CIM ZIA (certolizumab pegol) for injection, for subcutaneous use effectively. See full prescribing information for CIM ZIA. These highlights do not include all the information needed to use CIM ZIA® safely and effectively. See full prescribing information for CIM ZIA.

**HIGHLIGHS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use CIM ZIA® safely and effectively. See full prescribing information for CIM ZIA.

CIM ZIA (certolizumab pegol) for injection, for subcutaneous use

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use CIM ZIA® safely and effectively. See full prescribing information for CIM ZIA.

CIM ZIA (certolizumab pegol) for injection, for subcutaneous use

**INDICATIONS AND USAGE**

CIM ZIA is a tumor necrosis factor (TNF) blocker indicated for:

- Treatment of adults with moderately to severely active rheumatoid arthritis (1.2)
- Treatment of adults with moderately to severely active Crohn's disease (1.3)
- Treatment of adults with active ankylosing spondylitis (1.4)

**CONTRAINdications**

- None (4)

**WARNINGS AND PRECAUTIONS**

- Increased risk of serious infections leading to hospitalization or death including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens (5.1).
- CIM ZIA 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 CIM ZIA (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 CIM ZIA is a member (5.2). CIM ZIA is not indicated for use in pediatric patients (8.4).

**ADVERSE REACTIONS**

The most common adverse reactions (incidence ≥7% and higher than placebo): upper respiratory tract infection, rash, and urinary tract infection (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact UCB, Inc. at 1-866-822-0068 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**

- Use with Biological DMARDS – increased risk of serious infections (5.8, 7.1)
- Live vaccines – avoid use with CIM ZIA (5.10, 7.2)
- Laboratory tests – may interfere with aPTT tests (7.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

**DOSE FORMS AND STRENGTHS**

For injection: 200 mg lyophilized powder for reconstitution in a single-use vial, with 1 mL of sterile Water for Injection (3)

Injection: 200 mg/mL solution in a single-use prefilled syringe (3)

**CONTRAINdications**

- None (4)

**WARNINGS AND PRECAUTIONS**

- Serious infections – do not start CIMZIA during an active infection. If an infection develops, monitor carefully, and stop CIMZIA if infection becomes serious (5.1)
- Invasive fungal infections – for patients who develop a systemic illness on CIMZIA, consider empiric antifungal therapy for those who reside or travel to regions where mycoses are endemic (5.1)
- Cases of lymphoma and other malignancies have been observed among patients receiving TNF blockers (5.2)
- Heart failure, worsening or new onset may occur (5.3)
- Anaphylaxis or serious allergic reactions may occur (5.4)
- Hepatitis B virus reactivation – test for HBV infection before starting CIMZIA. Monitor HBV carriers carefully, and stop CIMZIA if infection becomes serious (5.7)
- Lupus-like syndrome – stop CIMZIA if syndrome develops (5.9)

**ADVERSE REACTIONS**

The most common adverse reactions (incidence ≥7% and higher than placebo): upper respiratory tract infection, rash, and urinary tract infection (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact UCB, Inc. at 1-866-822-0068 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**

- Use with Biological DMARDS – increased risk of serious infections (5.8, 7.1)
- Live vaccines – avoid use with CIMZIA (5.10, 7.2)
- Laboratory tests – may interfere with aPTT tests (7.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.
INDICATIONS AND USAGE

1.1 Crohn’s Disease
CIMZIA is indicated for reducing signs and symptoms of Crohn’s disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.

1.2 Rheumatoid Arthritis
CIMZIA is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA).

1.3 Psoriatic Arthritis
CIMZIA is indicated for the treatment of adult patients with active psoriatic arthritis (PsA).

1.4 Ankylosing Spondylitis
CIMZIA is indicated for the treatment of adults with active ankylosing spondylitis (AS). [see Clinical Studies (14.6)]

2 DOSAGE AND ADMINISTRATION

CIMZIA is administered by subcutaneous injection. Injection sites should be rotated and injections should not be given into areas where the skin is tender, bruised, red or hard. When a 400 mg dose is needed (given as two subcutaneous injections of 200 mg), injections should occur at separate sites in the thigh or abdomen.

The solution should be carefully inspected visually for particulate matter and discoloration prior to administration. The solution should be a clear colorless to yellow liquid, essentially free from particulates and should not be used if cloudy or if foreign particulate matter is present. CIMZIA does not contain preservatives; therefore, unused portions of drug remaining in the syringe or vial should be discarded.

2.1 Crohn’s Disease
The recommended initial adult dose of CIMZIA is 400 mg given as two subcutaneous injections of 200 mg initially and at Weeks 2 and 4. In patients who obtain a clinical response, the recommended maintenance regimen is 400 mg every four weeks.

2.2 Rheumatoid Arthritis
The recommended dose of CIMZIA for adult patients with rheumatoid arthritis is 400 mg (given as two subcutaneous injections of 200 mg) initially and at Weeks 2 and 4, followed by 200 mg every other week. For maintenance dosing, CIMZIA 400 mg every 4 weeks can be considered [see Clinical Studies (14.2)].

2.3 Psoriatic Arthritis
The recommended dose of CIMZIA for adult patients with psoriatic arthritis is 400 mg (given as 2 subcutaneous injections of 200 mg each) initially and at weeks 2 and 4, followed by 200 mg every other week. For maintenance dosing, CIMZIA 400 mg every 4 weeks can be considered [see Clinical Studies (14.3)].

2.4 Ankylosing Spondylitis
The recommended dose of CIMZIA for adult patients with ankylosing spondylitis is 400 mg (given as 2 subcutaneous injections of 200 mg each) initially and at weeks 2 and 4, followed by 200 mg every other week for 400 mg every 4 weeks.

2.5 Preparation and Administration of CIMZIA Using the Lysophosphatidyl Powder for Injection
CIMZIA Lysophosphatidyl powder should be prepared and administered by a health care professional. CIMZIA is provided in a package that contains everything required to reconstitute and inject the drug [see How Supplied/Storage and Handling (16)]. Step-by-step preparation and administration instructions are provided below.

Preparation and Storage

a. CIMZIA should be brought to room temperature before reconstituting.
b. Use appropriate aseptic technique when preparing and administering CIMZIA.
c. Reconstitute the vial(s) of CIMZIA with 1 mL of Sterile Water for Injection, USP using the 20-gauge needle provided.
d. Gently swirl each vial of CIMZIA without shaking, assuring that all of the powder comes in contact with the Sterile Water for Injection.
e. Leave the vial(s) undisturbed to fully reconstitute, which may take approximately 30 minutes.
f. The final reconstituted solution contains 200 mg/mL and should be clear to opalescent, colorless to pale yellow liquid essentially free from particulates.
g. Once reconstituted, CIMZIA can be stored in the vials for up to 24 hours between 2°C to 8°C (36°F to 46°F) prior to injection. Do not freeze.

Administration

a. Prior to injecting, reconstituted CIMZIA should be at room temperature but do not leave reconstituted CIMZIA at room temperature for more than two hours prior to administration.
b. Withdraw the reconstituted solution into a separate syringe for each vial using a new 20-gauge needle for each vial so that each syringe contains 1 mL of CIMZIA (200 mg of certolizumab pegol).
c. Replace the 20-gauge needle(s) on the syringes with a 23-gauge(s) for administration.
d. Inject the full contents of the syringe(s) subcutaneously into thigh or abdomen. Where a 400 mg dose is required, two injections are required, therefore, separate sites should be used for each 200 mg injection.

2.6 Preparation and Administration of CIMZIA Using the Prefilled Syringe
After proper training in subcutaneous injection technique, a patient may self-inject with the CIMZIA Prefilled Syringe if a physician determines that it is appropriate.

Patients using the CIMZIA Prefilled Syringe should be instructed to inject the full amount in the syringe (1 mL), according to the directions provided in the Instructions for Use booklet.

2.7 Monitoring to Assess Safety
Before initiation of therapy with CIMZIA, all patients must be evaluated for both active and inactive (latent) tuberculosis infection. The possibility of undetected latent tuberculosis should be considered in patients who have immigrated from or traveled to countries with a high prevalence of tuberculosis or had close contact with a person with active tuberculosis. Appropriate screening tests (e.g. tuberculin skin test and chest x-ray) should be performed in all patients.

2.8 Concomitant Medications
CIMZIA may be used as monotherapy or concomitantly with non-biological disease modifying anti-rheumatic drugs (DMARDs).

The use of CIMZIA in combination with biological DMARDs or other tumor necrosis factor (TNF) blocker therapy is not recommended.

3 DOSAGE FORMS AND STRENGTHS

• For Injection: Lyophilized Powder for Reconstitution
Sterile, white, lyophilized powder for reconstitution and then subcutaneous administration. Each single-use vial provides approximately 200 mg of CIMZIA.

• Injection: Prefilled Syringe
A single-use, 1 mL prefilled glass syringe with a fixed 25 gauge ½ inch thin wall needle, providing 200 mg per 1 mL of CIMZIA.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Serious Infections [see Boxed Warning]
Patients treated with CIMZIA are at an increased risk for developing serious infections involving various organ systems and sites that may lead to hospitalization or death.

Opportunistic infections due to bacterial, mycobacterial, invasive fungal, viral, parasitic, or other opportunistic pathogens including aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, legionellosis, listeriosis, pneumocystitis, and tuberculosis have been reported with TNF blockers. Patients have frequently presented with disseminated rather than localized disease.

Treatment with CIMZIA should not be initiated in patients with an active infection, including clinically important localized infections. Patients greater than 65 years of age, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants (e.g., corticosteroids or methotrexate) may be at a greater risk of infection. The benefits and risks of treatment should be considered prior to initiating therapy in patients:

• with chronic or recurrent infection
• who have been exposed to tuberculosis
• who have a history of an opportunistic infection
• who have resided or traveled in areas where tuberculosis is endemic
• who have resided or traveled in areas of endemically high risk for tuberculosis
• who have resided or traveled in areas of endemically high risk for tuberculosis
• who have resided or traveled in areas of endemically high risk for tuberculosis
• who have resided or traveled in areas of endemically high risk for tuberculosis
• who have resided or traveled in areas of endemically high risk for tuberculosis

5.2 Lymphoma and Other Malignancies
Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which CIMZIA is a member [see Warnings and Precautions (5.2)]. CIMZIA is not indicated for use in pediatric patients.

5.3 Opportunistic Infections
Opportunistic infections due to bacterial, mycobacterial, invasive fungal, viral, parasitic, or other opportunistic pathogens including aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, legionellosis, listeriosis, pneumocystis, and tuberculosis have been reported with TNF blockers. Patients have frequently presented with disseminated rather than localized disease.

Cases of reactivation of tuberculosis or new tuberculosis infections have been observed in patients receiving CIMZIA, including patients who have previously or concomitantly received treatment for latent or active tuberculosis. Reports included cases of pulmonary and extrapulmonary (i.e., disseminated) tuberculosis. Evaluate patients for tuberculosis risk factors and test for latent infection prior to initiating CIMZIA and periodically during therapy.
5.4 Hypersensitivity Reactions

The following situations that could be compatible with hypersensitivity reactions have been reported rarely following CIMZIA administration:

- angioedema
- dyspnea
- hypotension
- rash
- serum sickness
- and urticaria

Some of these reactions occurred after the first administration of CIMZIA. If such reactions occur, discontinue further administration of CIMZIA and institute appropriate therapy. There are no data on the risks of using CIMZIA in patients who have experienced a severe hypersensitivity reaction towards another TNF blocker; in these patients caution is needed [see Adverse Reactions (6.1)].

5.5 Hepatitis B Virus Reactivation

Use of TNF blockers, including CIMZIA, has been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. In some instances, HBV reactivation occurring in conjunction with TNF blocker therapy has been fatal. The majority of reports have occurred in patients concomitantly receiving other medications that suppress the immune system, which may also contribute to HBV reactivation.

Test patients for HBV infection before initiating treatment with CIMZIA. For patients who test positive for HBV infection, consult with a physician with expertise in the treatment of hepatitis B is recommended. Adequate data are not available on the safety or efficacy of treating patients who are carriers of HBV with anti-viral therapy in conjunction with TNF blocker therapy to prevent HBV reactivation. Patients who are carriers of HBV and require treatment with CIMZIA should be closely monitored for clinical and laboratory signs of active HBV infection throughout therapy and for several months following termination of therapy.

In patients who develop HBV reactivation, discontinue CIMZIA and initiate effective anti-viral therapy with appropriate supportive treatment. The safety of resuming TNF blocker therapy after HBV reactivation is controlled is not known. Therefore, exercise caution when considering resumption of CIMZIA therapy in this situation and monitor patients closely.

5.6 Neurologic Reactions

Use of TNF blockers has been associated with rare cases of new onset or exacerbation of seizures and/or radiographic evidence of central nervous system demyelinating disease, including multiple sclerosis, and with peripheral demyelinating disease, including Guillain-Barré syndrome. Exercise caution in considering the use of CIMZIA in patients with pre-existing or recent-onset central or peripheral nervous system demyelinating disorders. Rare cases of neurological disorders, including seizure disorder, optic neuritis, and peripheral neuropathy have been reported in treated patients with CIMZIA [see Adverse Reactions (6.1)].

5.7 Hematological Reactions

Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Adverse reactions of the hematologic system, including medically significant cytopenia (e.g., leukopenia, pancytopenia, thrombocytopenia) have been infrequently reported with CIMZIA [see Adverse Reactions (6.1)]. The causal relationship to TNF blockers has not been determined.

Although no high risk group has been identified, exercise caution in patients being treated with CIMZIA who have ongoing, or a history of, significant hematologic abnormalities. Advise all patients to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever, bruising, bleeding, pain) while on CIMZIA. Consider discontinuation of CIMZIA therapy in patients with confirmed significant hematologic abnormalities.

5.8 Use with Biological Disease-Modifying Antirheumatic Drugs (Biological DMARDs)

Serious infections were seen in clinical studies with concurrent use of anakinra (an interleukin-1 antagonist) and another TNF blocker; etanercept, with no added benefit compared to etanercept alone. A higher risk of serious infections was also observed in combination use of TNF blockers with abatacept and rituximab. Because of the nature of the adverse events seen with this combination therapy, similar toxicities may also result from use of CIMZIA in combination. Therefore, the use of CIMZIA in combination with other biological DMARDs is not recommended [see Drug Interactions (7.1)].

5.9 Autoimmunity

Treatment with CIMZIA may result in the formation of autoantibodies and rarely, in the development of a lupus-like syndrome. If a patient develops symptoms suggestive of a lupus-like syndrome following treatment with CIMZIA, discontinue treatment [see Adverse Reactions (6.1)].

5.10 Immunizations

Patients treated with CIMZIA may receive vaccinations, except for live or live attenuated vaccines. No data are available on the response to live vaccines or the secondary transmission of infection by live vaccines in patients receiving CIMZIA.

In a placebo-controlled clinical trial of patients with rheumatoid arthritis, no difference was detected in antibody response to vaccine between CIMZIA and placebo treatment groups when the pneumococcal polysaccharide vaccine and influenza vaccine were administered concurrently with CIMZIA. Similar proportions of patients developed protective levels of anti-vaccine antibodies between CIMZIA and placebo treatment groups; conversely, patients receiving CIMZIA and concomitant methotrexate had a lower humoral response compared with patients receiving CIMZIA alone. The clinical significance of this is unknown.

5.11 Immunosuppression

Since TNF mediates inflammation and modulates cellular immune responses, the possibility exists for TNF blockers, including CIMZIA, to affect host defenses against infections and malignancies. The impact of treatment with CIMZIA on the development and course of malignancies, as well as active and/or chronic infections, is primarily in patients who have experienced a severe infection reaction (5.1.2.5.5) and Adverse Reactions (6.1). The safety and efficacy of CIMZIA in patients with immunosuppression has not been formally evaluated.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

The most serious adverse reactions were:

- Malignancies [see Warnings and Precautions (5.1)]
- Heart Failure [see Warnings and Precautions (5.3)]

Because clinical studies are conducted under widely varying and controlled conditions, adverse reaction rates observed in clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug, and may not predict the rates observed in a broader patient population in clinical practice.

In premarketing controlled trials of all patient populations combined the most common adverse reactions (> 8%) were upper respiratory infections (18%), rash (9%) and urinary tract infections (8%).

Adverse Reactions Most Commonly Leading to Discontinuation of Treatment in Premarketing Controlled Trails

The proportion of patients with Crohn’s disease who discontinued treatment due to adverse reactions in the controlled clinical trials was 8% for CIMZIA and 7% for placebo. The most common adverse reactions leading to the discontinuation of CIMZIA (for at least 2 patients and with a higher incidence than placebo) were abdominal pain (0.4% CIMZIA, 0.2% placebo), diarrhea (0.4% CIMZIA, 0.0% placebo), and intestinal obstruction (0.4% CIMZIA, 0.0% placebo).

The proportion of patients with rheumatoid arthritis who discontinued treatment due to adverse reactions in the controlled clinical studies was 5% for CIMZIA and 2.5% for placebo. The most common adverse reactions leading to the discontinuation of CIMZIA were tuberculosis infections (0.5%), pyrexia, urticaria, pneumonia, and rash (0.3%).

Consider anti-tuberculosis therapy prior to initiation of CIMZIA in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a new test for latent tuberculosis but having risk factors for tuberculosis infection. Despite previous or concomitant treatment for latent tuberculosis, cases of active tuberculosis have occurred in patients treated with CIMZIA. Some patients who have been successfully treated for active tuberculosis have redeveloped tuberculosis while being treated with CIMZIA. Consultation with a physician with expertise in the treatment of tuberculosis is advised in the decision whether initiating anti-tuberculosis therapy is appropriate for an individual patient.

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

In controlled and open-labeled portions of CIMZIA studies of Crohn’s disease and other diseases, malignancies (excluding non-melanoma skin cancer) were observed at a rate (95% confidence interval) of 0.3% (0.0, 0.7) per 100 patient-years among 4,650 CIMZIA-treated patients versus a rate of 0.6 (0.1, 1.7) per 100 patient-years among 1,319 placebo-treated patients. The size of the control group and limited duration of the controlled portions of the studies precludes the ability to draw firm conclusions.

Malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blocking agents (initiation of therapy < 15 years of age), of which CIMZIA is included. In a meta-analysis of the cancer cases reported in 2,657 CIMZIA-treated patients, the incidence of lymphoma was 0.1% (13 lymphomas reported in patients treated with CIMZIA). In the CIMZIA RA clinical trials (placebo-controlled and open label) a total of three cases of lymphoma were observed among 2,367 patients. This is approximately 2-fold higher than expected in the general population.

In clinical trials for CIMZIA cannot be compared to the rates of clinical trials of other TNF blockers and may not predict the rates observed when CIMZIA is used in a broader patient population. Patients with Crohn’s disease that require chronic exposure to immunosuppressants may be at higher risk than the general population for the development of lymphoma, even in the absence of TNF blocker therapy [see Adverse Reactions (6.1)].

The potential role of TNF blocker therapy in the development of malignancies in patients with TNF blockers is not well understood.

Postmarketing cases of hepatosplenic T-cell lymphoma (HSTL), a rare type of T-cell lymphoma that has a very aggressive disease course and is usually fatal, have been reported in patients treated with TNF blockers, including CIMZIA. The majority of reported TNF blocker cases occurred in adolescent and young adult males with Crohn’s disease or ulcerative colitis. Almost all of these patients had received treatment with azathioprine and/or 6-mercaptopurine and/or methotrexate concomitantly with a TNF blocker at or prior to diagnosis. This is uncertain whether the occurrence of HSTL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants. The potential risk of using a TNF blocker in combination with azathioprine or 6-MP should be carefully considered.

Cases of acute and chronic leukemia have been reported in association with post-marketing TNF-blocker use in RA and other indications. Even in the absence of TNF-blocker therapy, patients with RA may be at a higher risk (approximately 2-fold) than the general population for the development of leukemia.

Periodic skin examinations are recommended for all patients, particularly those with risk factors for skin cancer.

5.3 Heart Failure

Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers, including CIMZIA. In RA, CHF has not been formally studied in patients with CHF; however, in clinical studies in patients with CHF with another TNF blocker, worsening congestive heart failure (CHF) and increased mortality due to CHF were observed. Exercise caution in patients with heart failure and monitor them carefully [see Adverse Reactions (6.1)].

5.4 Hypersensitivity Reactions

The following situations that could be compatible with hypersensitivity reactions have been reported rarely following CIMZIA administration:

- angioedema
- dyspnea
- hypotension
- rash
- serum sickness
- and urticaria

Some of these reactions occurred after the first administration of CIMZIA. If such reactions occur,
Controlled Studies with Crohn’s Disease

The data described below reflect exposure to CIMA Z in 400 mg subcutaneous dosing in studies of patients with Crohn’s disease. In the safety population in controlled studies, a total of 620 patients with Crohn’s disease received CIMA Z at a dose of 400 mg, and 614 subjects received placebo (including subjects randomized to placebo in Study CD2 following open-label dosing of CIMA Z at Weeks 0, 2, 4). In controlled and uncontrolled studies, 1,564 patients received CIMA Z at some dose level, of whom 1,355 patients received 400 mg CIMA Z. Approximately 55% of subjects were female, 45% were male, and 94% were Caucasian. The majority of patients in the active group were between the ages of 18 and 64.

During controlled clinical studies, the proportion of patients with serious adverse reactions was 10% for CIMA Z and 9% for placebo. The most common adverse reactions occurring in ≥5% of CIMA Z-treated patients, and with a higher incidence compared to placebo, in controlled clinical studies with CIMA Z were upper respiratory infections (e.g., nasopharyngitis, laryngitis, viral infection) in 20% of CIMA Z-treated patients and 13% of placebo-treated patients, urinary tract infections (e.g., bladder infection, bacteriuria, cystitis) in 7% of CIMA Z-treated patients and in 6% of placebo-treated patients, and arthralgia (6% CIMA Z, 4% placebo).

Other Adverse Reactions

The most commonly occurring adverse reactions in controlled trials of Crohn’s disease are described above. Other serious or significant adverse reactions reported in controlled and uncontrolled studies in Crohn’s disease and other diseases, occurring in patients receiving CIMA Z at doses of 400 mg or other doses include:

- Blood and lymphatic system disorders: Anemia, leukopenia, lymphadenopathy, pancytopenia, and thrombocytopenia.
- Cardiovascular disorders: Angina pectoris, arrhythmias, atrial fibrillation, cardiac failure, hypertensive heart disease, myocardial infarction, myocardial ischemia, pericardial effusion, pericarditis, stroke and transient ischemic attack.
- Eye disorders: Optic neuritis, retinal hemorrhage, and uveitis.
- General disorders and administration site conditions: Bleeding and injection site reactions.
- Hematopoietic disorders: Elevated liver enzymes and hepatitis.
- Immune system disorders: Alopecia totalis.
- Psychiatric disorders: Anxiety, bipolar disorder, and suicide attempt.
- Renal and urinary disorders: Nephrotic syndrome and renal failure.
- Reproductive system and breast disorders: Menstrual disorder.
- Skin and subcutaneous tissue disorders: Dermatitis, erythema nodosum, and urticaria.
- Vascular disorders: Thrombophlebitis, vasculitis.

Controlled Studies with Rheumatoid Arthritis

CIMA Z was studied primarily in placebo-controlled trials and in long-term follow-up studies. The data described below reflect the exposure to CIMA Z in 2,367 RA patients, including 2,030 exposed for ≥6 months, 2 years for ≥6 months, and 400 mg every 4 weeks dose group were 0.01 per patient-year and in the 400 mg every 4 weeks dose group were 0.01 per patient-year. Serious infections (e.g., tuberculosis, pneumonia, cellulitis, and pyelonephritis) in the placebo group, no serious infection occurred in more than one subject. There is no evidence of increased risk of infections with continued exposure over time [see Warnings and Precautions (5.1)].

Tuberculosis and Opportunistic Infections

In completed and ongoing global clinical studies in all indications including ≥15,700 CIMA Z-treated patients; the overall rate of tuberculosis is approximately 0.61 per 100 patient-years across all indications.

The majority of cases occurred in countries with high endemic rates of TB. Reports include cases of common medical conditions as follows:

- Malignancies
  - In clinical studies of CIMA Z, the overall incidence rate of malignancies was similar for CIMA Z-treated and control patients. For some TNF blockers, more cases of malignancies have been observed among patients treated with placebo than for TNF blockers compared to control patients [see Warnings and Precautions (5.2)].
  - Immunosuppressants at baseline. Patients treated with concomitant immunosuppressants had a lower rate of antibody development than patients not taking immunosuppressants at baseline (3% and 11%, respectively). The following adverse events were reported in clinical trials of CIMA Z: Malignancies: Skin and subcutaneous tissue disorders: Dermatitis, erythema nodosum, and urticaria.

In clinical trials of TNF blockers, including CIMA Z, in patients with RA, some patients have developed ANA. Four patients out of 2,367 patients treated with CIMA Z in RA clinical studies developed clinical signs suggestive of a lupus-like syndrome. The impact of long-term treatment with CIMA Z on the development of autoimmune disease is unknown [see Warnings and Precautions (5.2)].

Immunogenicity

Immunogenicity studies with CIMA Z in RA patients were described above. Other serious or significant adverse reactions reported in controlled and uncontrolled studies in Crohn’s disease and other diseases, occurring in patients receiving CIMA Z at doses of 400 mg or other doses include:

- Skin and subcutaneous tissue disorders: Dermatitis, erythema nodosum, and urticaria.
- Vascular disorders: Thrombophlebitis, vasculitis.

Controlled Studies with Crohn’s Disease

CIMA Z was studied primarily in placebo-controlled trials and in long-term follow-up studies. The data described below reflect the exposure to CIMA Z in 2,367 RA patients, including 2,030 exposed for at least 6 months, 1,663 exposed for at least one year and 282 for at least 2 years, and 1,774 in adequate and well-controlled studies. In placebo-controlled studies, the population had a median age of 53 years at study entry; approximately 80% were females, 93% were Caucasian and all patients were suffering from active rheumatoid arthritis, with a median disease duration of 6.5 years. Most patients received the recommended dose of CIMA Z or higher.

Table 1 summarizes the reactions reported at a rate of at least 3% in patients treated with CIMA Z 200 mg every other week compared to placebo (saline formulation), given concomitantly with methotrexate.

### Table 1: Adverse Reactions Reported by >3% of Patients Treated with CIMA Z Dosed Every Other Week During Placebo-Controlled Period of Rheumatoid Arthritis Studies, with Concomitant Methotrexate.

<table>
<thead>
<tr>
<th>Adverse Reaction (Preferred Term)</th>
<th>Placebo + MTX (%)</th>
<th>CIMA Z 200 mg EOW + MTX (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infection</td>
<td>68.7</td>
<td>68.7</td>
</tr>
<tr>
<td>Headache</td>
<td>5.7</td>
<td>5.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4.2</td>
<td>4.2</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>3.3</td>
<td>3.3</td>
</tr>
<tr>
<td>Acute bronchitis</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1.7</td>
<td>1.7</td>
</tr>
</tbody>
</table>

EOW = Every Other Week, MTX = Methotrexate.

Adverse reactions were observed more frequently in patients receiving CIMA Z than in controls. These adverse reactions occurred more frequently among patients with a baseline history of hypertension and among patients receiving concomitant corticosteroids and non-steroidal anti-inflammatory drugs.

Patients receiving CIMA Z 400 mg as monotherapy every 4 weeks in rheumatoid arthritis controlled clinical trials had similar adverse reactions to those patients receiving CIMA Z 200 mg every other week.

Other Adverse Reactions

Other infrequent adverse reactions (occurring in less than 3% of RA patients) were similar to those seen in Crohn’s disease patients.

Psoriatic Arthritis Clinical Study

CIMA Z had been studied in 409 patients with psoriatic arthritis (PsA) in a placebo-controlled trial. The safety profile for patients with PsA treated with CIMA Z was similar to the safety profile seen in patients with RA and previous experience with CIMA Z.

Ankylosing Spondylitis Clinical Study

CIMA Z has been studied in 325 patients with axial spondyloarthritides of whom the majority had ankylosing spondylitis (AS) in a placebo-controlled study (AS-1). The safety profile for patients in study AS-1 treated with CIMA Z was similar to the safety profile seen in patients with RA and previous experience with CIMA Z.

### 7 DRUG INTERACTIONS

#### 7.1 Use with Anakinra, Abatacept, Rituximab, and Natalizumab

An increased risk of serious infections has been seen in clinical studies of other TNF-blocking agents used in combination with anakinra or abatacept, with or without added benefit. Formal drug interaction studies have not been performed with rituximab or natalizumab. Because of the nature of the adverse events associated with these other biologic products, cases of the adverse events noted above may also result from the use of CIMA Z in these combinations. There is not enough information to assess the safety and efficacy of such combination therapy. Therefore, the use of CIMA Z in combination with anakinra, abatacept, rituximab, or natalizumab is not recommended [see Warnings and Precautions (5.8)].

#### 7.2 Live Vaccines

Avoid use of live (including attenuated) vaccines concurrently with CIMA Z [see Warnings and Precautions (5.1)].
Certolizumab pegol does not contain a fragment crystallizable (Fc) region, which is normally present in a complete antibody, and therefore does not fix complement or cause antibody-dependent cell-mediated cytotoxicity in vitro. It does not induce apoptosis in vitro in human peripheral blood mononuclear cells, nor does certolizumab pegol induce neutrophil degranulation.

A tissue reactivity study was carried out ex vivo to evaluate potential cross-reactivity of certolizumab pegol with cryosections of normal human tissues. Certolizumab pegol showed no reactivity with a designated standard panel of normal human tissues.

12.2 Pharmacodynamics

Biological activities ascribed to TNFα include the upregulation of cellular adhesion molecules and chemokines, upregulation of major histocompatibility complex (MHC) class I and class II molecules, and direct leukocyte activation. TNFα also appears to mediate the production of downstream inflammatory mediators, including interleukin-1, prostaglandins, platelet activating factor, and nitric oxide. Elevated levels of TNFα have been implicated in the pathology of Crohn's disease and rheumatoid arthritis. Certolizumab pegol binds to TNFα, inhibiting its role as a key mediator of inflammation. TNFα is strongly expressed in the bowel wall in areas involved by Crohn's disease and focal concentrations of TNFα in patients with Crohn's disease have been shown to reflect clinical severity of the disease. After treatment with certolizumab pegol, patients with Crohn's disease demonstrated a decrease in the levels of C-reactive protein (CRP). Increased TNFα levels are found in the synovial fluid of rheumatoid arthritis patients and play an important role in the joint destruction that is a hallmark of this disease.

12.3 Pharmacokinetics

Absorption A total of 126 healthy subjects received doses of up to 600 mg certolizumab pegol subcutaneously (sc) and up to 10 mg/kg intravenously (IV) in four pharmacokinetic studies. Data from these studies demonstrate that single intravenous and subcutaneous doses of certolizumab pegol have predictable dose-related pharmacokinetics. In healthy volunteers, the plasma concentration (Cmax), and the Area Under the curve (AUC), of certolizumab pegol are dose proportionally increased following IV and SC administration up to the maximum dose of 600 mg and 800 mg, respectively. These increases were accompanied by a decrease in the terminal serum half-life.

Distribution Distribution studies using exogenous tracers in rats and in humans demonstrated that certolizumab pegol is distributed almost entirely into the extracellular compartment. The plasma protein binding of certolizumab pegol is less than 5%. In vitro binding studies in humans showed that certolizumab pegol binds to anionic cell membranes with high affinity and specificity.

Metabolism Metabolism of certolizumab pegol has not been extensively studied. Some studies have suggested that certolizumab pegol is metabolized primarily by the liver, with some metabolism occurring in the bowel. The majority of the drug is excreted unchanged in the urine.

Elimination Elimination of certolizumab pegol is primarily via renal excretion. Approximately 75-85% of the dose is recovered in the urine within 48 hours of administration. The terminal elimination half-life of certolizumab pegol in healthy volunteers is approximately 14 days.

Residues of certolizumab pegol have been identified in human plasma, blood, urine, and feces. The major metabolites are the unmodified Fab fragment and the PEG component, which is excreted in the urine primarily as a conjugate with glutathione or glucuronide. In addition, minor metabolites, such as the Fab fragment conjugated to glutathione or glucuronide, have been identified.

10.5 Liver Disease Liver disease can affect the metabolism of certolizumab pegol. In patients with severe liver disease, the clearance of certolizumab pegol may be decreased, resulting in increased exposure to the drug. In patients with moderate liver disease, the clearance of certolizumab pegol may be increased, resulting in decreased exposure to the drug.

Renal Impairment: Specific clinical studies have not been performed to assess the effect of renal impairment on the pharmacokinetics of certolizumab pegol. The pharmacokinetics of the PEG (polyethylene glycol) fraction of certolizumab pegol is expected to be dependent on renal function but has not been assessed in renal impairment. There are insufficient data to provide a dosing recommendation in moderate and severe renal impairment.

Race: A specific clinical study showed no difference in pharmacokinetics between Caucasian and Japanese subjects.

Drug Interactions: Studies Methylene blue, photopheresis or methotrexate were not altered by concomitant administration with certolizumab pegol. Methylene blue and photopheresis may increase the effect of methotrexate on certolizumab pegol. However, methotrexate-treated patients have lower incidence of antibodies to certolizumab pegol. Thus, therapeutic plasma levels are more likely to be sustained when certolizumab pegol is administered with methotrexate in patients with rheumatoid arthritis.

Formal drug-drug interaction studies have not been conducted with certolizumab pegol.
14.1 Crohn's Disease

The efficacy and safety of CIMZIA were assessed in two double-blind, randomized, placebo-controlled studies in patients aged 18 years and older with moderately to severely active Crohn's disease, as defined by a Crohn's Disease Activity Index (CDAI) of 220 to 450 points, inclusive. CIMZIA was administered subcutaneously at a dose of 400 mg in both studies. Stable concomitant medications for Crohn's disease were permitted.

Study CD1

Study CD1 was a randomized placebo-controlled study in 682 patients with active Crohn's disease. CIMZIA or placebo was administered at Week 0, 2, and 4 and then every four weeks to Week 24. Assessments were done at Weeks 6 and 26. Clinical response was defined as at least a 100-point reduction in CDAI score compared to baseline, and clinical remission was defined as an absolute CDAI score of 150 points or lower.

The results for Study CD1 are provided in Table 2. At Week 6, the proportion of clinical responders was statistically significantly greater for CIMZIA-treated patients compared to controls. The difference in clinical remission rates was not statistically significant at Week 6. The difference in the proportion of patients who were in clinical response at both Weeks 6 and 26 was also statistically significant, demonstrating maintenance of clinical response.

Table 2 Study CD1 – Clinical Response and Remission, Overall Study Population

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>% Response or Remission (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (N = 328)</td>
</tr>
<tr>
<td>Week 6</td>
<td></td>
</tr>
<tr>
<td>Clinical Response</td>
<td>27% (22%, 32%)</td>
</tr>
<tr>
<td>Clinical Remission</td>
<td>17% (13%, 22%)</td>
</tr>
<tr>
<td>Week 26</td>
<td></td>
</tr>
<tr>
<td>Clinical Response</td>
<td>27% (22%, 31%)</td>
</tr>
<tr>
<td>Clinical Remission</td>
<td>18% (14%, 22%)</td>
</tr>
<tr>
<td>Both Weeks 6 &amp; 26</td>
<td></td>
</tr>
<tr>
<td>Clinical Response</td>
<td>16% (12%, 20%)</td>
</tr>
<tr>
<td>Clinical Remission</td>
<td>10% (7%, 13%)</td>
</tr>
</tbody>
</table>

* p-value < 0.05 logistic regression test
* Clinical response is defined as decrease in CDAI of at least 100 points, and clinical remission is defined as CDAI ≤ 150 points

Study CD2

Study CD2 was a randomized treatment-withdrawal study in patients with active Crohn's disease. All patients who entered the study were dosed initially with CIMZIA 400 mg at Weeks 0, 2, and 4 and then assessed for clinical response at Week 6 (as defined by at least a 100-point reduction in CDAI score). At Week 6, a group of 428 clinical responders was randomized to receive either CIMZIA 400 mg or placebo, every four weeks starting at Week 6, as maintenance therapy through Week 24. Non-responders at Week 6 were withdrawn from the study. Final evaluation was based on the CDAI score at Week 26. Patients who withdrew or who received rescue therapy were not be considered in clinical response. Three randomized responders received no study injections, and were excluded from the ITT analysis.

The results for clinical response and remission are shown in Table 3. At Week 26, a statistically significantly greater proportion of Week 6 responders were in clinical response and in clinical remission in the CIMZIA-treated group compared to the group treated with placebo.

Table 3 Study CD2 – Clinical Response and Clinical Remission

<table>
<thead>
<tr>
<th>% Response or Remission (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIMZIA 400 mg x3 + Placebo (N = 210)</td>
</tr>
<tr>
<td>Week 26</td>
</tr>
<tr>
<td>Clinical Response</td>
</tr>
<tr>
<td>Clinical Remission</td>
</tr>
</tbody>
</table>

* p < 0.05
* Clinical response is defined as decrease in CDAI of at least 100 points, and clinical remission is defined as CDAI ≤ 150 points

Baseline use of immunosuppressants or corticosteroids had no impact on the clinical response to CIMZIA.

14.2 Rheumatoid Arthritis

The efficacy and safety of CIMZIA were assessed in four randomized, placebo-controlled, double-blind studies (RA-I, RA-II, RA-III, and RA-IV) in patients ≥ 18 years of age with moderately to severely active rheumatoid arthritis diagnosed according to the American College of Rheumatology (ACR) criteria. Patients had ≥ 5 swollen and tender joints and had active RA for at least 6 months prior to baseline. CIMZIA was administered subcutaneously in combination with MTX at stable doses of at least 10 mg weekly in Studies RA-I, RA-II, and RA-III. CIMZIA was administered as monotherapy in Study RA-IV. RA-I and Study RA-II evaluated patients who had received MTX for at least 6 months prior to study medication, had an incomplete response to MTX alone. Patients were treated with a loading dose of 400 mg at Weeks 0, 2, and 4 (for both treatment arms) or placebo followed by either 200 mg or 400 mg of CIMZIA or placebo every other week, in combination with MTX for 52 weeks in Study RA-I and for 24 weeks in Study RA-II. Patients were evaluated for signs and symptoms and structural damage using the ACR20 response at Week 24 (RA-I and RA-II) and modified Total Sharp Score (mTSS) at Week 52 (RA-II). The open-label extension follow-up study enrolled 846 patients who received 400 mg of CIMZIA every other week.

Study RA-III evaluated 247 patients who had active disease despite receiving MTX for at least 6 months prior to study enrollment. Patients received 400 mg of CIMZIA every four weeks for 24 weeks without a prior loading dose. Patients were evaluated for signs and symptoms of RA using the ACR20 at Week 24.

Study RA-IV (monotherapy) evaluated 220 patients who had failed at least one DMARD use prior to receiving CIMZIA. Patients were treated with CIMZIA 400 mg or placebo every 4 weeks for 24 weeks. Patients were evaluated for signs and symptoms of active RA using the ACR20 at Week 24.
In the placebo group, 52% of patients experienced no radiographic progression (mTSS ≤ 0) at Week 52 compared to 69% in the CIMZIA 200 mg every other week treatment group. Study RA-II showed similar results at Week 24.

**Table 6: Radiographic Changes at 6 and 12 months in Study RA-I**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo + MTX (N=1199) Mean (SD)</th>
<th>CIMZIA 200 mg + MTX (N=393) Mean (SD)</th>
<th>CIMZIA 200 mg + MTX – Placebo + MTX Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>mTSS</td>
<td>Baseline: 40 (45)</td>
<td>38 (49)</td>
<td>-2.4</td>
</tr>
<tr>
<td></td>
<td>Week 24: 1.3 (3.8)</td>
<td>0.2 (3.2)</td>
<td>-1.1</td>
</tr>
<tr>
<td></td>
<td>Week 52: 2.8 (7.8)</td>
<td>0.4 (5.7)</td>
<td>-2.4</td>
</tr>
<tr>
<td>Erosion Score</td>
<td>Baseline: 14 (21)</td>
<td>15 (24)</td>
<td>-1</td>
</tr>
<tr>
<td></td>
<td>Week 24: 0.7 (2.1)</td>
<td>0.0 (1.5)</td>
<td>-0.7</td>
</tr>
<tr>
<td></td>
<td>Week 52: 1.5 (4.3)</td>
<td>0.1 (2.5)</td>
<td>-1.4</td>
</tr>
<tr>
<td>JSN Score</td>
<td>Baseline: 25 (27)</td>
<td>24 (28)</td>
<td>-1</td>
</tr>
<tr>
<td></td>
<td>Week 24: 0.7 (2.4)</td>
<td>0.2 (2.5)</td>
<td>-0.5</td>
</tr>
<tr>
<td></td>
<td>Week 52: 1.4 (5.0)</td>
<td>0.4 (4.2)</td>
<td>-1.0</td>
</tr>
</tbody>
</table>

An ANCOVA was fitted to the ranked change from baseline for each measure with region and treatment as factors and rank baseline as a covariate.

**Physical Function Responses**

In studies RA-I, RA-II, RA-III, and RA-IV, CIMZIA-treated patients achieved greater improvements from baseline than placebo-treated patients in physical function as assessed by the Health Assessment Questionnaire – Disability Index (HAQ-DI) at Week 24 (RA-II, RA-III and RA-IV) and at Week 52 (RA-I).

### 14.3 Psoriatic Arthritis

The efficacy and safety of CIMZIA were assessed in a multi-center, randomized, double-blind, placebo-controlled trial (PsA001) in 409 patients aged 18 years and older with active psoriatic arthritis despite DmARD therapy. Patients in this study had ≥ 3 swollen and tender joints and adult-onset PsA of at least 6 months duration as defined by the Classification Criteria for Psoriatic Arthritis (CASPAR) criteria, and increased acute phase reactants. Patients had failed one or more DmARDs. Previous treatment with one anti-TNF biologic therapy was allowed, and 20% of patients had prior anti-TNF biologic exposure. Patients receiving concomitant NSAIDs and conventional DmARDs were 73% and 70% respectively.

Patients received a loading dose of CIMZIA 400 mg at Weeks 0, 2 and 4 for both treatment arms or placebo followed by either CIMZIA 200 mg every other week or CIMZIA 400 mg every 4 weeks or placebo every other week. Patients were evaluated for signs and symptoms and structural damage using the ACR20 response at Week 12 and modified Total Sharp Score (mTSS) at Week 24.

**Clinical Response**

The percentage of CIMZIA-treated patients achieving ACR20, 50, and 70 responses in study PsA001 are shown in Table 7. ACR20 response rates at weeks 12 and 24 were higher for each CIMZIA dose group relative to placebo (95% confidence intervals for CIMZIA 200 mg minus placebo at weeks 12 and 24 of (23%, 45%) and (23%, 45%) respectively and 95% confidence intervals for CIMZIA 400 mg minus placebo at weeks 12 and 24 of (17%, 39%) and (22%, 44%), respectively). The results of the components of the ACR response criteria are shown in Table 8.

Patients with enthesitis at baseline were evaluated for mean improvement in Leeds Enthesitis Index (LE). CIMZIA-treated patients receiving either 200 mg every 2 weeks or 400 mg every 4 weeks showed a reduction in enthesitis of 1.6 and 1.7, respectively as compared with a reduction in placebo-treated patients of 0.9 at week 12. Similar results were observed for this endpoint at week 24. Treatment with CIMZIA resulted in improvement in skin manifestations in patients with PsA. However, the safety and efficacy of CIMZIA in the treatment of patients with plaque psoriasis has not been established.

The percent of patients achieving ACR20 responses by visit for PsA001 is shown in Figure 2.
Clinical Response

In study PaA001, inhibition of progression of structural damage was assessed radiographically and expressed as the change in modified total Sharp score (mTSS) and its components, the erosion score (ES) and joint space narrowing score (JSN) at week 24, compared to baseline. The mTSS score was modified for psoriatic arthritis by addition of hand distal interphalangeal (DIP) joints.

Patients treated with CIMZIA 200 mg every other week demonstrated greater reduction in radiographic progression compared with placebo-treated patients at Week 24 as assessed by change from baseline in total modified mTSS Score (estimated mean score was 1.16 in the placebo group compared with -0.02 in the CIMZIA 200 mg group; 95% CI for the difference was (-0.30, -0.01)). Patients treated with CIMZIA 400 mg every 4 weeks did not demonstrate greater inhibition of radiographic progression compared with placebo-treated patients at Week 24.

Physical Function Response

In Study PaA001, CIMZIA-treated patients showed improvement in physical function as assessed by the Health Assessment Questionnaire – Disability Index (HAQ-DI) at Week 24 as compared to placebo (estimated mean change from baseline was 0.19 in the placebo group compared with 0.54 in the CIMZIA 200 mg group; 95% CI for the difference was (-0.39, -0.14)).

14.4 Ankylosing Spondylitis

The efficacy and safety of CIMZIA were assessed in one multicenter, randomized, double-blind, placebo-controlled study (AS-1) in 325 patients >18 years of age with adult-onset active axial spondyloarthritis for at least 3 months. The majority of patients in the study had active AS.

Patients had active disease as defined by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) >4, and spinal pain >4 on a 0 to 10 Numerical Rating Scale (NRS). Patients must have been intolerant to or had an inadequate response to at least one NSAID. Patients were treated with a loading dose of CIMZIA 400 mg at Weeks 0, 2 and 4 (for both treatment arms) or placebo followed by either 200 mg of CIMZIA every 2 weeks or 400 mg of CIMZIA every 4 weeks or placebo. Concomitant NSAIDs were received by 91% of the AS patients. The primary efficacy variable was the proportion of patients achieving an ASAS20 response at Week 12.

Clinical Response

In study AS-1, at Week 12, a greater proportion of AS patients treated with CIMZIA 200 mg every 2 weeks or 400 mg every 4 weeks achieved ASAS 20 response compared to AS patients treated with placebo (Table 9). Responses were similar in patients receiving CIMZIA 200 mg every 2 weeks and CIMZIA 400 mg every 4 weeks. The results of the components of the ASAS response criteria and other measures of disease activity are shown in Table 10.

Table 9: ASAS Responses in AS patients at Weeks 12 and 24 in study AS-1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Placebo N=57</th>
<th>CIMZIA™ 200 mg every 2 weeks N=65</th>
<th>CIMZIA™ 400 mg every 4 weeks N=56</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 12</td>
<td>37%</td>
<td>57%</td>
<td>64%</td>
</tr>
<tr>
<td>Week 24</td>
<td>33%</td>
<td>68%</td>
<td>70%</td>
</tr>
<tr>
<td>ASAS40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 12</td>
<td>19%</td>
<td>40%</td>
<td>50%</td>
</tr>
<tr>
<td>Week 24</td>
<td>16%</td>
<td>48%</td>
<td>59%</td>
</tr>
</tbody>
</table>

* CIMZIA administered every 2 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
* CIMZIA administered every 4 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4

Table 10: Components of the ASAS response criteria and other measures of disease activity in AS patients at baseline and Week 12 in study AS-1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Placebo N=57</th>
<th>CIMZIA™ 200 mg every 2 weeks N=65</th>
<th>CIMZIA™ 400 mg every 4 weeks N=56</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS20 response criteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Patient Global Assessment (0-10)</td>
<td>6.9</td>
<td>5.6</td>
<td>7.3</td>
</tr>
<tr>
<td>- Total spinal pain (0-10)</td>
<td>7.3</td>
<td>5.8</td>
<td>7.0</td>
</tr>
<tr>
<td>- BASFI (0-10)</td>
<td>6.0</td>
<td>5.2</td>
<td>5.6</td>
</tr>
<tr>
<td>- Inflammation (0-10)</td>
<td>6.7</td>
<td>5.5</td>
<td>6.7</td>
</tr>
<tr>
<td>BASDAI (0-10)</td>
<td>6.4</td>
<td>5.4</td>
<td>6.5</td>
</tr>
<tr>
<td>BASMI</td>
<td>4.8</td>
<td>4.4</td>
<td>4.2</td>
</tr>
</tbody>
</table>

* CIMZIA administered every 2 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
* CIMZIA administered every 4 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4

The percent of AS patients achieving ASAS20 responses by visit for Study AS001 is shown in Figure 3. Among patients receiving CIMZIA, clinical responses were seen in some AS patients within one to two weeks after initiation of therapy.
CIMZIA® (CIM-zee-uhh) lyophilized powder or solution for subcutaneous use

Read the Medication Guide that comes with CIMZIA before you start using it, and before each injection of CIMZIA. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or treatment.

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

CIMZIA is a medicine that affects your immune system. CIMZIA can lower the ability of the immune system to fight infections. Serious infections have happened in patients taking CIMZIA. These infections include tuberculosis (TB) and infections caused by viruses, fungi or bacteria that have spread throughout the body. Some patients have died from these infections.

Your healthcare provider should test you for TB before starting CIMZIA.

Your healthcare provider should monitor you closely for signs and symptoms of TB during treatment with CIMZIA.

You should not start receiving CIMZIA if you have any kind of infection unless your healthcare provider says it is okay.

Before you receive CIMZIA, tell your healthcare provider if you:

- Think you have an infection, flu-like symptoms, or have any other symptoms of an infection such as:
  - fever, sweat, or chills
  - muscle aches
  - cough
  - shortness of breath
  - blood in phlegm
  - weight loss
- are being treated for an infection
- get a lot of infections or have infections that keep coming back
- have diabetes, HIV, or a weak immune system. People with these conditions have a higher chance for infections.
- have tuberculosis (TB), or have been in close contact with someone with TB
- were born in, lived in, or traveled to countries where there is more risk for getting TB. Tell your healthcare provider if you are not sure.
- live or have lived in certain parts of the country (such as the Ohio and Mississippi River valleys) where there is an increased risk for getting certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis). These infections may develop or become more severe if you take CIMZIA. If you do not know if you have lived in an area where histoplasmosis, coccidioidomycosis, or blastomycosis is common, ask your healthcare provider.
- have or have had hepatitis B
- use the medicine Kineret® (anakinra), Orencia® (abatacept), Rituxan® (rituximab), or Tysabri® (natalizumab)

After starting CIMZIA, if you get an infection, any sign of an infection including a fever, cough, flu-like symptoms, or have open cuts or sores on your body, call your healthcare provider right away.

CIMZIA can make you more likely to get infections or make any infection that you may have worse.

Certain types of Cancer

- There have been cases of unusual cancers in children and teenage patients using TNF-blocking agents.
- People taking TNF-blocker medicines, including CIMZIA, the chances of getting lymphoma or other cancers may increase.
- People with RA, especially more serious RA, may have a higher chance for getting a kind of cancer called lymphoma.

What is CIMZIA?

CIMZIA is a prescription medicine called a Tumor Necrosis Factor (TNF) blocker. CIMZIA is used in adult patients to:

- Treat active ankylosing spondylitis
- Treat active psoriatic arthritis

What should I tell my healthcare provider before starting treatment with CIMZIA?

CIMZIA may not be right for you. Before starting CIMZIA, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection. (See, “What is the most important information I should know about CIMZIA?”)
- have or have had any type of cancer.
- have congestive heart failure.
- have seizures, any numbness or tingling, or a disease that affects your nervous system such as multiple sclerosis.
- are scheduled to receive a vaccine. Do not receive a live vaccine while taking CIMZIA.
- are allergic to any of the ingredients in CIMZIA. See the end of this Medication Guide for a list of the ingredients in CIMZIA.
- are pregnant or planning to become pregnant. It is not known if CIMZIA will harm your unborn baby. Tell your healthcare provider right away if you become pregnant while receiving CIMZIA.

Pregnancy Registry: If you become pregnant while taking CIMZIA, tell your healthcare provider about registering in the pregnancy exposure registry for CIMZIA. You can enroll in this registry by calling 1-877-311-8972. The purpose of this registry is to collect information about the safety of CIMZIA during pregnancy.

- are breastfeeding or plan to breastfeed. It is not known if CIMZIA passes into your breast milk.
- You and your healthcare provider should decide if you will receive CIMZIA or breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements. Especially tell your healthcare provider if you take the following medicines due to a higher chance for serious infections:

- Kineret® (anakinra), Orencia® (abatacept), Rituxan® (rituximab), or Tysabri® (natalizumab)
- medicines called Tumor Necrosis Factor (TNF) blockers such as Remicade® (infliximab), Humira® (adalimumab), Enbrel® (etanercept), or Simponi® (golimumab)

Ask your healthcare provider if you are not sure.

You should not take CIMZIA while you take any of these medicines.

How should I receive CIMZIA?

- CIMZIA comes as lyophilized powder or as a solution in a prefilled syringe for injection.
- If your healthcare provider prescribes the CIMZIA powder, your CIMZIA should be injected by a healthcare provider. Each dose of CIMZIA will be given as 1 or 2 separate injections under the skin in your stomach area or upper thighs.
- If your healthcare provider prescribes the CIMZIA prefilled syringe, you will be trained on how to inject CIMZIA.
- You will receive a CIMZIA Prefilled Syringe Kit including a complete “Instructions for Use” booklet for the right way to inject CIMZIA.
- Read the detailed Instructions for Use booklet for instructions on how to prepare and inject your dose of CIMZIA, and how to properly throw away used syringes containing the needle.
- Do not give yourself an injection of CIMZIA unless you have been shown by your healthcare provider. A family member or friend can also be trained to help you give your injection. Talk to your healthcare provider if you have questions.
- CIMZIA is given by an injection under the skin. Your healthcare provider will tell you how much and how often to inject CIMZIA. Do not use more CIMZIA or inject more often than prescribed.
- You may need more than 1 injection at a time depending on your prescribed dose of CIMZIA.
- CIMZIA may be injected into your stomach or upper thighs. If you are prescribed more than 1 injection, each injection should be given at a different site in your stomach or upper thighs.
- Make sure the solution in the prefilled syringe is clear to colorless to light yellow. The solution should be mostly free from particles. Do not use the CIMZIA prefilled syringe if the medicine looks cloudy or if there are large or colored particles.
- Do not miss any doses of CIMZIA. If you miss a dose, call your healthcare provider or pharmacist for instructions.
- Make sure to keep all follow-up appointments with your healthcare provider.

What are the possible side effects of CIMZIA?

CIMZIA can cause serious side effects including:

- See “What is the most important information I should know about CIMZIA?”
- Heart Failure including new heart failure or worsening of heart failure you already have. Symptoms include shortness of breath, swelling of your ankles or feet, or sudden weight gain.
- Allergic Reactions. Signs of an allergic reaction include a skin rash, swelling or itching of the face, tongue, lips, or throat, or trouble breathing.
- Hepatitis B virus reactivation in patients who carry the virus in their blood. In some cases patients have died as a result of hepatitis B virus being reactivated. Your doctor should monitor you carefully before and during treatment with CIMZIA to see if you carry the hepatitis B virus in your blood. Tell your doctor if you have any of the following symptoms:
  - feel unwell
  - skin or eyes look yellow
  - tiredness (fatigue)
  - poor appetite or vomiting
  - pain on the right side of your stomach (abdomen)
New or worsening nervous system problems, such as multiple sclerosis (MS), Guillain-Barre syndrome, seizures, or inflammation of the nerves of the eyes. Symptoms may include:

- dizziness
- numbness or tingling
- problems with your vision
- weakness in your arms or legs

Blood Problems. Your body may not make enough of the blood cells that help fight infections or help stop bleeding. Symptoms include a fever that doesn’t go away, bruising or bleeding very easily, or looking very pale.

Immune reactions including a lupus-like syndrome. Symptoms include shortness of breath, joint pain, or a rash on the cheeks or arms that worsens with sun exposure.

Call your healthcare provider right away if you have any serious side effects listed above.

The most common side effects of CIMZIA include:

- upper respiratory infections (flu, cold)
- rash
- urinary tract infections (bladder infections)

Tell your healthcare provider about any side effect that bothers you or does not go away.

These are not all of the possible side effects of CIMZIA. For more information, ask your healthcare provider or pharmacist.

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

How should I store CIMZIA?

- Keep CIMZIA in the refrigerator between 36ºF to 46ºF (2ºC to 8ºC).
- Do not freeze CIMZIA.
- Protect CIMZIA from light. Store CIMZIA in the carton it came in.
- Do not use CIMZIA if the medicine is expired. Check the expiration date on the prefilled syringe or carton.
- The CIMZIA prefilled syringe is made of glass. Do not drop or crush the syringe.

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

General information about the safe and effective use of CIMZIA.

Meditations are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use CIMZIA for a condition for which it was not prescribed. Do not give CIMZIA to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about CIMZIA. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about CIMZIA that is written for health professionals.

For more information, go to www.CIMZIA.com or call 1-866-424-6942.

What are the ingredients in CIMZIA?

CIMZIA lyophilized powder:
Active ingredient: certolizumab pegol
Inactive ingredients: lactic acid, polysorbate, sucrose
CIMZIA lyophilized powder is mixed with sterile Water for Injection.

CIMZIA prefilled syringe:
Active ingredient: certolizumab pegol
Inactive ingredients: sodium acetate, sodium chloride, Water for Injection
CIMZIA has no preservatives.

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

Product manufactured by: UCB, Inc. • 1950 Lake Park Drive • Smyrna, GA 30080
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