



Therapeutic Class ReviewSM

Biologic Response Modifiers – certolizumab pegol (Cimzia[®])

October 2008

New Product for Review:
certolizumab pegol (Cimzia[®])
[UCB Inc.]

Dossier Provided by Manufacturer: Yes

Dossier Evaluation: (3)

- 1 - Dossier missing significant clinical trial(s).
- 2 - Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3 - Mfg. provided all relevant trials and information.

Executive Summary

Disease Background

- **Crohn's disease** is a transmural inflammatory disorder which can involve any part of the gastrointestinal tract and which is characterized by chronicity, recurrences and numerous complications.
 - There is no cure for Crohn's disease, and treatment regimens are directed toward inducing remission, maintaining remission and addressing complications.
 - The Crohn's Disease Activity Index (CDAI) is a research tool used to quantify the symptoms of patients with Crohn's disease.
 - Remission of Crohn's disease is defined as a fall in the CDAI of less than 150. Severe disease was defined as a value of greater than 450. Most major research studies on medications in Crohn's disease define response as a fall of the CDAI of greater than 70 points and/or 100 points. There is no absolute upper end to this assessment tool.
- **Rheumatoid arthritis** is a chronic inflammatory disease that affects the lining of the joints and results in significant chronic pain, loss of function and disability. Medications called disease modifying anti-rheumatic drugs (DMARDs) have become the primary therapy for rheumatoid arthritis.
 - DMARDs reduce disease activity, slow the erosion of affected joints and may improve the patients quality of life.
 - The older DMARDs are generally administered orally and include such medications as methotrexate, cyclosporine, and leflunomide.

- The biological DMARDs include self-administered medications such as etanercept (Enbrel) and adalimumab (Humira), and the infused medications such as infliximab (Remicade), abatacept (Orencia), and rituximab (Rituxan).

Comparison of FDA-approved indications for biologic immunomodulators used for Crohn’s disease and/or rheumatoid arthritis.

Drug	Formulary Status	Moderate-to-Severe Crohn’s disease	Rheumatoid Arthritis
etanercept (Enbrel)	F		✓
adalimumab (Humira)	F	✓	✓
anakinra (Kineret)	NF		✓
certolizumab pegol (Cimzia)	NF	✓	submitted
infliximab (Remicade)	Med	✓	✓
abatacept (Orencia)	Med		✓
rituximab (Rituxan)	Med		✓
natalizumab (Tysabri)	Med	✓	

F=formulary, NF=non-formulary, Med=covered under medical benefit

- Certolizumab pegol (Cimzia) is a pegylated anti-TNF agent.
 - Pegylation allows for dosing intervals of every 4 weeks after initial dosing.
 - Certolizumab pegol (Cimzia) is administered by subcutaneous (SC) injection every 4 weeks (after a regimen of 400 mg SC initially and at weeks 2 and 4).
 - Current labeling suggests that certolizumab pegol (Cimzia) should be administered by a health-care professional, but UCB is submitting data for self-administration.
- Certolizumab pegol (Cimzia) was approved for the treatment of moderate-to-severe Crohn’s disease. Additionally, two pivotal RCTs in rheumatoid arthritis have been conducted, and the manufacturer has submitted an NDA for approval in this indication.

Evidence

- The evidence from eight randomized controlled trials evaluating the efficacy and safety of certolizumab pegol (Cimzia) in the treatment of patients with Crohn’s disease or rheumatoid arthritis is uncertain or not useful.
- There is no useful evidence that certolizumab pegol (Cimzia) is more effective in the treatment of patients with Crohn’s disease or rheumatoid arthritis than other formulary alternatives.
- There is no useful evidence that certolizumab pegol (Cimzia) is safer or better tolerated than other preferred/formulary biological response modifiers in the treatment of Crohn’s disease or rheumatoid arthritis.

- Considerations in Subpopulations:
 - **Pediatrics:** Safety and effectiveness of certolizumab pegol (Cimzia) in pediatric patients have not been established.
 - **Geriatrics:** Clinical studies of certolizumab pegol (Cimzia) did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger subjects.
 - **Race, ethnicity and/or Gender:** Current clinical experience with certolizumab pegol (Cimzia) has not identified differences in safety or efficacy based on race, ethnicity or gender.

Decision

Certolizumab pegol (Cimzia) is non-preferred/non-formulary because:

- There is no useful evidence for the efficacy and safety of certolizumab pegol (Cimzia).
- There is no useful comparative evidence evaluating certolizumab pegol (Cimzia) against other more established biological response modifiers.
- There are existing formulary alternatives with better evidence and longer clinical experience.

Products ^[1-8]

Available Drug Products

Drug Products	FDA approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^d
certolizumab pegol (Cimzia)	4/2008	N/A	<ul style="list-style-type: none"> • Crohn's Disease 	400 mg SC every 4 weeks (given as two-200 mg injections)	<ul style="list-style-type: none"> • Rheumatoid arthritis • Psoriatic arthritis • Ankylosing spondylitis • Plaque psoriasis
etanercept (Enbrel [®])	11/98	N/A	<ul style="list-style-type: none"> • Rheumatoid Arthritis • Juvenile Rheumatoid Arthritis • Psoriatic Arthritis • Ankylosing spondylitis 	50 mg SC every week	<ul style="list-style-type: none"> • Bone metastasis - Pain from metastases • Graft versus host disease • Hemophagocytic lymphohistiocytosis, Reactive • Hidradenitis suppurativa,

Drug Products	FDA approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^d
			<ul style="list-style-type: none"> Moderate-to-severe plaque psoriasis 	50 mg SC twice weekly x 3 months, then 50 mg weekly	Severe, refractory <ul style="list-style-type: none"> Langerhans cell histiocytosis Myelosclerosis with myeloid metaplasia Nephrotic syndrome Pemphigoid Sarcoidosis TNF receptor-associated periodic fever syndrome (TRAPS)
adalimumab (Humira)	12/02	N/A	<ul style="list-style-type: none"> Rheumatoid Arthritis Psoriatic Arthritis Ankylosing spondylitis 	40 mg SC every other week up to 40 mg SC every week	<ul style="list-style-type: none"> None listed
			<ul style="list-style-type: none"> Crohn's Disease 	160 mg SC week 0, 80 mg SC week 2, then 40 mg SC every other week	
			<ul style="list-style-type: none"> Moderate-to-severe plaque psoriasis 	80 mg SC on week 0, then 40 mg SC every other week	
infliximab (Remicade®)	08/98	N/A	<ul style="list-style-type: none"> Rheumatoid Arthritis 	3 mg/kg IV every 8 weeks up to 10 mg/kg every 4 weeks	<ul style="list-style-type: none"> Behçet's syndrome Gastrointestinal tract transplanted organ rejection Giant cell arteritis Graft versus host disease Hidradenitis suppurativa, Severe, refractory Inflammatory bowel disease Juvenile chronic arthritis Juvenile
			<ul style="list-style-type: none"> Ankylosing Spondylitis 	5 mg/kg IV every 6 weeks	
			<ul style="list-style-type: none"> Crohn's Disease Psoriatic Arthritis Plaque Psoriasis Ulcerative Colitis 	5 mg/kg IV every 8 weeks	

Drug Products	FDA approval ^a	Patent Expiration(s) ^c	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^d
					<ul style="list-style-type: none"> idiopathic arthritis • Necrobiosis lipoidica diabetorum • Pyoderma gangrenosum • SAPHO syndrome Refractory • Sarcoidosis • Sprue, Refractory • Subcorneal pustular dermatosis • Wegener's granulomatosis,
rituximab (Rituxan [®])	11/1997	N/A (biologic)	Rheumatoid arthritis (RA)	1000 mg via IV infusion at week 0 and 2 (two infusions total)	
anakinra (Kineret [®])	11/2001	N/A (biologic)	Rheumatoid arthritis (RA)	100 mg via SQ injection once daily	
abatacept (Orencia [®])	12/2005	N/A (biologic)	Rheumatoid arthritis (RA)	Given via IV infusion at week 0, 2, and 4, and then every 4 weeks, thereafter: < 60 kg: 500 mg 60 to 100 kg: 750 mg > 100 kg: 1 Gm	

^a Date applies to approval date for the original brand name medication where there are now generics available.

^c Based on patents listed in Orange Book as of 01/2008.

^d As listed in © 1974 - 2008 Thomson MICROMEDEX database or as referenced.

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