SIMPONI® (golimumab)—Educational Program

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golimumab

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SIMPONI, a human IgG1κ monoclonal antibody against tumor necrosis factor (TNF), is indicated for the treatment of rheumatoid arthritis (RA),[a] psoriatic arthritis (PsA),[b] ankylosing spondylitis (AS),[c] and ulcerative colitis (UC).[1,d]

Summary

Key safety aspects to consider with respect to the Educational Program for SIMPONI[1]:

- The risk of serious infections, including opportunistic infections and tuberculosis (TB), in patients treated with SIMPONI
- The warning to not start SIMPONI during an active infection, such as TB or hepatitis B virus (HBV)
- The need to carefully monitor for any infection developments during treatment with SIMPONI and to stop treatment if infection becomes serious
- The need to adequately screen patients for TB prior to initiating treatment with SIMPONI in order to assess the potential risk of TB
- The need for all patients to undergo periodic skin examinations, particularly patients with risk factors for skin cancer
- The potential risk of HBV reactivation
- The potential risk of congestive heart failure (CHF); SIMPONI is contraindicated in New York Heart Association (NYHA) class III/IV
- The potential risk of acute injection-related reactions and serious hypersensitivity reactions (SHRs), including after first administration
- The technique to administer SIMPONI and guidance for health care professionals (HCPs) to report administration errors and to instruct their patients on techniques for self-administration
- The necessity for HCPs to provide the Patient Alert Card (PAC) and review it with their patients

Educational Program goal: Diminish the risk of adverse events by ensuring that physicians and their professional staff become aware of the most appropriate patient selection and management and administration technique for SIMPONI.

Background Information

As part of the Risk Management Plan for SIMPONI, Janssen Biologics and MSD have developed an Educational Program targeting prescribers of SIMPONI for RA, PsA, AS, and UC.

SIMPONI—Educational Program Objectives

Mitigate the risk of serious infections,[e] opportunistic infections, and new-onset or worsening congestive heart failure

- Ensure prescriber awareness of risk.
- Provide guidance on appropriate patient selection and management of risk.

Mitigate the risk of administration errors by physician and support staff

- Increase awareness of correct administration technique.
- Ensure reporting of any issues related to maladministration.
- Provide proper instruction to patients on self-administration techniques.

Mitigate the risk of serious hypersensitivity reactions

Ensure awareness of the following:

- Potential risk of acute injection-related reactions and delayed serious systemic hypersensitivity reactions, including after first administration
- Management and reporting of the risk
- Proper instructions to patients about this risk

Create awareness of the Patient Alert Card

- Ensure that the PAC is given to and reviewed with all patients treated with SIMPONI. The physician should also reinforce that the patient should carry the PAC and share it with other health care providers who may also be taking care of the patient.

This Educational Program will be conducted in the context of the approved labeling for SIMPONI. Therefore, the educational materials will contain information on the safety profile of SIMPONI in RA, PsA, AS, and UC in accordance with the Summary of Product Characteristics (SPC).

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[a]SIMPONI, in combination with methotrexate (MTX), is indicated for the treatment of moderate to severe, active rheumatoid arthritis in adults when the response to disease-modifying antirheumatic drug (DMARD) therapy, including MTX, has been inadequate. SIMPONI, in combination with MTX, is also indicated for the treatment of severe, active, and progressive RA in adults not previously treated with MTX.

[b]SIMPONI, alone or in combination with MTX, is indicated for the treatment of active and progressive PsA in adult patients when the response to previous DMARD therapy has been inadequate.

[c]SIMPONI is indicated for the treatment of severe, active AS in adults who have responded inadequately to conventional therapy.

[d]SIMPONI is indicated for treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies.

[e]TB and HBV reactivation.

Safety Aspects

1. The risk of **serious infections**, including **opportunistic infections** and **tuberculosis**, in patients treated with SIMPONI

Serious infections may occur in patients affected by autoimmune diseases such as RA, PsA, AS, or UC and in patients receiving anti-TNF treatment. Predisposition to serious infectious diseases and difficulty in the clearance of microorganisms are expected with TNF-antagonist treatment.[2] However, it is difficult to know whether there is a link between the existence of an autoimmune disease and the risk of developing an infection and/or whether the increased risk comes from the therapies used to treat such a disease (eg, corticosteroids, methotrexate [MTX]).[3–5] Anti-TNF treatment may increase the risk of infections.[1]

The use of SIMPONI in patients with active TB or other severe infections, such as sepsis, and opportunistic infections is contraindicated. Caution should be exercised when considering the use of SIMPONI in patients with a chronic infection or a history of recurrent infection. Patients should be advised of and avoid exposure to potential risk factors for infection as appropriate. For patients who have resided in or traveled to regions where invasive fungal infections such as histoplasmosis, coccidioidomycosis, or blastomycosis are endemic, the benefits and risks of treatment with SIMPONI should be carefully considered before initiation of therapy.[1]

Infections have been reported in patients receiving TNF-blocking agents, including SIMPONI. SIMPONI should not be given to patients with a clinically important active infection. Caution should be exercised when considering the use of SIMPONI in patients with a chronic infection or a history of recurrent infection. (See sections 4.3, 4.4, and 4.8 of the SPC for SIMPONI for information on serious infections.)

In controlled Phase 3 trials through Week 16 in patients with RA, PsA, and AS, serious infections were observed in 1.4% of patients treated with golimumab and 1.3% of control-treated patients. Through Week 16, the incidence of serious infections per 100 subject-years of follow-up was 7.4 (95% CI: 4.6, 11.1) for the golimumab 100-mg group, 3.3 (95% CI: 1.3, 6.9) for the golimumab 50-mg group, and 4.2 (95% CI: 1.8, 8.2) for the placebo group (see Table 1; golimumab 100-mg data not presented).[1]

In the controlled period of UC trials of golimumab induction, serious infections were observed in 0.8% of patients treated with golimumab and 1.5% of control-treated patients. In the controlled and uncontrolled portions of the pivotal trials with a median follow-up of approximately 2 years, the incidence of serious infections per 100 subject-years of follow-up was 4.9 (95% CI: 4.3, 5.7) for the golimumab 100-mg group and 3.1 (95% CI: 2.5, 3.9) for the golimumab 50-mg group (see Table 2).[1]

Table 1. Number of serious infections per 100 subject-years of follow-up during placebo-controlled portions of Phase 3 RA, PsA, and AS studies of SIMPONI[1]

	Placebo (± MTX)	SIMPONI (50 mg ± MTX)
Incidence of serious infections per 100 subject-years[a]	4.2	3.3
95% confidence interval	1.8, 8.2	1.3, 6.9

[a]Through Week 16.

Table 2. Number of serious infections per 100 subject-years of follow-up during controlled and uncontrolled portions of pivotal UC studies of SIMPONI[1]

	SIMPONI 50 mg	SIMPONI 100 mg
Incidence of serious infections per 100 subject-years[b]	3.1	4.9
95% confidence interval	2.5, 3.9	4.3, 5.7

[b]Median follow-up of approximately 2 years.

2. The need to **adequately screen patients for tuberculosis prior to initiating treatment** with SIMPONI in order to assess the potential risk of tuberculosis

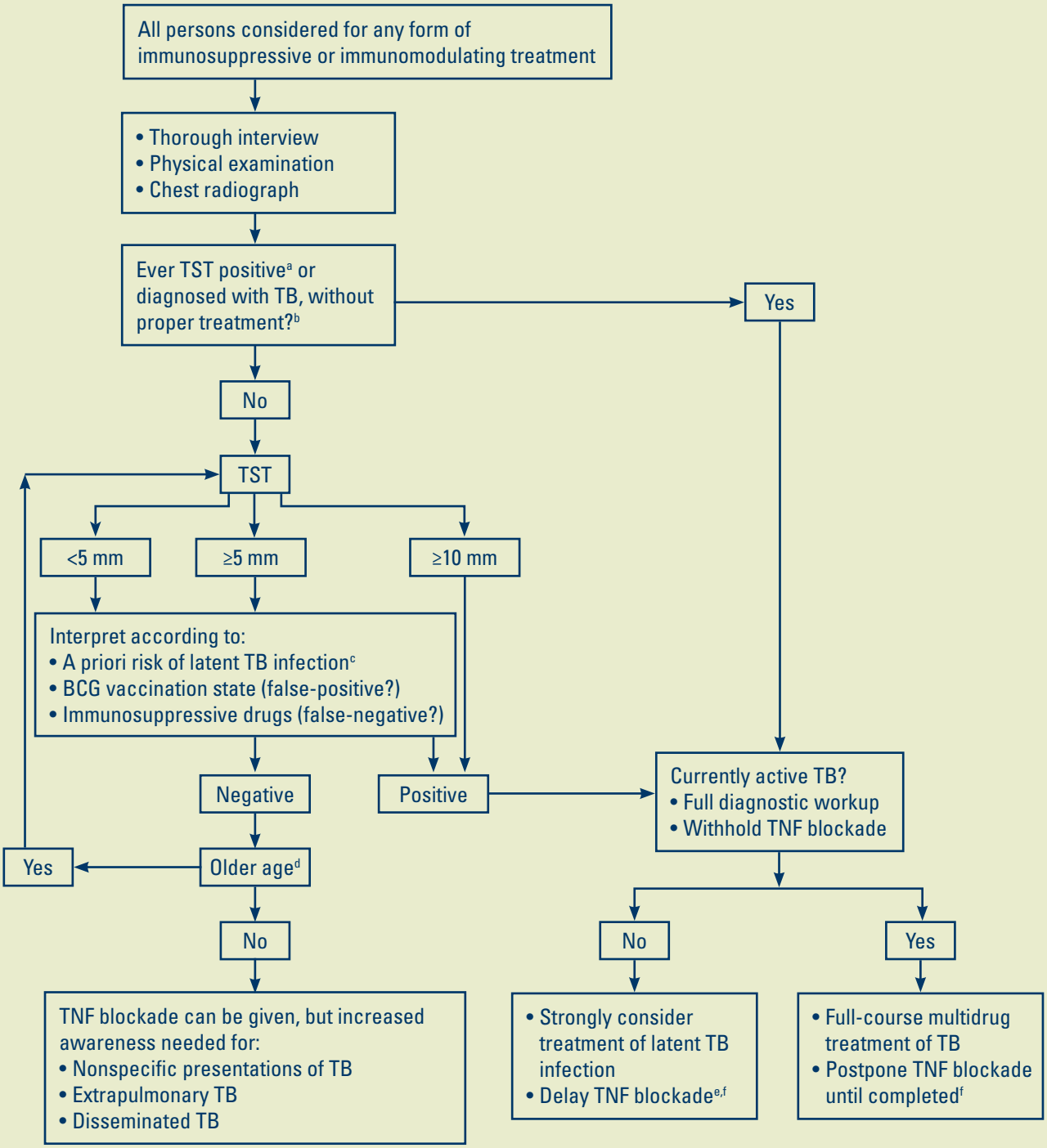
TNF is critical for prevention of the establishment of mycobacterial infection and the maintenance of latent TB.[6,7] Recommendations to prevent reactivation of latent TB can effectively lessen the likelihood of active TB in patients treated with TNF antagonists.[8]

The evaluation for TB risk should include a detailed medical history, with personal history of TB or possible previous contact with TB, and previous and/or current immunosuppressive therapy. Appropriate screening tests (ie, tuberculin skin or blood test and chest x-ray) defined by local guidelines should be performed in all patients. (See Figure 1.) It is recommended that the conduct of these tests be recorded on the PAC. If active TB is diagnosed, therapy with SIMPONI must not be initiated.[1] (See section 4.3 of the SPC for SIMPONI.)

Patients should be evaluated for TB risk factors and tested for TB infection according to local guidelines prior to treatment with SIMPONI. Treatment of latent TB infection should be initiated prior to therapy with SIMPONI. (See section 4.4 of the SPC for SIMPONI for information on TB.)

All patients should be instructed to seek medical advice if signs and symptoms suggestive of TB (eg, persistent cough, wasting/weight loss, low-grade fever) appear during or after treatment with SIMPONI.[1]

Figure 1. Tuberculosis screening algorithm[1, 9, 10]



TST=tuberculin skin test; BCG= Bacillus Calmette-Guérin.

[a]In vitro interferon-γ release assay (IGRA) screening has been recently introduced for the diagnosis of latent infection of TB.

[b]Adequate treatment of active TB is defined as ≥6 months of treatment, including ≥2 months of rifampin combined with pyrazinamide. Adequate treatment of latent TB infection consists of ≥6 months of isoniazid, ≥2 months of rifampin plus pyrazinamide, or ≥4 months of rifampin.

[c]The risk of latent TB infection, as deduced from the presence of risk factors for prior exposure, depends on age, country of origin, travel and occupational history, recognized exposure to a patient with pulmonary TB, or regular exposure to persons belonging to a risk group for TB (prison inmates, inhabitants of mental institutions, immigrants and asylum seekers from high-endemic countries, homeless persons, drug abusers).

[d]In persons who may have been infected long ago, the response to a first TST may be negative, but positive after a second test as a result of a booster phenomenon. Two-step testing could be useful in the cohort in which the prevalence of TB infection exceeds 5%; ie, in persons born before 1945. Two-step testing may also be valuable in immunosuppressed persons, irrespective of age.

[e]There are no evidence-based data to determine a safe interval between the start of treatment of latent TB infection and TNF blockade.

[f]Patients treated with SIMPONI are at increased risk for developing serious infections, such as TB, that may lead to hospitalization or death. All patients should be tested for TB prior to the start of treatment with SIMPONI. If latent or active TB is present, initiate treatment for TB prior to treatment with SIMPONI. Do not start SIMPONI during an active infection. Patients treated for active or latent TB should be re-evaluated before starting treatment with SIMPONI. Monitor all patients carefully during use of SIMPONI, and stop SIMPONI if infection becomes serious.

3. The potential risk of **hepatitis B virus reactivation**

Reactivation of hepatitis B has occurred in patients receiving a TNF antagonist, including SIMPONI, who are chronic carriers of this virus (ie, surface antigen positive). Some cases have had a fatal outcome. Patients at risk of HBV infection should be evaluated for prior evidence of HBV infection before initiating therapy with SIMPONI. Carriers of HBV who require treatment with SIMPONI should be closely monitored for signs and symptoms of active HBV infection throughout therapy and for several months following termination of therapy.[1]

Carriers of HBV who require treatment with SIMPONI should be closely monitored for signs and symptoms of active HBV infection. In patients who develop HBV reactivation, SIMPONI should be stopped and appropriate therapy should be initiated. (See section 4.4 of the SPC for SIMPONI for information on HBV reactivation.)

4. The potential risk of **congestive heart failure**

New and worsening CHF has been reported with TNF blockers, including SIMPONI. SIMPONI has not been studied in patients with CHF. SIMPONI is contraindicated in patients with moderate to severe CHF (NYHA class III/IV). SIMPONI should be used with caution in patients with mild heart failure (NYHA class I/II). Patients should be closely monitored, and SIMPONI must be discontinued in patients who develop new or worsening symptoms of heart failure.[1]

SIMPONI is contraindicated in patients with moderate or severe heart failure (NYHA class III/IV). SIMPONI should be used with caution in patients with mild heart failure (NYHA class I/II). (See sections 4.3, 4.4, and 4.8 of the SPC for SIMPONI for information on CHF.)

5. The potential risk of **acute injection-related reactions** and **serious hypersensitivity reactions, including after first administration**

In the controlled periods of pivotal trials, 5.1% of patients treated with SIMPONI had injection site reactions (ISRs) compared with 2.0% of control patients. The presence of antibodies to SIMPONI may increase the risk of ISRs. The majority of the ISRs were mild or moderate, and the most frequent manifestation was injection site erythema.[1]

In controlled Phase 2b and 3 trials in RA, PsA, AS, and severe persistent asthma and Phase 2/3 trials in UC, no patients treated with SIMPONI developed anaphylactic reactions. In postmarketing experience, serious systemic hypersensitivity reactions (including anaphylactic reaction) have been reported following administration of SIMPONI. Some of these reactions occurred after the first administration of SIMPONI. If an anaphylactic reaction or other serious allergic reactions occur, administration of SIMPONI should be discontinued immediately and appropriate therapy initiated.[1]

Patients treated with SIMPONI in clinical trials have reported ISRs more frequently than control patients. Serious systemic hypersensitivity reactions (including anaphylactic reaction) have been reported with SIMPONI during postmarketing experience. (See sections 4.4 and 4.8 of the SPC for SIMPONI for information on ISRs and SHRs.)

The needle covers on the prefilled pen and prefilled syringe are manufactured from dry natural rubber containing latex and may cause allergic reactions in individuals sensitive to latex.[1]

6. The **technique to administer SIMPONI** and guidance for health care professionals to **report administration errors** and to **instruct their patients on techniques for self-administration**

SIMPONI should be administered subcutaneously. Treatment with SIMPONI is to be initiated and supervised by qualified physicians experienced in the diagnosis and treatment of RA, PsA, AS, or UC. The patient will receive training from the HCP on how to self-inject SIMPONI according to the instructions for administration provided in the package leaflet. The full amount of SIMPONI should be administered at all times. Please report any failure to administer SIMPONI.[1]

At the start of therapy, medical or nursing staff may inject SIMPONI, then SIMPONI can be self-injected by the patient. (See the SPC for SIMPONI or the package leaflet for more detailed information on the technique to administer SIMPONI.)

SIMPONI is available both as a single-use prefilled syringe and as a single-use prefilled pen (SmartJect®). Each contains either 50-mg SIMPONI in 0.5-mL volume or 100-mg SIMPONI in 1.0-mL volume (dependent on availability).[1]

7. The necessity for health care professionals to **provide the Patient Alert Card and review it with their patients**

The PAC contains information on the risks associated with the use of SIMPONI, including TB screening information and results, and other relevant safety information. Patients should be instructed to show the PAC to any physician involved in their treatment.[1]

Patients treated with SIMPONI should be given the PAC. The PAC contains important safety information that the patient needs to be aware of before and during treatment with SIMPONI. If deemed appropriate by the physician, patients should be instructed to show the PAC to other HCPs involved in their treatment.

SIMPONI is manufactured by Janssen Biologics and is distributed by MSD.

We appreciate your interest in SIMPONI. If you have any questions or require additional information, please feel free to contact the Medical Information Center at your local telephone number.

References

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Important Safety Information About SIMPONI

Insert ISI for SIMPONI here.
The current ISI can be found in the Toolbox.

Selected Safety Information for SIMPONI

Insert local long balance for SIMPONI here.
The current global SSI can be found on the PRESTO teamsite.

For additional safety information, please consult the Summary of Product Characteristics.