

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

WARNINGS: SERIOUS INFECTIONS AND MALIGNANCY

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).
- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which SIMPONI is a member (5.2).

RECENT MAJOR CHANGES

Dosage and Administration (2.2)	8/2011
Warnings and Precautions, Serious Infections (5.1)	8/2011
Warnings and Precautions, Congestive Heart Failure (5.3)	3/2011
Warnings and Precautions, Demyelinating Disorders (5.4)	3/2011
Warnings and Precautions, Switching Between Biological Disease Modifying Antirheumatic Drugs (DMARDs) (5.7)	3/2011
Warnings and Precautions, Hematologic Cytopenias (5.8)	3/2011
Warnings and Precautions, Hypersensitivity Reactions (5.10)	8/2011

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

FULL PRESCRIBING INFORMATION: CONTENTS*

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7 DRUG INTERACTIONS

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 in 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).
- Hypersensitivity Reactions – Serious systemic hypersensitivity reactions including anaphylaxis may occur (5.10).

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.

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 (5.9, 7.3).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 8/2011

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*Sections or subsections omitted from the full prescribing information are not listed.

1 **FULL PRESCRIBING INFORMATION**
2

3 **WARNINGS: SERIOUS INFECTIONS and MALIGNANCY**

4 **SERIOUS INFECTIONS**

5 Patients treated with SIMPONI[®] are at increased risk for developing serious infections that
6 may lead to hospitalization or death [see *Warnings and Precautions (5.1)*]. Most patients who
7 developed these infections were taking concomitant immunosuppressants such as
8 methotrexate or corticosteroids.
9

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

11 **Reported infections include:**

- 12 • Active tuberculosis, including reactivation of latent tuberculosis. Patients with
13 tuberculosis have frequently presented with disseminated or extrapulmonary disease.
14 Patients should be tested for latent tuberculosis before SIMPONI use and during
15 therapy. Treatment for latent infection should be initiated prior to SIMPONI use.
16
- 17 • Invasive fungal infections, including histoplasmosis, coccidioidomycosis, and
18 pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may
19 present with disseminated, rather than localized, disease. Antigen and antibody
20 testing for histoplasmosis may be negative in some patients with active infection.
21 Empiric anti-fungal therapy should be considered in patients at risk for invasive
22 fungal infections who develop severe systemic illness.
23
- 24 • Bacterial, viral, and other infections due to opportunistic pathogens.
25

26 The risks and benefits of treatment with SIMPONI should be carefully considered prior to
27 initiating therapy in patients with chronic or recurrent infection.
28

29 Patients should be closely monitored for the development of signs and symptoms of infection
30 during and after treatment with SIMPONI, including the possible development of
31 tuberculosis in patients who tested negative for latent tuberculosis infection prior to
32 initiating therapy [see *Warning and Precautions (5.1)*].
33

34 **MALIGNANCY**

35 Lymphoma and other malignancies, some fatal, have been reported in children and
36 adolescent patients treated with TNF blockers, of which SIMPONI is a member [see *Warning*
37 *and Precautions (5.2)*].
38

39
40
41
42 **1 INDICATIONS AND USAGE**

43 **1.1 Rheumatoid Arthritis**

44 SIMPONI, in combination with methotrexate, is indicated for the treatment of adult patients with
45 moderately to severely active rheumatoid arthritis.
46

47 **1.2 Psoriatic Arthritis**

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

51 **1.3 Ankylosing Spondylitis**

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

54 **2 DOSAGE AND ADMINISTRATION**

55 **2.1 Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis**

56 The SIMPONI dose regimen is 50 mg administered by subcutaneous injection once a month.

57
58 For patients with rheumatoid arthritis (RA), SIMPONI should be given in combination with
59 methotrexate and for patients with psoriatic arthritis (PsA) or ankylosing spondylitis (AS),
60 SIMPONI may be given with or without methotrexate or other non-biologic Disease Modifying
61 Antirheumatic Drugs (DMARDs). For patients with RA, PsA, or AS, corticosteroids, non-
62 biologic DMARDs, and/or NSAIDs may be continued during treatment with SIMPONI.

64 **2.2 Monitoring to Assess Safety**

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

70 **2.3 General Considerations for Administration**

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

77 Prior to administration, visually inspect the solution for particles and discoloration through the
78 viewing window. SIMPONI should be clear to slightly opalescent and colorless to light yellow.

79 The solution should not be used if discolored, or cloudy, or if foreign particles are present. Any
80 leftover product remaining in the prefilled syringe or prefilled autoinjector should not be used.

81 NOTE: The needle cover on the prefilled syringe as well as the prefilled syringe in the
82 autoinjector contains dry natural rubber (a derivative of latex), which should not be handled by
83 persons sensitive to latex.

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

87 **3 DOSAGE FORMS AND STRENGTHS**

89 **SmartJect[®] Autoinjector**

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

93 **Prefilled Syringe**

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

96 4 CONTRAINDICATIONS

97 None.
98
99

100 5 WARNINGS AND PRECAUTIONS (see **Boxed WARNINGS**)

101 5.1 Serious Infections

102 Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral,
103 protozoal, or other opportunistic pathogens have been reported in patients receiving TNF-blockers
104 including SIMPONI. Among opportunistic infections, tuberculosis, histoplasmosis, aspergillosis,
105 candidiasis, coccidioidomycosis, listeriosis, and pneumocystosis were the most commonly
106 reported with TNF-blockers. Patients have frequently presented with disseminated rather than
107 localized disease, and were often taking concomitant immunosuppressants such as methotrexate or
108 corticosteroids. The concomitant use of a TNF-blocker and abatacept or anakinra was associated
109 with a higher risk of serious infections; therefore, the concomitant use of SIMPONI and these
110 biologic products is not recommended [see *Warning and Precautions (5.5, 5.6) and Drug*
111 *Interactions (7.2)*].
112

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

- 116 • with chronic or recurrent infection;
- 117 • who have been exposed to tuberculosis;
- 118 • with a history of an opportunistic infection;
- 119 • who have resided or traveled in areas of endemic tuberculosis or endemic mycoses, such as
120 histoplasmosis, coccidioidomycosis, or blastomycosis; or
- 121 • with underlying conditions that may predispose them to infection.
122

123 Patients should be closely monitored for the development of signs and symptoms of infection
124 during and after treatment with SIMPONI. SIMPONI should be discontinued if a patient develops
125 a serious infection, an opportunistic infection, or sepsis. A patient who develops a new infection
126 during treatment with SIMPONI should undergo a prompt and complete diagnostic workup
127 appropriate for an immunocompromised patient, appropriate antimicrobial therapy should be
128 initiated, and the patient should be closely monitored.
129

130 In controlled Phase 3 trials through Week 16 in patients with RA, PsA, and AS, serious infections
131 were observed in 1.4% of SIMPONI-treated patients and 1.3% of control-treated patients. In the
132 controlled Phase 3 trials through Week 16 in patients with RA, PsA, and AS, the incidence of
133 serious infections per 100 patient-years of follow-up was 5.7 (95% CI: 3.8, 8.2) for the SIMPONI
134 group and 4.2 (95% CI: 1.8, 8.2) for the placebo group. Serious infections observed in SIMPONI-
135 treated patients included sepsis, pneumonia, cellulitis, abscess, tuberculosis, invasive fungal
136 infections, and hepatitis B infection.
137

138 *Tuberculosis*

139 Cases of reactivation of tuberculosis or new tuberculosis infections have been observed in patients
140 receiving TNF-blockers, including patients who have previously received treatment for latent or
141 active tuberculosis. Patients should be evaluated for tuberculosis risk factors and tested for latent
142 infection prior to initiating SIMPONI and periodically during therapy.
143

144 Treatment of latent tuberculosis infection prior to therapy with TNF-blockers has been shown to
145 reduce the risk of tuberculosis reactivation during therapy. Induration of 5 mm or greater with
146 tuberculin skin testing should be considered a positive test result when assessing if treatment for
147 latent tuberculosis is needed prior to initiating SIMPONI, even for patients previously vaccinated
148 with Bacille Calmette-Guerin (BCG).
149

150 Anti-tuberculosis therapy should also be considered prior to initiation of SIMPONI in patients
151 with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot
152 be confirmed, and for patients with a negative test for latent tuberculosis but having risk factors
153 for tuberculosis infection. Consultation with a physician with expertise in the treatment of
154 tuberculosis is recommended to aid in the decision whether initiating anti-tuberculosis therapy is
155 appropriate for an individual patient.
156

157 Patients should be closely monitored for the development of signs and symptoms of tuberculosis
158 including patients who tested negative for latent tuberculosis infection prior to initiating therapy.
159

160 Tuberculosis should be strongly considered in patients who develop a new infection during
161 SIMPONI treatment, especially in patients who have previously or recently traveled to countries
162 with a high prevalence of tuberculosis, or who have had close contact with a person with active
163 tuberculosis.
164

165 In the controlled and uncontrolled portions of the Phase 2 RA and Phase 3 RA, PsA, and AS trials,
166 the incidence of active TB was 0.23 and 0 per 100 patient-years in 2347 SIMPONI-treated patients
167 and 674 placebo-treated patients, respectively. Cases of TB included pulmonary and extra
168 pulmonary TB. The overwhelming majority of the TB cases occurred in countries with a high
169 incidence rate of TB.
170

171 ***Invasive Fungal Infections***

172 For SIMPONI-treated patients who reside or travel in regions where mycoses are endemic,
173 invasive fungal infection should be suspected if they develop a serious systemic illness.
174 Appropriate empiric antifungal therapy should be considered while a diagnostic workup is being
175 performed. Antigen and antibody testing for histoplasmosis may be negative in some patients
176 with active infection. When feasible, the decision to administer empiric antifungal therapy in
177 these patients should be made in consultation with a physician with expertise in the diagnosis and
178 treatment of invasive fungal infections and should take into account both the risk for severe fungal
179 infection and the risks of antifungal therapy.
180

181 ***Hepatitis B Virus Reactivation***

182 The use of TNF-blockers including SIMPONI has been associated with reactivation of hepatitis B
183 virus (HBV) in patients who are chronic hepatitis B carriers (i.e., surface antigen positive). In
184 some instances, HBV reactivation occurring in conjunction with TNF-blocker therapy has been

185 fatal. The majority of these reports have occurred in patients who received concomitant
186 immunosuppressants.

187
188 All patients should be tested for HBV infection before initiating TNF-blocker therapy. For
189 patients who test positive for hepatitis B surface antigen, consultation with a physician with
190 expertise in the treatment of hepatitis B is recommended before initiating TNF-blocker therapy.
191 The risks and benefits of treatment should be considered prior to prescribing TNF-blockers,
192 including SIMPONI, to patients who are carriers of HBV. Adequate data are not available on
193 whether anti-viral therapy can reduce the risk of HBV reactivation in HBV carriers who are
194 treated with TNF-blockers. Patients who are carriers of HBV and require treatment with TNF-
195 blockers should be closely monitored for clinical and laboratory signs of active HBV infection
196 throughout therapy and for several months following termination of therapy.

197
198 In patients who develop HBV reactivation, TNF-blockers should be stopped and antiviral therapy
199 with appropriate supportive treatment should be initiated. The safety of resuming TNF-blockers
200 after HBV reactivation has been controlled is not known. Therefore, prescribers should exercise
201 caution when considering resumption of TNF-blockers in this situation and monitor patients
202 closely.

203 204 **5.2 Malignancies**

205 Malignancies, some fatal, have been reported among children, adolescents, and young adults who
206 received treatment with TNF-blocking agents (initiation of therapy \leq 18 years of age), of which
207 SIMPONI is a member. Approximately half the cases were lymphomas, including Hodgkin's and
208 non-Hodgkin's lymphoma. The other cases represented a variety of malignancies, including rare
209 malignancies that are usually associated with immunosuppression, and malignancies that are not
210 usually observed in children and adolescents. The malignancies occurred after a median of 30
211 months (range 1 to 84 months) after the first dose of TNF blocker therapy. Most of the patients
212 were receiving concomitant immunosuppressants. These cases were reported post-marketing and
213 are derived from a variety of sources, including registries and spontaneous postmarketing reports.

214
215 The risks and benefits of TNF-blocker treatment including SIMPONI should be considered prior
216 to initiating therapy in patients with a known malignancy other than a successfully treated non-
217 melanoma skin cancer (NMSC) or when considering continuing a TNF-blocker in patients who
218 develop a malignancy.

219
220 In the controlled portions of clinical trials of TNF-blockers including SIMPONI, more cases of
221 lymphoma have been observed among patients receiving anti-TNF treatment compared with
222 patients in the control groups. During the controlled portions of the Phase 2 trials in RA, and the
223 Phase 3 trials in RA, PsA and AS, the incidence of lymphoma per 100 patient-years of follow-up
224 was 0.21 (95% CI: 0.03, 0.77) in the combined SIMPONI group compared with an incidence of 0
225 (95% CI: 0., 0.96) in the placebo group. In the controlled and uncontrolled portions of these
226 clinical trials in 2347 SIMPONI-treated patients with a median follow-up of 1.4 years, the
227 incidence of lymphoma was 3.8-fold higher than expected in the general U.S. population
228 according to the SEER database (adjusted for age, gender, and race).¹ Patients with RA and other
229 chronic inflammatory diseases, particularly patients with highly active disease and/or chronic
230 exposure to immunosuppressant therapies, may be at higher risk (up to several fold) than the
231 general population for the development of lymphoma, even in the absence of TNF-blocking

232 therapy. Cases of acute and chronic leukemia have been reported with postmarketing TNF-
233 blocker use in rheumatoid arthritis and other indications. Even in the absence of TNF blocker
234 therapy, patients with rheumatoid arthritis may be at a higher risk (approximately 2-fold) than the
235 general population for the development of leukemia.

236
237 During the controlled portions of the Phase 2 trial in RA, and the Phase 3 trials in RA, PsA and
238 AS, the incidence of malignancies other than lymphoma per 100 patient-years of follow-up was
239 not elevated in the combined SIMPONI group compared with the placebo group. In the controlled
240 and uncontrolled portions of these trials, the incidence of malignancies, other than lymphoma, in
241 SIMPONI-treated patients was similar to that expected in the general U.S. population according to
242 the SEER database (adjusted for age, gender, and race).¹

243
244 In controlled trials of other TNF-blockers in patients at higher risk for malignancies (e.g., patients
245 with COPD, patients with Wegener's granulomatosis treated with concomitant cyclophosphamide)
246 a greater portion of malignancies occurred in the TNF-blocker group compared to the controlled
247 group. In an exploratory 1-year clinical trial evaluating the use of 50, 100 and 200 mg of
248 SIMPONI in 309 patients with severe persistent asthma, 6 patients developed malignancies other
249 than NMSC in the SIMPONI groups compared to none in the control group. Three of the 6
250 patients were in the 200 mg SIMPONI group.

251 252 **5.3 Congestive Heart Failure**

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

261 262 **5.4 Demyelinating Disorders**

263 Use of TNF-blockers, of which SIMPONI is a member, has been associated with cases of new
264 onset or exacerbation of central nervous system (CNS) demyelinating disorders, including
265 multiple sclerosis (MS) and peripheral demyelinating disorders, including Guillain-Barré
266 syndrome. In clinical trials, cases of central demyelination, MS, and peripheral demyelinating
267 polyneuropathy have been reported in patients treated with SIMPONI [see *Adverse Reactions*
268 (6.1)]. Prescribers should exercise caution in considering the use of TNF-blockers, including
269 SIMPONI, in patients with central or peripheral nervous system demyelinating disorders.
270 Discontinuation of SIMPONI should be considered if these disorders develop.

271 272 **5.5 Use with Abatacept**

273 In controlled trials, the concurrent administration of another TNF-blocker and abatacept was
274 associated with a greater proportion of serious infections than the use of a TNF-blocker alone; and
275 the combination therapy, compared to the use of a TNF-blocker alone, has not demonstrated
276 improved clinical benefit in the treatment of RA. Therefore, the combination of TNF-blockers
277 including SIMPONI and abatacept is not recommended [see *Drug Interactions* (7.2)].
278

279 **5.6 Use with Anakinra**
280 Concurrent administration of anakinra (an interleukin-1 antagonist) and another TNF-blocker, was
281 associated with a greater portion of serious infections and neutropenia and no additional benefits
282 compared with the TNF-blocker alone. Therefore, the combination of anakinra with TNF-
283 blockers, including SIMPONI, is not recommended [see *Drug Interactions 7.2*].
284

285 **5.7 Switching Between Biological Disease Modifying Antirheumatic Drugs (DMARDs)**
286 Care should be taken when switching from one biologic to another since overlapping biological
287 activity may further increase the risk of infection.
288

289 **5.8 Hematologic Cytopenias**
290 There have been post-marketing reports of pancytopenia, leukopenia, neutropenia, aplastic
291 anemia, and thrombocytopenia in patients receiving TNF-blockers. In clinical studies, cases of
292 pancytopenia, leukopenia, neutropenia, and thrombocytopenia have also occurred in SIMPONI-
293 treated patients. Caution should be exercised when using TNF-blockers, including SIMPONI, in
294 patients who have or have had significant cytopenias.
295

296 **5.9 Vaccinations**
297 Patients treated with SIMPONI may receive vaccinations, except for live vaccines. No data are
298 available on the response to live vaccination or the risk of infection, or transmission of infection
299 after the administration of live vaccines to patients receiving SIMPONI. In the Phase 3 PsA study,
300 after pneumococcal vaccination, a similar proportion of SIMPONI-treated and placebo-treated
301 patients were able to mount an adequate immune response of at least a 2-fold increase in antibody
302 titers to pneumococcal polysaccharide vaccine. In both SIMPONI-treated and placebo-treated
303 patients, the proportions of patients with response to pneumococcal vaccine were lower among
304 patients receiving MTX compared with patients not receiving MTX. The data suggest that
305 SIMPONI does not suppress the humoral immune response to the pneumococcal vaccine.
306

307 **5.10 Hypersensitivity Reactions**
308 In post-marketing experience, serious systemic hypersensitivity reactions (including anaphylactic
309 reaction) have been reported following SIMPONI administration. Some of these reactions
310 occurred after the first administration of SIMPONI. If an anaphylactic or other serious allergic
311 reaction occurs, administration of SIMPONI should be discontinued immediately and appropriate
312 therapy instituted.
313

314 **6 ADVERSE REACTIONS**

315 Because clinical trials are conducted under widely varying conditions, adverse reaction rates
316 observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of
317 another drug and may not reflect the rates observed in clinical practice.
318

319 **6.1 Clinical Studies Experience**

320 The safety data described below are based on 5 pooled, randomized, double-blind, controlled
321 Phase 3 trials in patients with RA, PsA, and AS (Studies RA-1, RA-2, RA-3, PsA, and AS) [see
322 *Clinical Studies (14.1, 14.2 and 14.3)*]. These 5 trials included 639 control-treated patients and
323 1659 SIMPONI-treated patients including 1089 with RA, 292 with PsA, and 278 with AS. The
324 proportion of patients who discontinued treatment due to adverse reactions in the controlled Phase

325 3 trials through Week 16 in RA, PsA and AS was 2% for SIMPONI-treated patients and 3% for
326 placebo-treated patients. The most common adverse reactions leading to discontinuation of
327 SIMPONI in the controlled Phase 3 trials through Week 16 were sepsis (0.2%), alanine
328 aminotransferase increased (0.2%), and aspartate aminotransferase increased (0.2%).
329

330 The most serious adverse reactions were:

- 331 • Serious Infections [see *Warnings and Precautions (5.1)*]
 - 332 • Malignancies [see *Warnings and Precautions (5.2)*]
- 333

334 Upper respiratory tract infection and nasopharyngitis were the most common adverse reactions
335 reported in the combined Phase 3 RA, PsA and AS trials through Week 16, occurring in 7% and
336 6% of SIMPONI-treated patients as compared with 6% and 5% of control-treated patients,
337 respectively.
338

339 ***Infections***

340 In controlled Phase 3 trials through Week 16 in RA, PsA, and AS, infections were observed in
341 28% of SIMPONI-treated patients compared to 25% of control-treated patients [for Serious
342 Infections, see *Warnings and Precautions (5.1)*].
343

344 ***Liver Enzyme Elevations***

345 There have been reports of severe hepatic reactions including acute liver failure in patients
346 receiving TNF-blockers. In controlled Phase 3 trials of SIMPONI in patients with RA, PsA, and
347 AS through Week 16, ALT elevations $\geq 5 \times$ ULN occurred in 0.2% of control-treated patients and
348 0.7% of SIMPONI-treated patients and ALT elevations $\geq 3 \times$ ULN occurred in 2% of control-
349 treated patients and 2% of SIMPONI-treated patients. Since many of the patients in the Phase 3
350 trials were also taking medications that cause liver enzyme elevations (e.g., NSAIDs, MTX), the
351 relationship between SIMPONI and liver enzyme elevation is not clear.
352

353 ***Autoimmune Disorders and Autoantibodies***

354 The use of TNF-blockers, including SIMPONI, has been associated with the formation of
355 autoantibodies and, rarely, with the development of a lupus-like syndrome. In the controlled
356 Phase 3 trials in patients with RA, PsA, and AS through Week 14, there was no association of
357 SIMPONI treatment and the development of newly positive anti-dsDNA antibodies.
358

359 ***Injection Site Reactions***

360 In controlled Phase 3 trials through Week 16 in RA, PsA and AS, 6% of SIMPONI-treated
361 patients had injection site reactions compared with 2% of control-treated patients. The majority of
362 the injection site reactions were mild and the most frequent manifestation was injection site
363 erythema. In controlled Phase 2 and 3 trials in RA, PsA, and AS, no patients treated with
364 SIMPONI developed anaphylactic reactions.
365

366 ***Immunogenicity***

367 Antibodies to SIMPONI were detected in 57 (4%) of SIMPONI-treated patients across the Phase 3
368 RA, PsA, and AS trials through Week 24. Similar rates were observed in each of the three
369 indications. Patients who received SIMPONI with concomitant MTX had a lower proportion of
370 antibodies to SIMPONI than patients who received SIMPONI without MTX (approximately 2%

371 versus 7%, respectively). Of the patients with a positive antibody response to SIMPONI in the
372 Phase 2 and 3 trials, most were determined to have neutralizing antibodies to golimumab as
373 measured by a cell-based functional assay. The small number of patients positive for antibodies to
374 SIMPONI limits the ability to draw definitive conclusions regarding the relationship between
375 antibodies to golimumab and clinical efficacy or safety measures.
376

377 The data above reflect the percentage of patients whose test results were considered positive for
378 antibodies to SIMPONI in an ELISA assay, and are highly dependent on the sensitivity and
379 specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay
380 may be influenced by several factors including sample handling, timing of sample collection,
381 concomitant medications, and underlying disease. For these reasons, comparison of the incidence
382 of antibodies to SIMPONI with the incidence of antibodies to other products may be misleading.
383

384 ***Other Adverse Reactions***

385 Table 1 summarizes the adverse drug reactions that occurred at a rate of at least 1% in the
386 SIMPONI ± DMARD group and with a higher incidence than in the placebo ± DMARD group
387 during the controlled period of the 5 pooled Phase 3 trials through Week 16 in patients with RA,
388 PsA, and AS.
389

Table 1. Adverse Drug Reactions Reported by ≥ 1% of SIMPONI-Treated Patients and with a Higher Incidence than Placebo-Treated Patients in the Phase 3 Trials of RA, PsA, and AS through Week 16^a

	SIMPONI ± DMARDs	Placebo ± DMARDs
Patients treated	1659	639
Adverse Reaction		
Infections and Infestations		
Upper respiratory tract infection (nasopharyngitis, pharyngitis, laryngitis, and rhinitis)	16%	13%
Viral infections (such as influenza and herpes)	5%	3%
Bronchitis	2%	1%
Superficial fungal infections	2%	1%
Sinusitis	2%	1%
General disorders and administration site conditions		
Injection site reaction (injection site erythema, urticaria, induration, pain, bruising, pruritus, irritation, paresthesia)	6%	2%
Investigations		
Alanine aminotransferase increased	4%	3%
Aspartate aminotransferase increased	3%	2%

Table 1. Adverse Drug Reactions Reported by $\geq 1\%$ of SIMPONI-Treated Patients and with a Higher Incidence than Placebo-Treated Patients in the Phase 3 Trials of RA, PsA, and AS through Week 16^a

	SIMPONI \pm DMARDs	Placebo \pm DMARDs
Vascular disorders		
Hypertension	3%	2%
Nervous system disorders		
Dizziness	2%	1%
Paresthesia	2%	1%
Gastrointestinal Disorders		
Constipation	1%	<1%

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

Less common clinical trial adverse drug reactions

Adverse drug reactions that occurred $<1\%$ in SIMPONI-treated patients during the SIMPONI clinical trials that do not appear in the Warnings and Precautions section included the following events listed by system organ class:

Infections and infestations: Septic shock, atypical mycobacterial infection, pyelonephritis, arthritis bacterial, bursitis infective

Neoplasms benign, malignant and unspecified: leukemia

Skin and subcutaneous tissue disorders: psoriasis (new onset or worsening, palmar/plantar and pustular), vasculitis (cutaneous)

Vascular disorders: Vasculitis (systemic)

6.2 Post-marketing Experience

The following adverse reactions have been identified during post-approval use of SIMPONI. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to SIMPONI exposure.

Immune System Disorders: Serious systemic hypersensitivity reactions (including anaphylactic reaction) [see *Warnings and Precautions (5.10)*].

7 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

426 higher rate of serious infections has also been observed in RA patients treated with rituximab who
427 received subsequent treatment with a TNF-blocker. There is insufficient information to provide
428 recommendations regarding the concomitant use of SIMPONI and other biologic products
429 approved to treat RA, PsA, or AS.

430

431 **7.3 Live Vaccines**

432 Live vaccines should not be given concurrently with SIMPONI [see *Warnings and Precautions*
433 (5.9)].

434

435 Infants born to women treated with SIMPONI during their pregnancy may be at increased risk of
436 infection for up to 6 months. Administration of live vaccines to infants exposed to SIMPONI *in*
437 *utero* is not recommended for 6 months following the mother's last SIMPONI injection during
438 pregnancy (see *Use in Specific Populations* (8.1)).

439

440 **7.4 Cytochrome P450 Substrates**

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

448

449 **8 USE IN SPECIFIC POPULATIONS**

450 **8.1 Pregnancy**

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

456

457 An embryofetal developmental toxicology study was performed in which pregnant cynomolgus
458 monkeys were treated subcutaneously with golimumab during the first trimester with doses up to
459 50 mg/kg twice weekly (360 times greater than the maximum recommended human dose-MHRD)
460 and has revealed no evidence of harm to maternal animals or fetuses. Umbilical cord blood
461 samples collected at the end of the second trimester showed that fetuses were exposed to
462 golimumab during gestation. In this study, *in utero* exposure to golimumab produced no
463 developmental defects to the fetus.

464

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

472
473 IgG antibodies are known to cross the placenta during pregnancy and have been detected in the
474 serum of infants born to patients treated with these antibodies. Since SIMPONI is an IgG
475 antibody, infants born to women treated with SIMPONI during their pregnancy may be at
476 increased risk of infection for up to 6 months. Administration of live vaccines to infants exposed
477 to SIMPONI *in utero* is not recommended for 6 months following the mother's last SIMPONI
478 injection during pregnancy [see *Warnings and Precautions (5.9)*].
479

480 **8.3 Nursing Mothers**

481 It is not known whether SIMPONI is excreted in human milk or absorbed systemically after
482 ingestion. Because many drugs and immunoglobulins are excreted in human milk, and because of
483 the potential for adverse reactions in nursing infants from SIMPONI, a decision should be made
484 whether to discontinue nursing or to discontinue the drug, taking into account the importance of
485 the drug to the mother.
486

487 In the pre- and post-natal development study in cynomolgus monkeys in which golimumab was
488 administered subcutaneously during pregnancy and lactation, golimumab was detected in the
489 breast milk at concentrations that were approximately 400-fold lower than the maternal serum
490 concentrations.
491

492 **8.4 Pediatric Use**

493 Safety and effectiveness of SIMPONI in pediatric patients less than 18 years of age have not been
494 established.
495

496 **8.5 Geriatric Use**

497 In the Phase 3 trials in RA, PsA, and AS, there were no overall differences in SAEs, serious
498 infections, and AEs in SIMPONI-treated patients ages 65 or older (N = 155) compared with
499 younger SIMPONI-treated patients. Because there is a higher incidence of infections in the
500 geriatric population in general, caution should be used in treating geriatric patients with
501 SIMPONI.
502

503 **10 OVERDOSAGE**

504 In a clinical study, 5 patients received protocol-directed single infusions of 10 mg/kg of
505 intravenous SIMPONI without serious adverse reactions or other significant reactions. The
506 highest weight patient was 100 kg, and therefore received a single intravenous infusion of 1000
507 mg of SIMPONI. There were no SIMPONI overdoses in the clinical studies.
508

509 **11 DESCRIPTION**

510 SIMPONI (golimumab) is a human IgG1 κ monoclonal antibody specific for human tumor
511 necrosis factor alpha (TNF α) that exhibits multiple glycoforms with molecular masses of
512 approximately 150 to 151 kilodaltons. SIMPONI was created using genetically engineered mice
513 immunized with human TNF, resulting in an antibody with human-derived antibody variable and
514 constant regions. SIMPONI is produced by a recombinant cell line cultured by continuous
515 perfusion and is purified by a series of steps that includes measures to inactivate and remove
516 viruses.
517

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

524
525 SIMPONI does not contain preservatives. The solution is clear to slightly opalescent, colorless to
526 light yellow with a pH of approximately 5.5. SIMPONI is provided in one strength: 50 mg of the
527 golimumab antibody in 0.5 mL of solution. Each 0.5 mL of SIMPONI contains 50 mg of the
528 golimumab antibody, 0.44 mg of L-histidine and L-histidine monohydrochloride monohydrate,
529 20.5 mg of sorbitol, 0.08 mg of polysorbate 80, and Water for Injection.

530 531 **12 CLINICAL PHARMACOLOGY**

532 **12.1 Mechanism of Action**

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

539
540 Elevated TNF α levels in the blood, synovium, and joints have been implicated in the
541 pathophysiology of several chronic inflammatory diseases such as rheumatoid arthritis, psoriatic
542 arthritis, and ankylosing spondylitis. TNF α is an important mediator of the articular inflammation
543 that is characteristic of these diseases. Golimumab modulated the *in vitro* biological effects
544 mediated by TNF in several bioassays, including the expression of adhesion proteins responsible
545 for leukocyte infiltration (E-selectin, ICAM-1 and VCAM-1) and the secretion of
546 proinflammatory cytokines (IL-6, IL-8, G-CSF and GM-CSF).

547 548 **12.2 Pharmacodynamics**

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

553 554 **12.3 Pharmacokinetics**

555 Following subcutaneous administration of SIMPONI to healthy subjects and patients with active
556 RA, the median time to reach maximum serum concentrations (T_{max}) ranged from 2 to 6 days. A
557 subcutaneous injection of 50 mg SIMPONI to healthy subjects produced a mean maximum serum
558 concentration (C_{max}) of approximately 2.5 μ g/mL. SIMPONI exhibited dose-proportional
559 pharmacokinetics (PK) in patients with active RA over the dose range of 0.1 to 10.0 mg/kg
560 following a single intravenous (IV) dose. Following a single IV administration over the same
561 dose range in patients with active RA, mean systemic clearance of SIMPONI was estimated to be
562 4.9 to 6.7 mL/day/kg, and mean volume of distribution ranged from 58 to 126 mL/kg. The
563 volume of distribution for SIMPONI indicates that SIMPONI is distributed primarily in the

564 circulatory system with limited extravascular distribution. Median terminal half-life values were
565 estimated to be approximately 2 weeks in healthy subjects and patients with active RA, PsA or
566 AS. By cross-study comparisons of mean AUC_{inf} values following an IV or subcutaneous
567 administration of SIMPONI, the absolute bioavailability of subcutaneous SIMPONI was estimated
568 to be approximately 53%.

569
570 When 50 mg SIMPONI was administered subcutaneous to patients with RA, PsA, or AS every 4
571 weeks, serum concentrations appeared to reach steady state by Week 12. With concomitant use of
572 methotrexate (MTX), treatment with 50 mg SIMPONI subcutaneous every 4 weeks resulted in a
573 mean steady-state trough serum concentration of approximately 0.4-0.6 $\mu\text{g/mL}$ in patients with
574 active RA, approximately 0.5 $\mu\text{g/mL}$ in patients with active PsA, and approximately 0.8 $\mu\text{g/mL}$ in
575 patients with active AS. Patients with RA, PsA, and AS treated with SIMPONI 50 mg and MTX
576 had approximately 52%, 36% and 21% higher mean steady-state trough concentrations of
577 golimumab, respectively compared with those treated with SIMPONI 50 mg without MTX. The
578 presence of MTX also decreased anti-golimumab antibody incidence from 7% to 2% [*see Adverse*
579 *Reactions (6.1)*]. For RA, SIMPONI should be used with MTX. In the PsA and AS trials, the
580 presence or absence of concomitant MTX did not appear to influence clinical efficacy and safety
581 parameters [*see Drug Interactions (7.1) and Clinical Studies (14.1)*].

582
583 Population PK analyses indicated that concomitant use of NSAIDs, oral corticosteroids, or
584 sulfasalazine did not influence the apparent clearance of SIMPONI.

585
586 Population PK analyses showed there was a trend toward higher apparent clearance of SIMPONI
587 with increasing weight. However, across the PsA and AS populations, no meaningful differences
588 in clinical efficacy were observed among the subgroups by weight quartile. The RA trial in MTX-
589 experienced and TNF-blocker-naïve patients (Study RA-2) did show evidence of a reduction in
590 clinical efficacy with increasing body weight, but this effect was observed for both tested doses of
591 SIMPONI (50 mg and 100 mg). Therefore, there is no need to adjust the dosage of SIMPONI
592 based on a patient's weight.

593
594 Population PK analyses suggested no PK differences between male and female patients after body
595 weight adjustment in the RA and PsA trials. In the AS trial, female patients showed 13% higher
596 apparent clearance than male patients after body weight adjustment. Subgroup analysis based on
597 gender showed that both female and male patients achieved clinically significant response at the
598 proposed clinical dose. Dosage adjustment based on gender is not needed.

599
600 Population PK analyses indicated that PK parameters of SIMPONI were not influenced by age in
601 adult patients. Patients with age ≥ 65 years had apparent clearance of SIMPONI similar to
602 patients with age < 65 years. No ethnicity-related PK differences were observed between
603 Caucasians and Asians, and there were too few patients of other races to assess for PK differences.

604
605 Patients who developed anti-SIMPONI antibodies generally had lower steady-state serum trough
606 concentrations of SIMPONI.

607
608 No formal study of the effect of renal or hepatic impairment on the PK of golimumab was
609 conducted.

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13 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 α antibody showed no impairment of fertility.

14 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 445 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 = 150), SIMPONI 50 mg (n = 147), or SIMPONI 100 mg (n = 148). 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.

656 In Studies RA-1, RA-2, and RA-3, the median duration of RA disease was 9.4, 5.7, and 1.2 years;
657 and 99%, 75%, and 54% of the patients used at least one DMARD in the past, respectively.
658 Approximately 77% and 57% of patients received concomitant NSAIDs and low dose
659 corticosteroids, respectively, in the 3 pooled RA trials.
660

661 ***Clinical Response***

662 In the 3 RA trials, a greater percentage of patients treated with the combination of SIMPONI and
663 MTX achieved ACR responses at Week 14 (Studies RA-1 and RA-2) and Week 24 (Studies RA-
664 1, RA-2, and RA-3) versus patients treated with the MTX alone. There was no clear evidence of
665 improved ACR response with the higher SIMPONI dose group (100 mg) compared to the lower
666 SIMPONI dose group (50 mg). In Studies RA-2 and RA-3, the SIMPONI monotherapy groups
667 were not statistically different from the MTX monotherapy groups in ACR responses. [Table 2](#)
668 shows the proportion of patients with the ACR response for the SIMPONI 50 mg and control
669 groups in Studies RA-1, RA-2, and RA-3. In the subset of patients who received SIMPONI in
670 combination with MTX in Study RA-1, the proportion of patients achieving ACR 20, 50 and 70
671 responses at week 14 were 40%, 18%, and 12%, respectively, in the SIMPONI 50 mg + MTX
672 group (N = 101) compared with 17%, 6%, and 2%, respectively, in the placebo + MTX group (N
673 = 103). [Table 3](#) shows the percent improvement in the components of the ACR response criteria
674 for the SIMPONI 50 mg + MTX and MTX groups in Study RA-2. The percent of patients
675 achieving ACR 20 responses by visit for Study RA-2 is shown in Figure 1. ACR 20 responses
676 were observed in 38% of patients in the SIMPONI 50 mg + MTX group at the first assessment
677 (Week 4) after the initial SIMPONI administration.
678

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 680

Table 2. Studies RA-1, RA-2, and RA-3 Proportion of Patients with an ACR Response^a

	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 ^b	SIMPONI 50 mg ± DMARDs ^b	Background MTX	SIMPONI 50 mg + Background MTX	MTX	SIMPONI 50 mg + MTX
N ^c	150	147	133	89	160	159
ACR 20						
Week 14	18%	35%	33%	55%	NA ^c	NA ^c
Week 24	16%	31%	28%	60%	49%	62%
ACR 50						
Week 14	7%	15%	10%	35%	NA ^c	NA ^c
Week 24	4%	16%	14%	37%	29%	40%
ACR 70						
Week 14	2%	10%	4%	13%	NA ^c	NA ^c
Week 24	2%	9%	5%	20%	16%	24% ^d
^a	Approximately 78% and 58% of the patients received concomitant NSAIDs and low dose corticosteroids (equivalent to ≤ 10 mg of prednisone a day), 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.					
^e	NA = Not applicable, as data was not collected at Week 14 in Study RA-3.					

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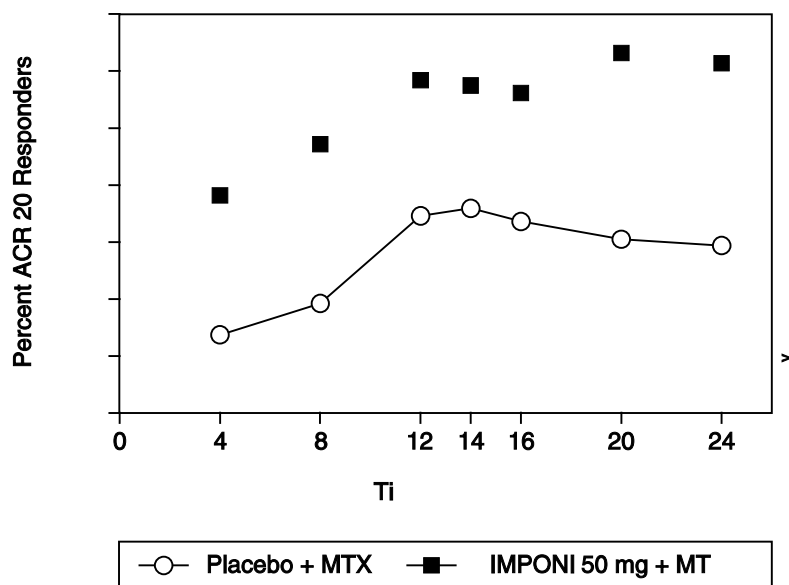
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Table 3. Study RA-2 – Median Percent Improvement from Baseline in the Individual ACR Components at Week 14^a

	Background MTX	SIMPONI 50 mg + Background MTX
N ^b	133	89
Number of swollen joints (0-66)		
Baseline	12	13
Week 14	38%	62%
Number of tender joints (0-68)		
Baseline	21	26
Week 14	30%	60%
Patient’s assessment of pain (0-10)		
Baseline	5.7	6.1
Week 14	18%	55%
Patient’s global assessment of disease activity (0-10)		
Baseline	5.3	6.0
Week 14	15%	45%
Physician’s global assessment of disease activity (0-10)		
Baseline	5.7	6.1
Week 14	35%	55%
HAQ score (0-3)		
Baseline	1.25	1.38
Week 14	10%	29%
CRP (mg/dL)		
Baseline	0.8	1.0
Week 14	2%	44%
Note: Baseline values are medians. ^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. ^b N reflects randomized patients; actual number of patients evaluable for each endpoint may vary.		

686
 687
 688

689 **Figure 1. Study RA - 2 – Percent of Patients Achieving ACR 20 Response by Visit: Randomized**
690 **Patients***
691



692
693 * The same patients may not have responded at each timepoint.
694
695
696

697 ***Physical Function Response in Patients with RA***

698 In Studies RA-1 and RA-2, the SIMPONI 50 mg groups demonstrated a greater improvement
699 compared to the control groups in the change in mean Health Assessment Questionnaire Disability
700 Index (HAQ-DI) score from baseline to Week 24: 0.23 vs. 0.03 in RA-1, 0.47 vs. 0.13 in RA-2,
701 respectively. Also in Studies RA-1 and RA-2, the SIMPONI 50 mg groups compared to the
702 control groups had a greater proportion of HAQ responders (change from baseline > 0.22) at
703 Week 24: 43% vs. 27%, 65% vs. 35%, respectively.
704

705 **14.2 Psoriatic Arthritis**

706 The safety and efficacy of SIMPONI were evaluated in a multi-center, randomized, double-blind,
707 placebo-controlled trial in 405 adult patients with moderately to severely active PsA (≥ 3 swollen
708 joints and ≥ 3 tender joints) despite NSAID or DMARD therapy (Study PsA). Patients in this
709 study had a diagnosis of PsA for at least 6 months with a qualifying psoriatic skin lesion of at least
710 2 cm in diameter. Previous treatment with a biologic TNF-blocker was not allowed. Patients
711 were randomly assigned to placebo (n = 113), SIMPONI 50 mg (n = 146), or SIMPONI 100 mg
712 (n = 146) given subcutaneously every 4 weeks. Patients were allowed to receive stable doses of
713 concomitant MTX (≤ 25 mg/week), low dose oral corticosteroids (equivalent to ≤ 10 mg of
714 prednisone a day), and/or NSAIDs during the trial. The use of other DMARDs including SSZ,
715 HCQ, cytotoxic agents, or other biologics was prohibited. The primary endpoint was the
716 percentage of patients achieving ACR 20 response at Week 14. Placebo-controlled efficacy data
717 were collected and analyzed through Week 24.
718

719 Patients with each subtype of PsA were enrolled, including polyarticular arthritis with no
720 rheumatoid nodules (43%), asymmetric peripheral arthritis (30%), distal interphalangeal (DIP)

721 joint arthritis (15%), spondylitis with peripheral arthritis (11%), and arthritis mutilans (1%). The
722 median duration of PsA disease was 5.1 years, 78% of patients received at least one DMARD in
723 the past, and approximately 48% of patients received MTX, and 16% received low dose oral
724 steroids.

725

726 ***Clinical Response in Patients with PsA***

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

739

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

743

744

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

	Placebo ± MTX ^a	SIMPONI 50 mg ± MTX ^a
N ^b	113	146
ACR 20		
Week 14	9%	51%
Week 24	12%	52%
ACR 50		
Week 14	2%	30%
Week 24	4%	32%
ACR 70		
Week 14	1%	12%
Week 24	1%	19%
^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. ^b N reflects randomized patients. Bold text indicates primary endpoint		

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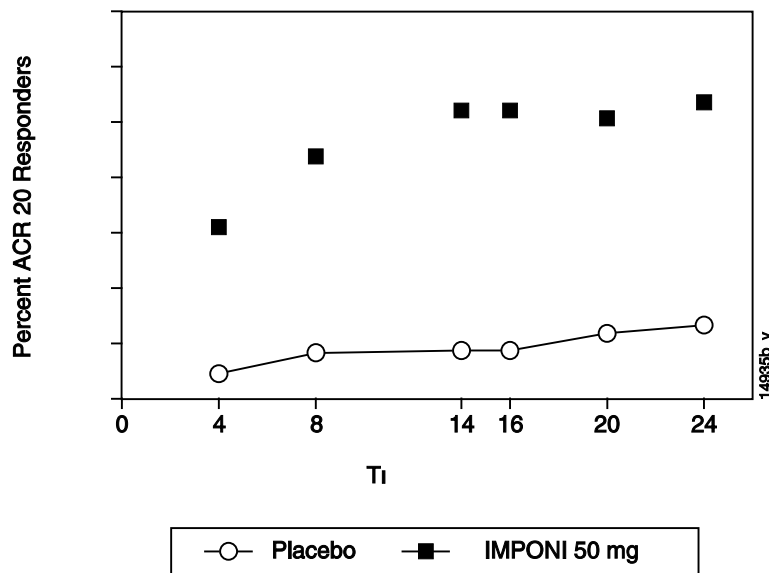
Table 5. Study PsA - Percent Improvement in ACR Components at Week 14

	Placebo± MTX ^a	SIMPONI 50 mg ± MTX ^a
N ^b	113	146
Number of swollen joints (0-66)		
Baseline	10.0	11.0
Week 14	8%	60%
Number of tender joints (0-68)		
Baseline	18.0	19.0
Week 14	0%	54%
Patient's assessment of pain (0-10)		
Baseline	5.4	5.8
Week 14	-1%	48%
Patient's global assessment of disease activity (0-10)		
Baseline	5.2	5.2
Week 14	2%	49%
Physician's global assessment of disease activity (0-10)		
Baseline	5.2	5.4
Week 14	7%	59%
HAQ score (0-10)		
Baseline	1.0	1.0
Week 14	0%	28%
CRP (mg/dL) (0-10)		
Baseline	0.6	0.6
Week 14	0%	40%
Note: Baseline are median values ^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. ^b N reflects randomized patients; actual number of patients evaluable for each endpoint may vary by timepoint		

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



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

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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 (≥ 0.3 change from baseline) at Week 24: 43% vs. 22%, respectively.

760

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) ≥ 4 and VAS for total back pain of ≥ 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.

773

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

777

778 In Study AS, the median duration of AS disease was 5.6 years, median duration of inflammatory
779 back pain was 12 years, 83% were HLA-B27 positive, 24% had prior joint surgery or procedure,
780 and 55% received at least one DMARD in the past. During the trial, the use of concomitant
781 DMARDs and/or NSAIDs was as follows: MTX (20%), SSZ (26%), HCQ (1%), low dose oral
782 steroids (16%), and NSAIDs (90%).
783

784 ***Clinical Response in Patients with AS***

785 In Study AS, SIMPONI ± DMARDs treatment, compared with placebo ± DMARDs, resulted in a
786 significant improvement in signs and symptoms as demonstrated by the proportion of patients with
787 an ASAS 20 response at Week 14 (see Table 6). There was no clear evidence of improved ASAS
788 response with the higher SIMPONI dose group (100 mg) compared to the lower SIMPONI dose
789 group (50 mg). Table 7 shows the percent improvement in the components of the ASAS response
790 criteria for the SIMPONI 50 mg ± DMARDs and placebo ± DMARDs groups in Study AS.
791

792 The percent of patients achieving ASAS 20 responses by visit for Study AS is shown in Figure 3.
793 ASAS 20 responses were observed in 48% of patients in the SIMPONI 50 mg + MTX group at the
794 first assessment (Week 4) after the initial SIMPONI administration.
795

796 **Table 6. Study AS – Proportion of ASAS Responders at Weeks 14 and 24**
797

	Placebo ± DMARDs ^a	SIMPONI 50 mg ± DMARDs ^a
N ^b	78	138
Responders, % of patients		
ASAS 20		
Week 14	22%	59%
Week 24	23%	56%
ASAS 40		
Week 14	15%	45%
Week 24	15%	44%
^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. Bold text indicates primary endpoint		

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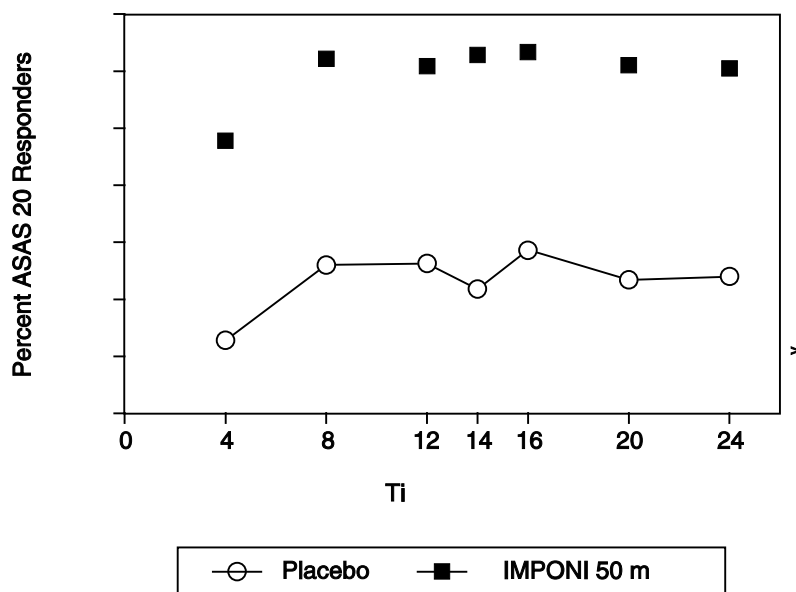
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Table 7. Study AS – Median Percent Improvement in ASAS Components at Week 14

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

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



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

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15 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 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 PATIENT COUNSELING INFORMATION

See [FDA-Approved Patient Labeling \(Medication Guide and Patient Instructions for Use\)](#)

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).

854 ***Other Medical Conditions***

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

858

859 **17.2 Instruction on Injection Technique**

860 The first self-injection should be performed under the supervision of a qualified healthcare
861 professional. If a patient or caregiver is to administer SIMPONI, he/she should be instructed in
862 injection techniques and their ability to inject subcutaneously should be assessed to ensure the
863 proper administration of SIMPONI (*see FDA-Approved Patient Labeling (Medication Guide and*
864 *Patient Instructions for Use)*).

865

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

869

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

872

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

875

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

881

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

885

886

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

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893
894
895 **MEDICATION GUIDE**
896 **SIMPONI® (SIM-po-nee)**
897 **(golimumab)**
898

899 Read the Medication Guide that comes with SIMPONI before you start taking it and each time
900 you get a refill. There may be new information. This Medication Guide does not take the place of
901 talking with your doctor about your medical condition or treatment. It is important to remain
902 under your doctor's care while using SIMPONI.
903

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

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

- 909 • Your doctor should test you for TB and hepatitis B before starting SIMPONI.
- 910 • Your doctor should monitor you closely for signs and symptoms of TB during treatment
911 with SIMPONI.

912
913 You should not start taking SIMPONI if you have any kind of infection unless your doctor says it
914 is okay.
915

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

- 917 • 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
- 918 • are being treated for an infection
- 919 • get a lot of infections or have infections that keep coming back
- 920 • have diabetes, HIV, or a weak immune system. People with these conditions have a higher
921 chance for infections.
- 922 • have TB, or have been in close contact with someone with TB
- 923 • live, have lived, or traveled to certain parts of the country (such as the Ohio and
924 Mississippi River valleys and the Southwest) where there is an increased chance for getting
925 certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis).
926 These infections may happen or become more severe if you use SIMPONI. Ask your
927 doctor if you do not know if you have lived in an area where these infections are common.
- 928 • have or have had hepatitis B
- 929 • use the medicine ORENCIA (abatacept), KINERET (anakinra), ACTEMRA (tocilizumab)
930 or RITUXAN (rituximab)
931

932
933 **After starting SIMPONI**, call your doctor right away if you have any symptoms of an
934 infection. SIMPONI can make you more likely to get infections or make worse any infection
935 that you have.

- 936
937 **Cancer**
- 938 • For children and adults taking TNF-blocker medicines, including SIMPONI, the chances of
939 getting cancer may increase.
 - 940 • There have been cases of unusual cancers in children and teenage patients taking TNF-
941 blocking agents.
 - 942 • People with inflammatory diseases including rheumatoid arthritis, psoriatic arthritis, or
943 ankylosing spondylitis, especially those with very active disease, may be more likely to get
944 lymphoma.

945
946 **What is SIMPONI?**

947 SIMPONI is a prescription medicine called a Tumor Necrosis Factor (TNF) blocker. SIMPONI is
948 used in adults:

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

952
953 You may continue to use other medicines that help treat your condition while taking SIMPONI, such
954 as non-steroidal anti-inflammatory drugs (NSAIDs) and prescription steroids, as recommended by
955 your doctor.

956
957 **What should I tell my doctor before starting treatment with SIMPONI?**

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

- 960 • have an infection (see “[What is the most important information I should know about SIMPONI?](#)”).
- 961 • have or have had lymphoma or any other type of cancer.
- 962 • have or had heart failure.
- 963 • have or have had a condition that affects your nervous system, such as multiple sclerosis or
964 Guillain-Barré syndrome.
- 965 • have recently received or are scheduled to receive a vaccine. People taking SIMPONI should not
966 receive live vaccines. People taking SIMPONI can receive non-live vaccines.
- 967 • have a baby and you were using SIMPONI during your pregnancy. Tell your baby’s doctor before
968 your baby receives any vaccine. Your baby may have an increased chance of getting an infection
969 for up to 6 months after birth.
- 970 • are allergic to rubber or latex. The needle cover on the prefilled syringe and SmartJect[®]
971 autoinjector contains dry natural rubber.
- 972 • are pregnant or planning to become pregnant. It is not known if SIMPONI will harm your unborn
973 baby.
- 974 • are breastfeeding. You and your doctor should decide if you will take SIMPONI or breastfeed.
975 You should not do both without talking to your doctor first.

976

- 977 **Tell your doctor about all the medicines you take**, including prescription and non-prescription
978 medicines, vitamins, and herbal supplements. Especially, tell your doctor if you:
979 • use ORENCIA (abatacept) or KINERET (anakinra). You should not take SIMPONI while you are
980 also taking ORENCIA (abatacept) or KINERET (anakinra).
981 • use other TNF-blocker medicines, including REMICADE (infliximab), HUMIRA (adalimumab),
982 ENBREL (etanercept), or CIMZIA (certolizumab pegol).
983 • receive RITUXAN (rituximab) or ACTEMRA (tocilizumab).
984

985 Ask your doctor if you are not sure if your medicine is one listed above.
986

987 Keep a list of all your medications with you to show your doctor and pharmacist each time you get a
988 new medicine.
989

990 **How should I use SIMPONI?**

- 991 • SIMPONI is given as an injection under the skin (subcutaneous injection).
992 • SIMPONI should be injected one time each month.
993 • If your doctor decides that you or a caregiver may be able to give your injections of SIMPONI at
994 home, you should receive training on the right way to prepare and inject SIMPONI. Do not try to
995 inject SIMPONI yourself until you have been shown the right way to give the injections by your
996 doctor or nurse.
997 • Use SIMPONI exactly as prescribed by your doctor.
998 • SIMPONI comes in a prefilled syringe or SmartJect autoinjector. Your doctor will prescribe the
999 type that is best for you.
1000 • See the detailed *Patient Instructions for Use* at the end of this Medication Guide for instructions
1001 about the right way to prepare and give your SIMPONI injections at home.
1002 • Do not miss any doses of SIMPONI. If you forget to use SIMPONI, inject your dose as soon as
1003 you remember. Then, take your next dose at your regular scheduled time. In case you are not sure
1004 when to inject SIMPONI, call your doctor or pharmacist.
1005

1006 **What are the possible side effects with SIMPONI?**

1007 SIMPONI can cause serious side effects, including:
1008

1009 See “**What is the most important information I should know about SIMPONI?**”
1010

1011 **Hepatitis B infection in people who carry the virus in their blood.**

- 1012 • If you are a carrier of the hepatitis B virus (a virus that affects the liver), the virus can become
1013 active while you use SIMPONI. Your doctor should do blood tests before you start treatment
1014 with SIMPONI and while you are using SIMPONI. Tell your doctor if you have any of the
1015 following symptoms of a possible hepatitis B infection:
- feel very tired
 - dark urine
 - skin or eyes look yellow
 - little or no appetite
 - vomiting
 - muscle aches
 - clay-colored bowel movements
 - fevers
 - chills
 - stomach discomfort
 - skin rash

1016

1017 **Heart failure, including new heart failure or worsening of heart failure that you already have.**

1018 New or worse heart failure can happen in people who use TNF-blocker medicines including
1019 SIMPONI.

1020 • If you have heart failure, your condition should be watched closely while you take SIMPONI.

1021 • Call your doctor right away if you get new or worsening symptoms of heart failure while taking
1022 SIMPONI (such as shortness of breath or swelling of your lower legs or feet).

1023

1024 **Nervous System Problems**

1025 Rarely, people using TNF-blocker medicines, including SIMPONI, have nervous system problems
1026 such as multiple sclerosis or Guillain-Barré syndrome.

1027 • Tell your doctor right away if you get any of these symptoms:

1028 • vision changes

1029 • weakness in your arms or legs

1030 • numbness or tingling in any part of your body

1031

1032 **Liver Problems**

1033 Liver problems can happen in people who use TNF-blocker medicines, including SIMPONI. These
1034 problems can lead to liver failure and death. Call your doctor right away if you have any of these
1035 symptoms:

1036 • feel very tired

1037 • skin or eyes look yellow

1038 • poor appetite or vomiting

1039 • pain on the right side of your stomach (abdomen)

1040

1041 **Blood Problems**

1042 Low blood counts have been seen with TNF-blockers, including SIMPONI. Your body may not make
1043 enough blood cells that help fight infections or help stop bleeding. Symptoms include fever, bruising
1044 or bleeding easily, or looking pale. Your doctor will check your blood counts before and during
1045 treatment with SIMPONI.

1046

1047 **Common side effects with SIMPONI include:**

1048

1049 • upper respiratory infection (runny nose, sore throat, and hoarseness or laryngitis)

1050 • reaction at the site of injection (redness, swelling, itching, pain, bruising, or tingling)

1051 • viral infections such as flu and oral cold sores

1052

1053 Other side effects with SIMPONI include:

1054

1055 • **Immune System Problems.** Rarely, people using TNF-blocker medicines have developed
1056 symptoms that are like the symptoms of Lupus. Tell your doctor if you have any of these
1057 symptoms:

1058 • a rash on your cheeks or other parts of the body

1059 • sensitivity to the sun

1060 • new joint or muscle pains

- 1061 • becoming very tired
- 1062 • chest pain or shortness of breath
- 1063 • swelling of the feet, ankles, or legs
- 1064
- 1065 • **Psoriasis.** Some people using SIMPONI had new psoriasis or worsening of psoriasis they already
- 1066 had. Tell your doctor if you develop red scaly patches or raised bumps that are filled with pus.
- 1067 Your doctor may decide to stop your treatment with SIMPONI.
- 1068
- 1069 • **Allergic Reactions.** Allergic reactions can happen in people who use TNF-blocker medicines
- 1070 including SIMPONI. Some reactions may be serious and can be life-threatening. Some of these
- 1071 reactions can happen after receiving your first dose of SIMPONI. Call your doctor right away if
- 1072 you have any of these symptoms of an allergic reaction:
- 1073 • hives
- 1074 • swollen face
- 1075 • breathing trouble
- 1076 • chest pain
- 1077

1078 These are not all of the side effects with SIMPONI. Tell your doctor about any side effect that bothers

1079 you or does not go away. Call your doctor for medical advice about side effects. You may report side

1080 effects to the FDA at 1-800-FDA-1088.

1081

1082 **How do I store SIMPONI?**

- 1083 • Refrigerate SIMPONI at 36°F to 46°F (2°C to 8°C).
 - 1084 • Do not freeze SIMPONI.
 - 1085 • Keep SIMPONI in the carton to protect it from light when not being used.
 - 1086 • Do not shake SIMPONI.
- 1087

1088 **Keep SIMPONI and all medicines out of the reach of children.**

1089

1090 **General Information about SIMPONI**

- 1091 • Medicines are sometimes prescribed for purposes other than those listed in the Medication Guide.
 - 1092 Do not use SIMPONI for a condition for which it was not prescribed.
 - 1093 • Do not give SIMPONI to other people, even if they have the same condition that you have. It may
 - 1094 harm them.
 - 1095 • This Medication Guide summarizes the most important information about SIMPONI. If you
 - 1096 would like more information, talk to your doctor. You can ask your doctor or pharmacist for
 - 1097 information about SIMPONI that is written for health professionals. For more information go to
 - 1098 www.simpONI.com or call 1-800-457-6399.
- 1099

1100 **What are the ingredients in SIMPONI?**

1101 Active ingredient: golimumab.

1102 Inactive ingredients: L-histidine, L-histidine monohydrochloride monohydrate, sorbitol, polysorbate

1103 80, and water for injection. SIMPONI does not contain preservatives.

1104

1105 Revised: 8/2011

1106 This Medication Guide has been approved by the U.S. Food and Drug Administration.