The percentage of the maternal dose (200 mg CIMZIA dosed once every 2 weeks), that reaches an infant ranged from 0.56% to 4.25% based on samples with measurable certolizumab pegol concentration. No serious adverse reactions were noted in the 17 breastfed infants in the study.

In a separate study, plasma certolizumab pegol concentrations were collected 4 weeks after birth in 9 breastfed infants whose mothers had been currently taking CIMZIA (regardless of being exclusively breastfed or not). Certolizumab pegol in infant plasma was not measurable i.e., below 0.032 mcg/mL.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established. Due to its inhibition of TNFα, CIMZIA administered during pregnancy could affect immune responses in the *in utero*-exposed newborn and infant *[see Use in Specific Populations (8.1)]*.

8.5 Geriatric Use

Clinical studies of CIMZIA did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Population pharmacokinetic analyses of patients enrolled in CIMZIA clinical studies concluded that there was no apparent difference in drug concentration regardless of age. Because there is a higher incidence of infections in the elderly population in general, use caution when treating the elderly with CIMZIA *[see Warnings and Precautions (5.1)]*.

10 OVERDOSAGE

The maximum tolerated dose of certolizumab pegol has not been established. Doses of up to 800 mg subcutaneous and 20 mg/kg intravenous have been administered without evidence of dose-limiting toxicities. In cases of overdosage, it is recommended that patients be monitored closely for any adverse reactions or effects, and appropriate symptomatic treatment instituted immediately.

11 DESCRIPTION

Certolizumab pegol is a TNF blocker. CIMZIA is a recombinant, humanized antibody Fab' fragment, with specificity for human tumor necrosis factor alpha (TNFα), conjugated to an approximately 40kDa polyethylene glycol (PEG2MAL40K). The Fab' fragment is manufactured in *E. coli* and is subsequently subjected to purification and conjugation to PEG2MAL40K, to generate certolizumab pegol. The Fab' fragment is composed of a light chain with 214 amino acids and a heavy chain with 229 amino acids. The molecular weight of certolizumab pegol is approximately 91 kiloDaltons.

CIMZIA (certolizumab pegol) for injection is supplied as a sterile white, lyophilized powder in a single-dose vial for subcutaneous use. After reconstitution of the lyophilized powder with 1 mL Sterile Water for Injection, USP, the final concentration is 200 mg/mL with a deliverable volume of 1 mL (200 mg) and a pH of approximately 5.2. Each single-dose vial provides 200 mg certolizumab pegol, lactic acid (0.9 mg), polysorbate (0.1 mg), and sucrose (100 mg).

CIMZIA (certolizumab pegol) injection is supplied as a sterile, clear to opalescent, colorless to pale yellow solution that may contain particulates in a single-dose prefilled syringe for subcutaneous use. Each prefilled syringe delivers 1 mL of solution containing 200 mg certolizumab pegol, sodium acetate (1.36 mg), sodium chloride (7.31 mg), and Water for Injection, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Certolizumab pegol binds to human TNFα with a KD of 90pM. TNFα is a key pro-inflammatory cytokine with a central role in inflammatory processes. Certolizumab pegol selectively neutralizes TNFα

(IC_{90} of 4 ng/mL for inhibition of human TNFα in the *in vitro* L929 murine fibrosarcoma cytotoxicity assay) but does not neutralize lymphotoxin α (TNFβ). Certolizumab pegol cross-reacts poorly with TNF from rodents and rabbits, therefore *in vivo* efficacy was evaluated using animal models in which human TNFα was the physiologically active molecule.

Certolizumab pegol was shown to neutralize membrane-associated and soluble human TNFα in a dose-dependent manner. Incubation of monocytes with certolizumab pegol resulted in a dose-dependent inhibition of LPS-induced TNFα and IL-1β production in human monocytes.

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-derived monocytes or lymphocytes, 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 stimulates 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 fecal 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 800 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 plasma concentrations with a linear relationship between the dose administered and the maximum plasma concentration (C_{max}), and the Area Under the certolizumab pegol plasma concentration versus time Curve (AUC). A mean C_{max} of approximately 43 to 49 mcg/mL occurred at Week 5 during the initial loading dose period using the recommended dose regimen for the treatment of patients with rheumatoid arthritis (400 mg sc at Weeks 0, 2 and 4 followed by 200 mg every other week).

Certolizumab pegol plasma concentrations were broadly dose-proportional and pharmacokinetics observed in patients with rheumatoid arthritis, Crohn's disease, and plaque psoriasis were consistent with those seen in healthy subjects.

Following subcutaneous administration, peak plasma concentrations of certolizumab pegol were attained between 54 and 171 hours post-injection. Certolizumab pegol has bioavailability (F) of approximately 80% (ranging from 76% to 88%) following subcutaneous administration compared to intravenous administration.

Distribution

The steady state volume of distribution (Vss) was estimated as 4.7 to 8 L in the population pharmacokinetic analysis for patients with Crohn's disease, patients with rheumatoid arthritis, and adult patients with plaque psoriasis.

Metabolism

The metabolism of certolizumab pegol has not been studied in human subjects. Data from animals indicate that once cleaved from the Fab' fragment the PEG moiety is mainly excreted in urine without further metabolism.

Elimination

PEGylation, the covalent attachment of PEG polymers to peptides, delays the metabolism and elimination of these entities from the circulation by a variety of mechanisms, including decreased renal clearance, proteolysis, and immunogenicity. Accordingly, certolizumab pegol is an antibody Fab' fragment conjugated with PEG in order to extend the terminal plasma elimination half-life ($t_{1/2}$) of the Fab'. The terminal elimination phase half-life ($t_{1/2}$) was approximately 14 days for all doses tested. The clearance following IV administration to healthy subjects ranged from 9.21 mL/h to 14.38 mL/h. The clearance following sc dosing was estimated 17 mL/h in the Crohn's disease population PK analysis with an inter-subject variability of 38% (CV) and an inter-occasion variability of 16%. Similarly, the clearance following sc dosing was estimated as 21.0 mL/h in the RA population PK analysis, with an inter-subject variability of 30.8% (%CV) and inter-occasion variability 22.0%. The clearance following subcutaneous dosing in patients with plaque psoriasis was 14 mL/h with an inter-subject variability of 22.2% (CV). The route of elimination of certolizumab pegol has not been studied in human subjects. Studies in animals indicate that the major route of elimination of the PEG component is via urinary excretion.

Special Populations

Population pharmacokinetic analysis was conducted on data from patients with rheumatoid arthritis and patients with Crohn's disease, to evaluate the effect of age, race, gender, methotrexate use, concomitant medication, creatinine clearance and presence of anti-certolizumab antibodies on pharmacokinetics of certolizumab pegol. A population pharmacokinetic analysis was also conducted on data from patients with plaque psoriasis to evaluate the effect of age, gender, body weight, and presence of anti-certolizumab pegol antibodies. Only bodyweight and presence of anti-certolizumab antibodies significantly affected certolizumab pegol pharmacokinetics. Pharmacokinetic exposure was inversely related to body weight but pharmacodynamic exposure-response analysis showed that no additional therapeutic benefit would be expected from a weight-adjusted dose regimen. The presence of anti-certolizumab antibodies was associated with a $\geq$3 to 4-fold increase in clearance.

Age: Pharmacokinetics of certolizumab pegol was not different in elderly compared to young adults.

Gender: Pharmacokinetics of certolizumab pegol was similar in male and female subjects.

Renal Impairment: Specific clinical studies have not been performed to assess the effect of renal impairment on the pharmacokinetics of CIMZIA. 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 Interaction Studies

Methotrexate pharmacokinetics is not altered by concomitant administration with CIMZIA in patients with rheumatoid arthritis. The effect of methotrexate on CIMZIA pharmacokinetics was not studied. However, methotrexate-treated patients have lower incidence of antibodies to CIMZIA. Thus, therapeutic plasma levels are more likely to be sustained when CIMZIA is administered with methotrexate in patients with rheumatoid arthritis.

Formal drug-drug interaction studies have not been conducted with CIMZIA upon concomitant administration with corticosteroids, nonsteroidal anti-inflammatory drugs, analgesics or immunosuppressants.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term animal studies of CIMZIA have not been conducted to assess its carcinogenic potential. Certolizumab pegol was not genotoxic in the Ames test, the human peripheral blood lymphocytes chromosomal aberration assay, or the mouse bone marrow micronucleus assay.

Since certolizumab pegol does not cross-react with mouse or rat TNFα, reproduction studies were performed in rats using a rodent anti-murine TNFα pegylated Fab fragment (cTN3 PF), similar to certolizumab pegol. The cTN3 PF had no effects on the fertility and general reproductive performance of male and female rats at intravenous doses up 100 mg/kg, administered twice weekly.

14 CLINICAL STUDIES

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[1]) 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 662 patients with active Crohn's disease. CIMZIA or placebo was administered at Weeks 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 3. 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 3: Study CD1 – Clinical Response and Remission, Overall Study Population

Timepoint	% Response or Remission (95% CI)	
	Placebo (N = 328)	**CIMZIA 400 mg (N = 331)**
Week 6		
Clinical Response[#]	**27%** (22%, 32%)	**35%** (30%, 40%)*
Clinical Remission[#]	**17%** (13%, 22%)	**22%** (17%, 26%)
Week 26		
Clinical Response	**27%** (22%, 31%)	**37%** (32%, 42%)*
Clinical Remission	**18%** (14%, 22%)	**29%** (25%, 34%)*
Both Weeks 6 & 26		
Clinical Response	**16%** (12%, 20%)	**23%** (18%, 28%)*
Clinical Remission	**10%** (7%, 13%)	**14%** (11%, 18%)

* 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 8, 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 considered not to be 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 4. 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 4: Study CD2 - Clinical Response and Clinical Remission

	% Response or Remission (95% CI)	
	CIMZIA 400 mg x3 + Placebo N = 210	**CIMZIA 400 mg N = 215**
Week 26		
Clinical Response[#]	**36%** (30%, 43%)	**63%** (56%, 69%)*
Clinical Remission[#]	**29%** (22%, 35%)	**48%** (41%, 55%)*

* 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 ≥ 9 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.

Study RA-I and Study RA-II evaluated patients who had received MTX for at least 6 months prior to study medication, but 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-I). 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.

Clinical Response

The percent of CIMZIA-treated patients achieving ACR20, 50, and 70 responses in Studies RA-I and RA-IV are shown in Table 5. CIMZIA-treated patients had higher ACR20, 50 and 70 response rates at 6 months compared to placebo-treated patients. The results in study RA-II (619 patients) were similar to the results in RA-I at Week 24. The results in study RA-III (247 patients) were similar to those seen in study RA-IV. Over the one-year Study RA-I, 13% of CIMZIA-treated patients achieved a major clinical response, defined as achieving an ACR70 response over a continuous 6-month period, compared to 1% of placebo-treated patients.

Table 5: ACR Responses in Studies RA-I, and RA-IV (Percent of Patients)

Response	Study RA-I Methotrexate Combination (24 and 52 weeks)			Study RA-IV Monotherapy (24 weeks)		
	Placebo + MTX N=199	CIMZIA[a] 200 mg + MTX q 2 weeks N=393	CIMZIA[a] 200 mg + MTX - Placebo + MTX (95% CI)[d]	Placebo N=109	CIMZIA[b] 400 mg q 4 weeks N=111	CIMZIA[b] 400 mg - Placebo (95% CI)[d]
ACR20						
Week 24	14%	59%	45% (38%, 52%)	9%	46%	36% (25%, 47%)
Week 52	13%	53%	40% (33%, 47%)	N/A	N/A	
ACR50						
Week 24	8%	37%	30% (24%, 36%)	4%	23%	19% (10%, 28%)
Week 52	8%	38%	30% (24%, 37%)	N/A	N/A	
ACR70						
Week 24	3%	21%	18% (14%, 23%)	0%	6%	6% (1%, 10%)
Week 52	4%	21%	18% (13%, 22%)	N/A	N/A	

Major Clinical Response[(c)]	1%	13%	12% (8%, 15%)	

[(a)] CIMZIA administered every 2 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[(b)] CIMZIA administered every 4 weeks not preceded by a loading dose regimen
[(c)] Major clinical response is defined as achieving ACR70 response over a continuous 6-month period
[(d)] 95% Confidence Intervals constructed using the large sample approximation to the Normal Distribution.

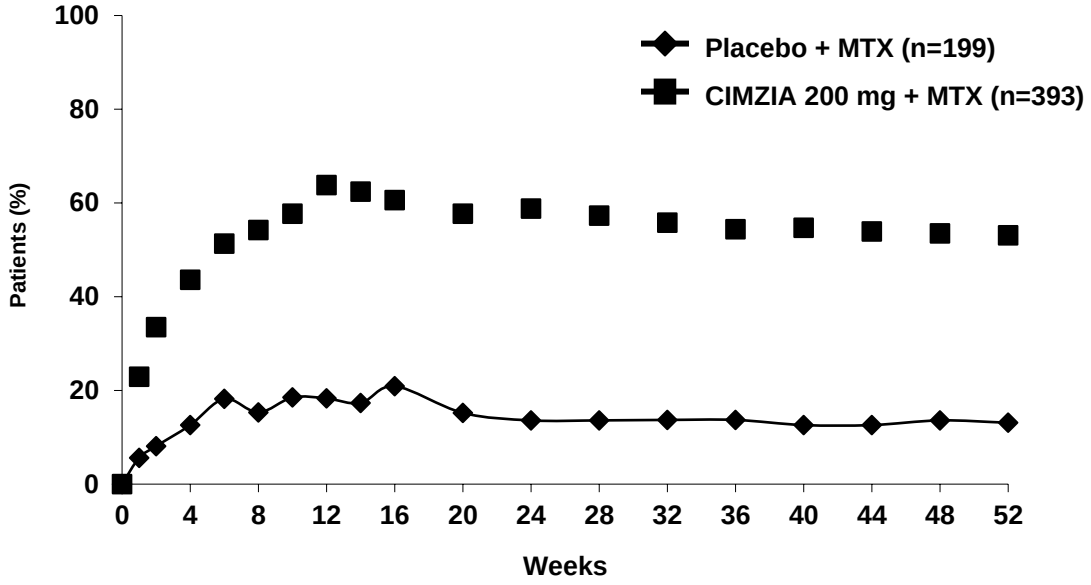
Table 6: Components of ACR Response in Studies RA-I and RA-IV

Parameter[+]	Study RA-I				Study RA-IV			
	Placebo + MTX N=199		CIMZIA[(a)] 200 mg + MTX q 2 weeks N=393		Placebo N=109		CIMZIA[(b)] 400 mg q 4 weeks Monotherapy N=111	
	Baseline	Week 24	Baseline	Week 24	Baseline	Week 24	Baseline	Week 24
Number of tender joints (0-68)	28	27	29	9	28 (12.5)	24 (15.4)	30 (13.7)	16 (15.8)
Number of swollen joints (0-66)	20	19	20	4	20 (9.3)	16 (12.5)	21 (10.1)	12 (11.2)
Physician global assessment[(c)]	66	56	65	25	4 (0.6)	3 (1.0)	4 (0.7)	3 (1.1)
Patient global assessment[(c)]	67	60	64	32	3 (0.8)	3 (1.0)	3 (0.8)	3 (1.0)
Pain[(c)(d)]	65	60	65	32	55 (20.8)	60 (26.7)	58 (21.9)	39 (29.6)
Disability index (HAQ)[(e)]	1.75	1.63	1.75	1.00	1.55 (0.65)	1.62 (0.68)	1.43 (0.63)	1.04 (0.74)
CRP (mg/L)	16.0	14.0	16.0	4.0	11.3	13.5	11.6	6.4

[(a)] CIMZIA administered every 2 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[(b)] CIMZIA administered every 4 weeks not preceded by a loading dose regimen
[(c)] Study RA-I - Visual Analog Scale: 0 = best, 100 = worst. Study RA-IV - Five Point Scale: 1 = best, 5 = worst
[(d)] Patient Assessment of Arthritis Pain**.** Visual Analog Scale: 0 = best, 100 = worst
[(e)] Health Assessment Questionnaire Disability Index; 0 = best, 3 = worst, measures the patient's ability to perform the following: dress/groom, arise, eat, walk, reach, grip, maintain hygiene, and maintain daily activity
All values are last observation carried forward.
[+]For Study RA-I, median is presented. For Study RA-IV, mean (SD) is presented except for CRP which presents geometric mean

The percent of patients achieving ACR20 responses by visit for Study RA-I is shown in Figure 1. Among patients receiving CIMZIA, clinical responses were seen in some patients within one to two weeks after initiation of therapy.

Figure 1 Study RA-I ACR20 Response Over 52 Weeks*



*The same patients may not have responded at each time point

Radiographic Response

In Study RA-I, 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 (JSN) score, at Week 52, compared to baseline. CIMZIA inhibited the progression of structural damage compared to placebo plus MTX after 12 months of treatment as shown in Table 7. In the placebo group, 52% of patients experienced no radiographic progression (mTSS $\leq$0.0) 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 7: Radiographic Changes at 6 and 12 months in Study RA-I

	Placebo + MTX N=199 Mean (SD)	CIMZIA 200 mg + MTX N=393 Mean (SD)	CIMZIA 200 mg + MTX – Placebo + MTX Mean Difference
mTSS			
Baseline	40 (45)	38 (49)	--
Week 24	1.3 (3.8)	0.2 (3.2)	-1.1
Week 52	2.8 (7.8)	0.4 (5.7)	-2.4
Erosion Score			
Baseline	14 (21)	15 (24)	--
Week 24	0.7 (2.1)	0.0 (1.5)	-0.7
Week 52	1.5 (4.3)	0.1 (2.5)	-1.4
JSN Score			
Baseline	25 (27)	24 (28)	--
Week 24	0.7 (2.4)	0.2 (2.5)	-0.5
Week 52	1.4 (5.0)	0.4 (4.2)	-1.0

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 Response

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 8. 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 (30%, 51%), 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 9.

Patients with enthesitis at baseline were evaluated for mean improvement in Leeds Enthesitis Index (LEI). CIMZIA-treated patients receiving either 200 mg every 2 weeks or 400 mg every 4 weeks showed a reduction in enthesitis of 1.8 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.

Table 8: ACR Responses in Study PsA001 (Percent of Patients)

Response[c]	**Placebo N=136**	**CIMZIA[a] 200 mg Q2W N=138**	**CIMZIA[b] 400 mg Q4W N=135**
ACR20			
Week 12	24%	58%	52%
Week 24	24%	64%	56%
ACR50			
Week 12	11%	36%	33%
Week 24	13%	44%	40%
ACR70			
Week 12	3%	25%	13%
Week 24	4%	28%	24%

[a] CIMZIA administered every 2 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[b] CIMZIA administered every 4 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[c] Results are from the randomized set. Non-responder Imputation (NRI) is used for patients who escaped therapy or had missing data.

Table 9: Components of ACR Response in Study PsA001

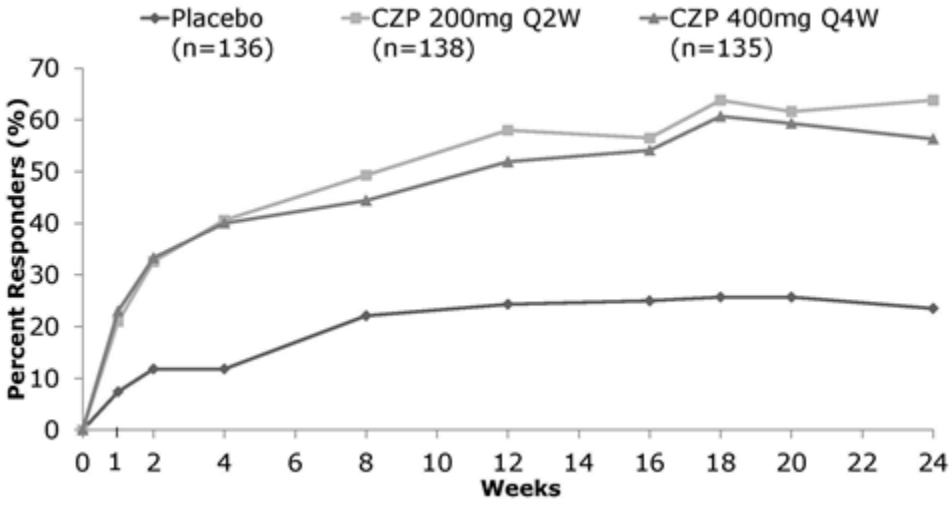
Parameter	**Placebo[c] N=136**		**CIMZIA[a] 200 mg Q2W N=138**		**CIMZIA[b] 400 mg Q4W N=135**	
	Baseline	**Week 12**	**Baseline**	**Week 12**	**Baseline**	**Week 12**
Number of tender joints (0-68)[d]	20	17	22	11	20	11
Number of swollen joints (0-66)[d]	10	9	11	4	11	5
Physician global assessment[d, e]	59	44	57	25	58	29
Patient global assessment[d, e]	57	50	60	33	60	40

Pain[(d, f)]	60	50	60	33	61	39
Disability index (HAQ)[(d, g)]	1.30	1.15	1.33	0.87	1.29	0.90
CRP (mg/L)	18.56	14.75	15.36	5.67	13.71	6.34

[(a)] CIMZIA administered every 2 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[(b)] CIMZIA administered every 4 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[(c)] Results are from the entire placebo group
[(d)] Last Observation Carried Forward is used for missing data, early withdrawals or placebo escape
[(e)] Patient and Physician Global Assessment of Disease Activity, VAS 0=best 100= worst
[(f)] The Patient Assessment of Arthritis Pain, VAS 0=no pain and 100= most severe pain
[(g)] The HAQ-DI, 4 point scale 0=without difficulty and 3=unable to do
All values presented represent the mean
Results are from the randomized set (either with imputation or observed case)

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

Figure 2: Study PsA001-ACR20 Response Over 24 Weeks*



Randomized Set. Non-responder imputation used for patients with missing data or those who escaped therapy.
*The same patients may not have responded at each time point.

Radiographic Response

In study PsA001, 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 measured by change from baseline in total modified mTSS Score (estimated mean score was 0.18 in the placebo group compared with -0.02 in the CIMZIA 200 mg group; 95% CI for the difference was (-0.38, -0.04)). Patients treated with CIMZIA

400 mg every four weeks did not demonstrate greater inhibition of radiographic progression compared with placebo-treated patients at Week 24.

Physical Function Response

In Study PsA001, 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 (-0.47, -0.22) and 0.46 in the CIMZIA 400 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 10). 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 11.

Table 10: ASAS Responses in AS patients at Weeks 12 and 24 in study AS-1

Parameters	Placebo N=57	CIMZIA[(a)] 200 mg every 2 weeks N=65	CIMZIA[(b)] 400 mg every 4 weeks N=56
ASAS20			
Week 12	37%	57%	64%
Week 24	33%	68%	70%
ASAS40			
Week 12	19%	40%	50%
Week 24	16%	48%	59%

[(a)]CIMZIA administered every 2 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[(b)] CIMZIA administered every 4 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
All percents reflect the proportion of patients who responded in the full analysis set

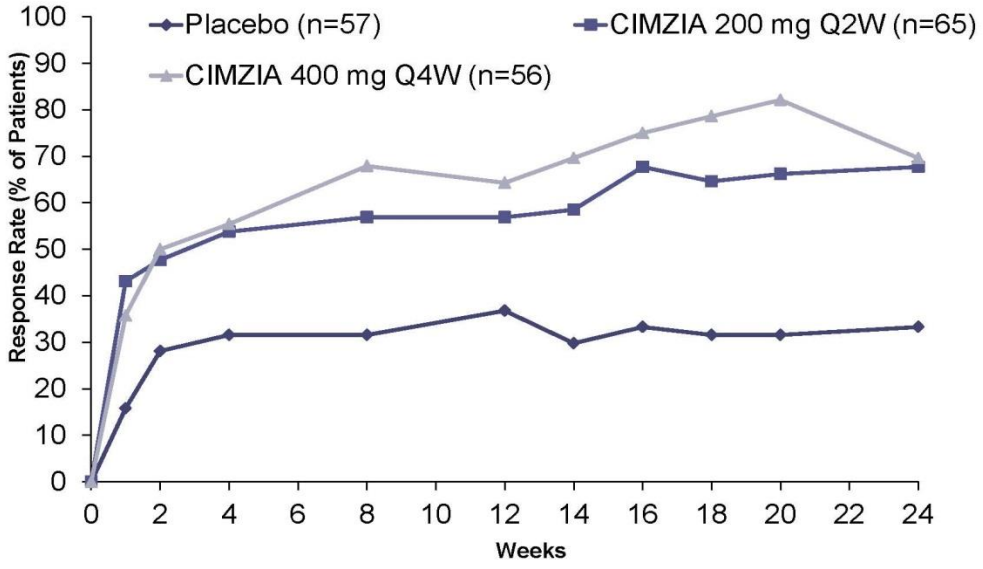
Table 11: Components of the ASAS response criteria and other measures of disease activity in AS patients at baseline and Week 12 in study AS-1

	Placebo N=57		CIMZIA[(a)] 200 mg every 2 weeks N=65		CIMZIA[(b)] 400 mg every 4 weeks N=56	
	Baseline	Week 12	Baseline	Week 12	Baseline	Week 12
ASAS20 response criteria						
-Patient Global Assessment (0-10)	6.9	5.6	7.3	4.2	6.8	3.8
-Total spinal pain (0-10)	7.3	5.8	7.0	4.3	6.9	4.0
-BASFI (0-10)[(c)]	6.0	5.2	5.6	3.8	5.7	3.8
-Inflammation (0-10)	6.7	5.5	6.7	3.8	6.4	3.4
BASDAI (0-10)[(d)]	6.4	5.4	6.5	4.0	6.2	3.7
BASMI [(e)]	4.8	4.4	4.2	3.6	4.3	3.9

[(a)]CIMZIA administered every 2 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[(b)]CIMZIA administered every 4 weeks preceded by a loading dose of 400 mg at Weeks 0, 2 and 4
[(c)]BASFI is Bath Ankylosing Spondylitis Functional Index
[(d)]BASDAI is Bath Ankylosing Spondylitis Disease Activity Index
[(e)]BASMI is Bath Ankylosing Spondylitis Metrology Index
All values presented represent the mean in the full analysis set

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.

Figure 3: Study AS-1: ASAS20 response over 24 weeks in AS patients *



*The same patients may not have responded at each time point.

14.5 Plaque Psoriasis

Three multicenter, randomized, double-blind studies (Study PS-1 [NCT02326298], Study PS-2 [NCT02326272], and Study PS-3 [NCT02346240]) enrolled subjects 18 years of age or older with moderate-to-severe plaque psoriasis who were eligible for systemic therapy or phototherapy. Subjects had a Physician Global Assessment (PGA) of ≥ 3 ("moderate") on a 5-category scale of overall disease severity, a Psoriasis Area and Severity Index (PASI) score ≥ 12, and body surface area (BSA) involvement of ≥ 10%.

Studies PS-1 (234 subjects) and PS-2 (227 subjects) randomized subjects to placebo, CIMZIA 200 mg every other week (following a loading dose of CIMZIA 400 mg at Weeks 0, 2, and 4), or CIMZIA 400 mg every other week. Studies PS-1 and PS-2 assessed the co-primary endpoints of the proportion of patients who achieved a PASI 75 and PGA of "clear" or "almost clear" with at least a 2-point improvement at Week 16. Other evaluated outcomes were PASI 90 at Week 16 and maintenance of efficacy to Week 48.

Study PS-3 randomized 559 subjects to receive placebo, CIMZIA 200 mg every other week (following a loading dose of CIMZIA 400 mg at Weeks 0, 2, and 4), CIMZIA 400 mg every other week up to Week 16, or a biologic comparator (up to Week 12). Study PS-3 assessed the proportion of patients who achieved a PASI 75 at Week 12 as the primary endpoint. Other evaluated outcomes were PGA of "clear" or "almost clear" at Week 16, PASI 75 at Week 16, PASI 90 at Week 16, and maintenance of efficacy to Week 48.

Of the 850 subjects randomized to receive placebo or CIMZIA in these placebo-controlled studies, 29% of patients were naïve to prior systemic therapy for the treatment of psoriasis, 47% had received prior phototherapy or chemophototherapy, and 30% had received prior biologic therapy for the treatment of psoriasis. Of the 850 subjects, 14% had received at least one TNF alpha agent and 16% had received an anti-IL agent. Eighteen percent of subjects reported a history of psoriatic arthritis at baseline.

Across all studies and treatment groups, the mean PASI score at baseline was 20 and ranged from 12 to 69. The baseline PGA score ranged from moderate (70%) to severe (30%). Mean baseline BSA was 25% and ranged from 10% to 96%. Subjects were predominantly men (64%) and White (94%), with a mean age of 46 years.

Clinical Response
Table 12 presents the efficacy results of PS-1, PS-2, and PS-3 at Week 16.

Table 12: Efficacy Results at Week 16 in Adults with Plaque Psoriasis in PS-1, PS-2, and PS-3 [MI[(a)]]

	Study PS-1			Study PS-2			Study PS-3[(e)]		
	Placebo (N=51)	CIMZIA 200mg[(c)] Q2W (N=95)	CIMZIA 400mg Q2W (N=88)	Placebo (N=49)	CIMZIA 200mg Q2W (N=91)	CIMZIA 400mg Q2W (N=87)	Placebo (N=57)	CIMZIA 200mg Q2W (N=165)	CIMZIA 400mg Q2W (N=167)
PGA of 0 or 1[(b, d)]	4%	45%	55%	3%	61%	65%	4%	52%	62%
PASI 75[(b)]	7%	65%	75%	13%	81%	82%	4%	69%	75%
PASI 90	0%	36%	44%	5%	50%	52%	0%	40%	49%

[(a)] Missing data was imputed using multiple imputation based on the MCMC method.
[(b)] The co-primary efficacy endpoints at Week 16 in PS-1 and PS-2.
[(c)] Subjects received 400 mg of CIMZIA at Weeks 0, 2, and 4, followed by 200 mg every other week.
[(d)] PGA score of 0 (clear) or 1 (almost clear).
[(e)] The primary endpoint in PS-3 was PASI 75 at Week 12.

Examination of age, gender, prior use of biologics, and prior use of systemic therapies did not identify difference in response to CIMZIA among these subgroups.

Based on a post-hoc subgroup analysis in subjects with moderate-to-severe psoriasis, stratified by ≤90 kg or >90 kg, subjects with both lower body weight and lower disease severity may achieve an acceptable response with CIMZIA 200 mg.

Maintenance of Response

In PS-1 and PS-2, among subjects who were PASI 75 responders at Week 16 and received CIMZIA 400 mg every other week, the PASI 75 response rates at Week 48 were 94% and 81%, respectively. In subjects who were PASI 75 responders at Week 16 and received CIMZIA 200 mg every other week, the PASI 75 response rates at Week 48 were 81% and 74%, respectively.

In PS-1 and PS-2, among subjects who were PGA clear or almost clear responders at Week 16 and received CIMZIA 400 mg every other week, the PGA response rates at Week 48 were 79% and 73%, respectively. In subjects who were PGA clear or almost clear responders at Week 16 and received CIMZIA 200 mg every other week, the PGA response rates at Week 48 were 79% and 76%, respectively.

In PS-3 study, subjects who achieved a PASI 75 response at Week 16 were re-randomized to either continue treatment with CIMZIA or be withdrawn from therapy (i.e., receive placebo). At Week 48, 98% of subjects who continued on CIMZIA 400 mg every other week were PASI 75 responders as compared to 36% of subjects who were re-randomized to placebo. Among PASI 75 responders at Week 16 who received CIMZIA 200 mg every other week and were re-randomized to either CIMZIA 200 mg every other week or placebo, there was also a higher percentage of PASI 75 responders at Week 48 in the CIMZIA group as compared to placebo (80% and 46%, respectively).

15 REFERENCES

1. Best WR, Becktel JM, Singleton JW, Kern F: Development of a Crohn's Disease Activity Index, National Cooperative Crohn's Disease Study. Gastroenterology 1976; 70(3): 439-444

16 HOW SUPPLIED/STORAGE AND HANDLING

Storage and Stability

Refrigerate carton between 2 to 8 °C (36 to 46 °F). Do not freeze. Do not separate contents of carton prior to use. Do not use beyond expiration date, which is located on the drug label and carton. Protect solution from light.

Lyophilized Powder for Reconstitution:

NDC 50474-700-62

CIMZIA (certolizumab pegol) for injection is supplied as a sterile white, lyophilized powder in a single-dose vial for subcutaneous use.

Pack Content

Qty.	Item
2	Type I glass vials with rubber stopper and overseals each containing 200 mg of lyophilized CIMZIA for reconstitution.
2	2 mL Type I glass vials containing 1 mL sterile Water for Injection
2	3 mL plastic syringes
4	20 gauge needles (1 inch)
2	23 gauge needles (1 inch)
8	Alcohol swabs

Prefilled Syringe

NDC 50474-710-79

CIMZIA (certolizumab pegol) injection is supplied as a sterile, clear to opalescent, colorless to pale yellow solution in a single-dose prefilled syringe for subcutaneous use.

2 alcohol swabs and 2 single use prefilled glass syringes with a fixed 25 ½ gauge thin-wall needle, each containing 200 mg (1 mL) of CIMZIA.

Prefilled Syringe Starter Kit

NDC 50474-710-81

6 alcohol swabs and 6 single dose prefilled glass syringes with a fixed 25 ½ gauge thin-wall needle. The Starter Kit contains 3 sets of 2 prefilled syringes to provide sufficient drug supply for the initial 3 induction doses at the start of treatment. Each prefilled syringe contains 200 mg (1 mL) of CIMZIA.

When necessary, CIMZIA prefilled syringes may be stored at room temperature up to 77^{O}F (25^{O}C) in the original carton to protect from light for a single period of up to 7 days. Once a CIMZIA prefilled syringe has been stored at room temperature, do not place back in refrigerator. Write the date removed from the refrigerator in the space provided on the carton and discard if not used within the 7-day period.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Medication Guide)

Patient Counseling

Advise patients of the potential risks and benefits of CIMZIA therapy. Be sure that patients receive the Medication Guide and allow them time to read it prior to starting CIMZIA therapy and to review it periodically. Any questions resulting from the patient's reading of the Medication Guide should be discussed. Because caution should be exercised in prescribing CIMZIA to patients with clinically important active infections, advise patients of the importance of informing their health care providers about all aspects of their health.

Immunosuppression

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

Counsel patients about the possible risk of lymphoma and other malignancies while receiving CIMZIA.

Allergic Reactions

Advise patients to seek immediate medical attention if they experience any symptoms of severe allergic reactions. The prefilled syringe components are not made with natural rubber latex.

Other Medical Conditions

Advise patients to report any signs of new or worsening medical conditions such as heart disease, neurological disease, or autoimmune disorders. Advise patients to report promptly any symptoms suggestive of a cytopenia such as bruising, bleeding, or persistent fever.

Pregnancy

Advise patients that there is a pregnancy registry that monitors pregnancy outcomes in women exposed to CIMZIA during pregnancy, patients can call 1-877-311-8972 *[see Use in Specific Populations 8.1]*.

Instruction on Prefilled Syringe Self-Injection Technique

After proper training by a qualified healthcare professional in subcutaneous injection technique, a patient may self-inject with CIMZIA using the Prefilled Syringe if a healthcare provider determines that it is appropriate. A patient's ability to administer CIMZIA subcutaneous injections should be checked to ensure correct administration. Suitable sites for injection include the thigh or abdomen. CIMZIA should be injected when the liquid is at room temperature.

Full injection instructions are provided in the Instructions for Use booklet for the Prefilled Syringe, packaged in each CIMZIA Prefilled Syringe kit.

To avoid needle-stick injury, patients and healthcare providers should not attempt to place the needle cover back on the syringe or otherwise recap the needle. Be sure to properly dispose of needles and syringes in a puncture-proof container, and instruct patients and caregivers in proper syringe and needle disposal technique. Actively discourage any reuse of the injection materials.

Manufactured by:
UCB, Inc.
1950 Lake Park Drive
Smyrna, GA 30080

US License No. 1736

Medication Guide

CIMZIA® (CIM-zee-uh)

(certolizumab pegol)

lyophilized powder or solution for subcutaneous use

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

CIMZIA may cause serious side effects, including:

- **CIMZIA is a prescription medicine called a Tumor Necrosis Factor (TNF) blocker** that can lower the ability of your immune system to fight infections. Some people who received CIMZIA have developed serious infections, including tuberculosis (TB) and infections caused by viruses, fungi, or bacteria that have spread throughout the body. Some of these serious infections have caused hospitalization and death.
  - 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.

  Before starting CIMZIA, tell your healthcare provider if you:
  - think you have an infection or have symptoms of an infection such as:
    - fever, sweat, or chills
    - cough
    - blood in phlegm
    - warm, red, or painful skin or sores on your body
    - burning when you urinate or urinate more often than normal
    - muscle aches
    - shortness of breath
    - weight loss
    - diarrhea or stomach pain
    - feeling very tired
  - are being treated for an infection
  - get a lot of infections or have infections that keep coming back
  - have diabetes, HIV-1 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, live, have lived, or traveled to certain countries where there is more risk for getting TB. Ask your healthcare provider if you are not sure.
  - live, have lived, or traveled to certain parts of the country (such as the Ohio and Mississippi River valleys and the Southwest) where there is an increased risk for getting certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis). These infections may develop or become more severe if you receive CIMZIA. Ask your healthcare provider if you do not know if you have lived in an area where these infections are common.
  - have or have had hepatitis B
  - use the medicine Kineret (anakinra), Orencia® (abatacept), Rituxan® (rituximab), or Tysabri® (natalizumab)

  Stop using CIMZIA, and tell your healthcare provider right away if have any of the symptoms of an infection listed above.
- **Cancer.**
  - For people who receive TNF blockers, including CIMZIA, the chances of getting certain types of cancers may increase.
  - Some children, teenagers, and young adults who received TNF blockers, including CIMZIA, have developed lymphoma and other certain types of rare cancers, some of which have caused death. These cancers are not usually seen in this age group. **CIMZIA is not for use in children.**
  - People with inflammatory diseases including rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis, especially those with very active disease, may be more likely to get lymphoma.
  - Some people who receive TNF blockers, including CIMZIA, have developed a rare type of cancer which may cause death, called hepatosplenic T-cell lymphoma. Most of these people were male teenagers and young adult males with Crohn's disease or ulcerative colitis. Also, most of these people had been treated with both a TNF blocker and another medicine called IMURAN® (azathioprine) or PURINETHOL® (6-mercaptopurine, 6-MP).
  - Some people who receive CIMZIA, have developed certain types of skin cancer. Tell your healthcare provider if you develop any changes in the appearance of your skin, including growths on your skin, during or after treatment with

CIMZIA. You should see your healthcare provider periodically during treatment for skin examinations, especially if you have a history of skin cancer.

What is CIMZIA?

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

- Lessen the signs and symptoms of moderately to severely active Crohn's disease (CD) in adults who have not been helped enough by usual treatments
- Treat moderately to severely active rheumatoid arthritis (RA)
- Treat active psoriatic arthritis (PsA)
- Treat active ankylosing spondylitis (AS)
- Treat moderate to severe plaque psoriasis (PsO) in adults who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet light alone or with pills)

It is not known if CIMZIA is safe and effective in children.

Before receiving CIMZIA, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection
- have or have had lymphoma or any other type of cancer
- have or had congestive heart failure
- have or have had seizures, any numbness or tingling, or a disease that affects your nervous system such as multiple sclerosis or Guillain-Barre syndrome.
- are scheduled to receive a vaccine. Do not receive a live vaccine while receiving CIMZIA.
- are allergic to certolizumab pegol or any of the ingredients in CIMZIA. See the end of this Medication Guide for a complete list of the ingredients in CIMZIA.
- are pregnant or plan to become pregnant. Tell your healthcare provider right away if you become pregnant during treatment with CIMZIA.

  Pregnancy Registry: If you become pregnant during treatment with CIMZIA, talk to 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. Talk to your healthcare provider about the best way to feed your baby during treatment with CIMZIA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

How will 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 (subcutaneous injection) in your stomach area (abdomen) 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 instructions on how to inject CIMZIA the right way.
- Read the detailed "Instructions for Use" for instructions about 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 prefilled syringe is given as an injection under the skin (subcutaneous injection) in your stomach area (abdomen) or upper thighs. 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. 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 CIMZIA prefilled syringe is clear and colorless to yellow and free from particles. **Do not use the CIMZIA prefilled syringe if the medicine is cloudy, discolored, or contains 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 people who carry the virus in their blood.** In some cases, people who received CIMZIA have died because of the hepatitis B virus being reactivated. Your healthcare provider should monitor you carefully before and during treatment with CIMZIA to see if you carry the hepatitis B virus in your blood. Tell your healthcare provider if you have any of the following symptoms:
  - feel unwell
  - tiredness (fatigue)
  - pain on the right side of your stomach (abdomen)
  - skin or eyes look yellow
  - poor appetite or vomiting
- **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
  - problems with your vision
  - numbness or tingling
  - 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 does not 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).

These are not all of the possible side effects of CIMZIA.

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.

Medicines 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. You can ask your pharmacist or healthcare provider for information about CIMZIA that is written for health professionals.

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.

Product manufactured by:
UCB, Inc.
1950 Lake Park Drive
Smyrna, GA 30080
US License No. 1736

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

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: May 2018