called lymphoma were more frequent in patients on  
801 SIMPONI than expected for people in general. People who have been treated for rheumatoid arthritis,  
802 psoriatic arthritis or ankylosing spondylitis for a long time, particularly those with highly active  
803 disease may be more prone to develop lymphoma. Cancers, other than lymphoma, have also been  
804 reported in patients treated with SIMPONI or other TNF blockers. In a study of SIMPONI in patients  
805 with severe persistent asthma, cancers occurred in SIMPONI treated patients but not in control treated  
806 patients. If you have severe persistent asthma you should discuss with your doctor whether SIMPONI  
807 is appropriate for you.

808

809 If you take SIMPONI or other TNF blockers, your risk of developing lymphoma or other cancers may  
810 increase. You should also tell your doctor if you have had or develop lymphoma or other cancers  
811 while you are taking SIMPONI. Whether you decide to use SIMPONI or not, you should discuss with  
812 your doctor the cancer screening measures and impact of the life style choices on the risk of  
813 developing cancer.

814

815 **Congestive heart failure**

816 Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF-  
817 blocking agents. SIMPONI has not been studied in patients with CHF. Tell your doctor if you have  
818 heart failure. If you have heart failure and doctor decides to administer SIMPONI, your condition  
819 should be closely monitored during treatment. If you develop new or worsening symptoms of heart  
820 failure (such as shortness of breath or swelling of your feet), you should contact your doctor right  
821 away.

822

823 **Neurological Events**

824 In rare instances patients treated with TNF blocking agents may develop diseases such as multiple  
825 sclerosis. Tell your doctor if you have a history of a neurological disease. If you develop symptoms  
826 of neurological disease such as changes in your vision, weakness in your arms or legs, numbness or  
827 tingling in any part of your body, you should contact your doctor right away.

828

829 **Vaccinations**

830 You should not receive certain vaccines while using SIMPONI. If you have recently received or are  
831 scheduled to receive a vaccine, please inform your doctor.

832

833 **Liver Problems**

834 There have been cases where patients taking SIMPONI developed liver problems. Signs that you  
835 could be having a problem include: skin and eyes turning yellow, dark brown-colored urine, right-  
836 sided abdominal pain, fever, nausea, vomiting, and severe fatigue. You should contact your doctor  
837 right away if you experience these symptoms.

838

839 **Common side effects with SIMPONI include:**

840 Flu, bronchitis, infection of soft tissues, sore throat, upper respiratory infection, sinus infection, runny  
841 nose, cold sores, abnormal liver tests, dizziness, numbness or tingling, high blood pressure, fever and  
842 redness at the site of injection.

843

844 Any medicine may have side effects. These are not all of the side effects with SIMPONI. Tell your  
845 doctor about any side effect that bothers you or does not go away. Ask your doctor or pharmacist for  
846 more information.

847

848 **How do I store SIMPONI?**

849 If you are using SIMPONI at home, it is important that it is stored in your refrigerator although not in  
850 the freezer compartment. SIMPONI should not be frozen. Keep the product in the original carton to  
851 protect from light until the time of use. Do not shake.

852

853 **What are the ingredients in SIMPONI?**

854 The active ingredient is golimumab. The inactive ingredients in SIMPONI are: sorbitol, L-histidine,  
855 L-histidine monohydrochloride monohydrate, polysorbate 80 and water for injection. No preservatives  
856 are present.

857

858 **Other important points**

859 SIMPONI is a clear to slightly clear, colorless to light yellow solution. This appearance is not unusual  
860 for solutions containing protein.

SIMPONI (golimumab)

861

862 SIMPONI should not be used:

863 - after the expiration date on the label;

864 - if the product is damaged;

865 - if the liquid is discolored, cloudy or you can see other particulate matter floating in it;

866 - if you know, or think that it may have been exposed to extreme temperatures (such as accidentally  
867 frozen or heated);

868 Always keep medicine out of the reach of children.

869

870 **Instructions for Injecting SIMPONI under the skin yourself**

871 At the start of your therapy, SIMPONI may be injected by medical or nursing staff. However, your

872 doctor may decide that it is right for you or your caregiver to learn how to inject SIMPONI under the

873 skin (subcutaneously) yourself. Make sure you (or your caregiver) have been trained how to inject

874 SIMPONI before you do it yourself. Call your doctor if you have any questions about giving yourself

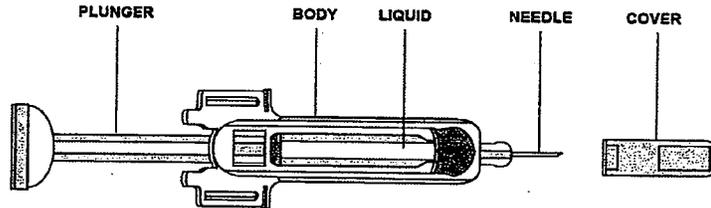
875 an injection.

876

876 **INSTRUCTIONS FOR INJECTING SIMPONI USING A PRE-FILLED SYRINGE**

877

878 **STEP 1: PREPARING FOR PRE-FILLED SYRINGE USE**



879

880

881

882

883

884

885

If you would like to self-inject SIMPONI, you must be trained by a healthcare professional to prepare an injection and give it to yourself. If you have not been trained, please contact your healthcare provider to schedule a training session.

886

**Check Expiration Date**

887

888

889

890

Open the box and remove the pre-filled syringe. Check the expiration date on the pre-filled syringe and the label of the box. If the expiration date has passed, do not use the pre-filled syringe and please contact your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for assistance.

891

**DO NOT** shake the pre-filled syringe at any time.

892

893

**DO NOT** remove the needle cover from the pre-filled syringe.

894

895

**Use Syringe at Room Temperature**

896

897

898

899

900

To ensure proper injection, allow the pre-filled syringe to sit at room temperature outside of the box for 30 minutes out of the reach of children. **DO NOT** warm the pre-filled syringe in any other way. (For example, do not warm it in a microwave or in hot water.) **DO NOT** remove the pre-filled syringe needle cover while allowing it to reach room temperature.



901

902

**Assemble Additional Supplies**

903

904

905

Assemble the additional supplies you will need for your injection. These include an alcohol swab, a cotton ball or gauze, and a sharps container for syringe disposal.

906

**Check Solution in Syringe**

907

908

909

910

911

912

913

914

915

916

Hold the pre-filled syringe with the covered needle pointing upward. Look at the solution or liquid in the syringe to make sure that it is clear to slightly opalescent and colorless to slightly yellow. **DO NOT** use if it is discolored, cloudy or contains particles. If the solution is not clear to slightly opalescent and colorless to slightly yellow or contains particles, please contact your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for assistance.

917 **STEP 2: CHOOSING AND PREPARING THE INJECTION SITE**

918

919 **Choose the Injection Site**

920 The recommended injection site is the front of the middle thighs.

921 You can also use the abdomen, except for the two-inch area

922 around the belly button. If a caregiver is giving you the injection,

923 the caregiver can also use the outer area of the upper arms. Do

924 not inject into areas where the skin is tender, bruised, red, scaly

925 or hard. Avoid areas with scars or stretch marks.

926

927 **Preparing Injection Site**

928 Thoroughly wash your hands with soap and warm water. Wipe the injection site with an alcohol swab.

929 **DO NOT** touch this area again before giving the injection. Allow the skin to dry before injecting. Do

930 not fan or blow on the clean area.

931

932 **STEP 3: INJECTING THE DRUG**

933

934 **Remove the Needle Cover**

935 When you are ready to inject, pick up the pre-filled syringe, hold

936 the body of the syringe with one hand and pull the needle cover

937 straight off. Throw the needle cover into the trash. You may

938 notice a small air bubble in the pre-filled syringe. You do not

939 need to remove the air bubble. You may also see a drop of liquid

940 at the end of the needle – this is normal. Do not touch the needle or allow it to touch any surface.

941 **Note:** The needle cover should **NOT** be removed until you are ready to inject the dose. The dose

942 should be injected within 5 minutes after the needle cover has been removed. Do not use syringe, if it

943 is dropped without the needle cover in place. If you drop the syringe without the needle cover in

944 place, please contact your doctor, pharmacist or call 1 888-xxx-xxxx (US only) for assistance.

945

946 **Position the Syringe to Inject**

947 Hold the syringe with one hand like a pencil, and use the other hand to gently pinch the area of skin

948 that you previously cleaned. Hold firmly.

949

950 **Inject the Medication**

951 Place the needle at approximately a 45-degree angle to the pinched

952 skin. In a single and swift motion, insert the needle through the skin

953 as far as it will go. Push in the plunger and inject the medication.

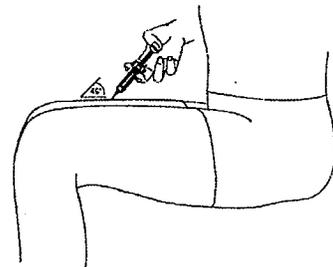
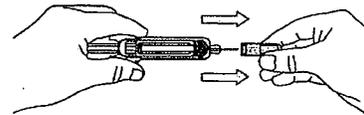
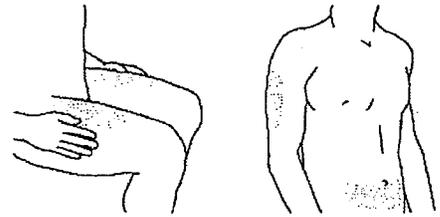
954 When the plunger meets the end of the syringe barrel and all of the

955 medication has been injected, release the pinched skin and gently

956 remove the needle. Following complete injection, the needle guard

957 will automatically extend over the needle and lock as you relax your

958 hand.



SIMPONI (golimumab)

959

960 **STEP 4: AFTER THE INJECTION**

961

962 **Disposing of the Empty Syringe**

963 Immediately dispose of the empty syringe into the sharps container. For your  
964 safety and health and for the safety of others, needles and syringes **must**  
965 **NEVER** be re-used. Dispose of sharps container according to your local  
966 regulations.

967

968 **Use Cotton Ball or Gauze**

969 There may be a small amount of blood or liquid at the injection site, which is  
970 normal. You can press a cotton ball or gauze over the injection site and hold  
971 for 10 seconds. Do not rub the injection site. You may cover the injection site  
972 with a small adhesive bandage, if necessary.

973

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975

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977

**INSTRUCTIONS FOR INJECTING SIMPONI USING AN AUTOINJECTOR**

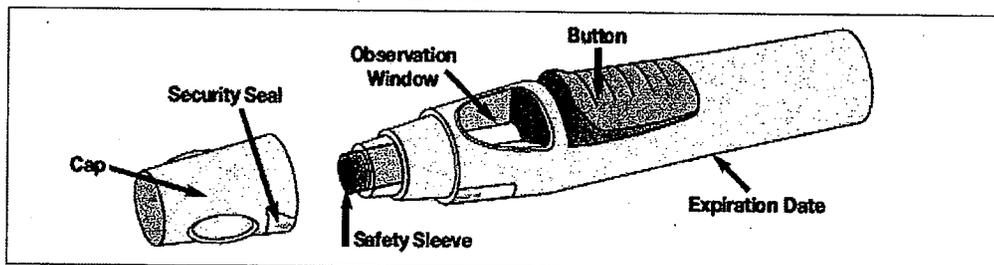
978

979 **Autoinjector Instructions for Use for the Patient and Caregiver**

980

981

**STEP 1: PREPARING FOR USE OF AUTOINJECTOR**



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987

988

**If you would like to self-inject SIMPONI, you must be trained by a healthcare professional to prepare an injection and give it to yourself. If you have not been trained, please contact your healthcare provider to schedule a training session.**

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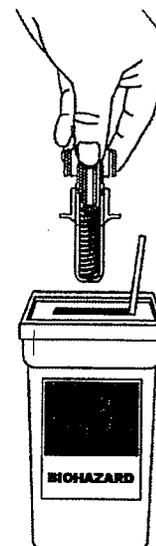
997

**Check Expiration Date**

Check the expiration date on the single-use autoinjector and the label of the box. If the expiration date has passed, do not use the autoinjector and please contact your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for assistance.

**DO NOT** shake the autoinjector at any time.

**DO NOT** remove the autoinjector cap at this point.



998

999 **Check Security Seal**

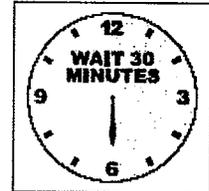
1000 Check the security seal around the cap of the autoinjector. If the security seal is broken, do not use the  
 1001 autoinjector and please contact your doctor or pharmacist or call 1-888-xxx-xxxx (US only) for  
 1002 assistance.

1003

1004 **Use Autoinjector at Room Temperature**

1005 To ensure proper injection, allow the autoinjector to sit at room temperature outside  
 1006 the box for 30 minutes out of the reach of children. **DO NOT** warm the autoinjector  
 1007 in any other way. (For example, do not warm it in a microwave or in hot water.)

1008 **DO NOT** remove the autoinjector cap while allowing it to reach room temperature.  
 1009



1010 **Assemble Additional Supplies**

1011 Assemble additional supplies you will need for your injection. These include an alcohol swab, a cotton  
 1012 ball or gauze, and a sharps container.  
 1013

1014 **Check the Solution in Autoinjector**

1015 Look through the observation window to make sure that the solution or liquid in the autoinjector is  
 1016 clear to slightly opalescent and colorless to slightly yellow. You may also notice an air bubble, which  
 1017 is normal. **DO NOT** use if the solution or liquid is discolored, cloudy, or contains particles. If the  
 1018 solution is not clear to slightly opalescent and colorless to slightly yellow, or contains particles, please  
 1019 contact your doctor or pharmacist or call 1-888—xxx-xxxx (US only) for assistance.  
 1020

1021

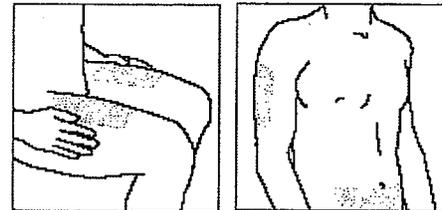
1022

1022 **STEP 2: CHOOSING AND PREPARING THE INJECTION SITE**

1023

1024 **Choose the Injection Site**

1025 The recommended injection site is the front of the middle  
 1026 thighs. You can also use the abdomen, except for the two-inch  
 1027 area around the belly button. If a caregiver is giving you the  
 1028 injection, the caregiver can also use the outer area of the upper  
 1029 arms. Do not inject into areas where the skin is tender, bruised,  
 1030 red, scaly or hard. Avoid areas with scars or stretch marks.  
 1031



1032

1032 **Preparing Injection Site**

1033 Thoroughly wash your hands with soap and warm water. Wipe the injection site with an alcohol swab.  
 1034 **DO NOT** touch this area again before giving the injection. Allow the skin to dry before injecting. Do  
 1035 not fan or blow on the clean area.  
 1036

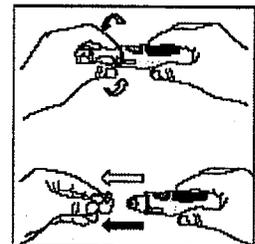
1037

1037 **STEP 3: INJECTING THE DRUG**

1038

1039 **Remove the Cap**

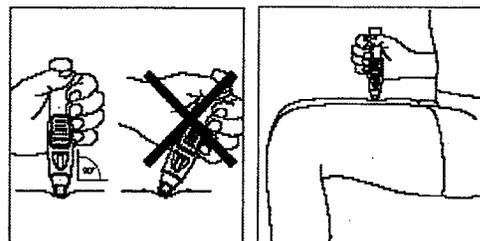
1040 When you are ready to inject, twist the cap slightly to break the security seal. Pull  
 1041 the cap off and discard it immediately. **DO NOT** put the cap back on because it  
 1042 may damage the needle inside the autoinjector. **Note:** The dose should be injected  
 1043 within 5 minutes after the needle cap has been removed. Do not use autoinjector if



1044 it is dropped without the cap in place. If you drop the autoinjector without the cap in place, please  
 1045 contact your doctor, pharmacist or call 1 888-xxx-xxxx (US only) for assistance.  
 1046

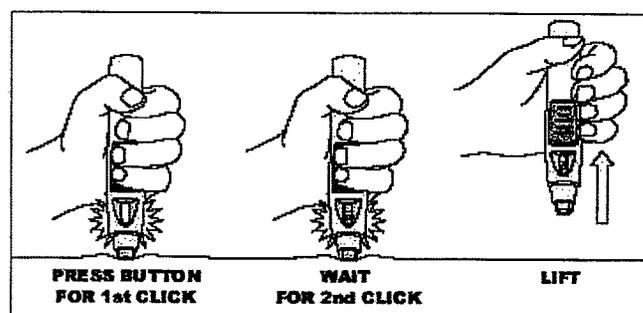
1047  
 1048 **Push the Autoinjector Against the Skin**

1049 Hold the autoinjector comfortably in your hand. Without pressing  
 1050 the button, push the open end of the autoinjector firmly against the  
 1051 skin at a 90-degree angle. **Note:** Some people find that using their  
 1052 free hand to pinch and hold the skin at the injection site during  
 1053 administration makes injecting easier.  
 1054



1055 **Press Button to Inject**

1056 Continue to hold the autoinjector firmly against  
 1057 the skin, and press the button. The first loud 'click'  
 1058 begins the injection. **DO NOT** lift the autoinjector  
 1059 yet. **Note:** You will not be able to push in the  
 1060 button unless the autoinjector is pushed firmly  
 1061 against the skin.  
 1062



1063 **Wait for Second "Click"**

1064 Continue to hold the autoinjector against the skin  
 1065 until you hear the second 'click' (up to 15  
 1066 seconds). The second click indicates that the  
 1067 injection is finished and the needle is retracted into the autoinjector. Lift the autoinjector from the  
 1068 injection site. **Note:** If you have hearing impairment, count 15 seconds from the time you press the  
 1069 button and then lift the autoinjector from the injection site.  
 1070

1071  
 1072 **STEP 4: AFTER THE INJECTION**

1073  
 1074 **Check Observation Window**

1075 After injecting, check the observation window to make sure that the yellow  
 1076 indicator is visible. This indicates that the autoinjector has worked properly. If the  
 1077 yellow indicator is not visible in the observation window, call 1-888-xxx-xxxx for  
 1078 assistance.  
 1079



1080 **Disposing of the Autoinjector**

1081 Immediately dispose of the autoinjector in the sharps container. Dispose of sharps  
 1082 container according to your local regulations.  
 1083

1084 **Use Cotton Ball or Gauze**

1085 There may be a small amount of blood or liquid at the injection site, which is  
 1086 normal. You can press a cotton ball or gauze over the injection site for 10 seconds.  
 1087 Do not rub the injection site. You may cover the injection site with a small adhesive  
 1088 bandage, if necessary.

