POLICY: Inflammatory Conditions – Cimzia® (certolizumab pegol for subcutaneous injection [lyophilized powder or solution] – UCB)

DATE REVIEWED: 04/22/2020

OVERVIEW

Cimzia, a tumor necrosis factor inhibitor (TNFi), is a recombinant humanized antibody Fab´ fragment (fragment antigen binding) that is a covalent conjugate to polyethylene glycol (PEG).[1] Pegylation delays the elimination of PEG polymers and the antibody, thus increasing the terminal elimination half-life of the Fab fragment. Unlike infliximab and adalimumab, Cimzia does not contain an Fc portion of the antibody.

Cimzia is indicated for the following uses:[1]

1. Crohn's disease, for reducing signs and symptoms and maintaining clinical responses in adults with moderate to severe active disease who have had an inadequate response to conventional therapy; AND
2. Rheumatoid arthritis (RA), for the treatment of adults with moderately to severely active disease; AND
3. Psoriatic arthritis (PsA), for the treatment of adult patients with active disease; AND
4. Ankylosing spondylitis, for the treatment of adults with active disease; AND
5. Plaque psoriasis, for the treatment of adults with moderately to severely active disease who are candidates for systemic therapy or phototherapy; AND
6. Non-radiographic axial spondyloarthritis (nr-axSpA), in patients with objective signs of inflammation.

Cimzia may be used as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs).

Disease Overview

TNF is a naturally occurring cytokine that mediates inflammation and modulates cellular immune responses. Increased levels of TNF have been implicated in the pathology of inflammatory conditions such as Crohn's disease, psoriatic arthritis, and rheumatoid arthritis (RA). Increased levels of TNF are found in the synovial fluid of patients with RA and TNF has an important role in both the pathologic inflammation and the joint destruction that are characteristic of this disease. In Crohn's disease, increased levels of TNF are found in the bowel wall in areas involved by Crohn's disease. Cimzia neutralizes the biological activity of TNFα and inhibits binding of TNFα with its receptors.

Dosing Information

Approved induction dosing is 400 mg given subcutaneously at Weeks 0, 2, and 4. For psoriasis, maintenance dosing is 400 mg given every 2 weeks. For other indications, maintenance dosing is generally given as 400 mg subcutaneously per 28 day period. This dose may be administered as a single 200-mg injection given once every 2 weeks or as two 200-mg doses (400-mg dose) given once every 4 weeks.

Guidelines

TNFis feature prominently in guidelines for treatment of inflammatory conditions.

- Spondyloarthritis: Guidelines for ankylosing spondylitis and nonradiographic axial spondylitis are published by the American College of Rheumatology (ACR)/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network (2019).[2] TNFis are recommended for the

initial biologic. In those who are secondary nonresponders to a TNFi, a second TNFi is recommended over switching out of the class.

- Crohn's Disease: The American College of Gastroenterology (ACG) has guidelines for Crohn's disease (2018).[3] TNFis are listed as an option for disease that is resistant to corticosteroids, severely active disease, perianal fistulizing disease, and maintenance of remission. In post-operative Crohn's disease, a TNFi should be started within 4 weeks of surgery to prevent recurrence.
- Plaque Psoriasis: Guidelines from the American Academy of Dermatologists (AAD) and National Psoriasis Foundation (NPF) recommend adalimumab as a monotherapy treatment option for adults with moderate to severe disease.[4]
- Psoriatic Arthritis: Guidelines from ACR (2019) recommend TNFis over other biologics for use in treatment-naïve patients with PsA and in those who were previously treated with an oral therapy.[5]
- Rheumatoid Arthritis: Guidelines from the American College of Rheumatology (ACR) [2015] have TNF inhibitors and non-TNF biologics, administered with or without MTX, equally positioned as a recommended therapy following a trial of a conventional synthetic DMARD (e.g., MTX, leflunomide, hydroxychloroquine, sulfasalazine).[6]

Safety

Cimzia has Boxed Warnings concerning risks of serious infection and the risk of malignancy.[1] Prior to initiating therapy with Cimzia, patients should be evaluated for active tuberculosis (TB) infection; in addition, patients should be assessed for latent TB infection periodically during therapy. Patients should also be monitored for signs and symptoms of infection during and after treatment with Cimzia; if a serious infection or sepsis develops, Cimzia should be discontinued. Lymphoma and other malignancies have been reported in patients who have taken TNFis such as Cimzia.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Cimzia. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with infliximab products as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Cimzia to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. **Ankylosing Spondylitis (AS).** Approve Cimzia for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if Cimzia is prescribed by or in consultation with a rheumatologist.
   - **B)** Patients Currently Receiving Cimzia. Approve for 1 year if the patient has had a response, as determined by the prescriber.

Note: Examples of a response include decreased pain or stiffness, improved function or activities of daily living. The patient may not have a full response, but there should have been a recent or past response to Cimzia.

Dosing. Approve the following regimens (A or B):
A) Initial Therapy. Approve up to 400 mg as a subcutaneous injection followed by additional similar doses at 2 and 4 weeks after the first injection, then up to a maximum dose of 400 mg per 28 days.
B) Patients Currently Receiving Cimzia. Do not exceed 400 mg per 28-day period.

---

2. Crohn's Disease. Approve Cimzia for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i, ii, and iii):
i. The patient is ≥ 18 years of age; AND
ii. The patient meets one of the following conditions (a or b):
a) The patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
b) The patient has tried one other systemic agent for Crohn's disease.
Note: Examples of systemic therapies for Crohn's disease include azathioprine, 6-mercaptopurine, and methotrexate (MTX). A previous trial of a biologic also counts as a trial of one other agent for Crohn's disease. Refer to Appendix for examples of biologics used for Crohn's disease. A trial of mesalamine does not count as a systemic agent for Crohn's disease; AND
iii. Cimzia is prescribed by or in consultation with a gastroenterologist.
B) Patients Currently Receiving Cimzia. Approve for 1 year if the patient has had a response, as determined by the prescriber.
Note: The patient may not have a full response, but there should have been a recent or past response to Cimzia. Patients with fistulizing Crohn's disease or Crohn's disease of the ileal pouch must meet the above criteria for Crohn's disease in adults.

Dosing. Approve the following regimens (A or B):
A) Initial Therapy. Approve up to 400 mg as a subcutaneous injection followed by additional similar doses at 2 and 4 weeks after the first injection, followed by 400 mg administered no more frequently than once every 4 weeks thereafter.
B) Patients Currently Receiving Cimzia. Do not exceed 400 mg per 28-day period.

---

3. Non-Radiographic Axial Spondyloarthritis (nr-axSpA). Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 3 months if the patient meets BOTH of the following (i and ii):
i. The patient has objective signs of inflammation, defined as at least one of the following (a or b):
a) C-reactive protein (CRP) elevated beyond the upper limit of normal for the reporting laboratory; OR
b) Sacroiliitis reported on magnetic resonance imaging (MRI); AND
ii. Cimzia is prescribed by or in consultation with a rheumatologist.
B) Patients Currently Receiving Cimzia. Approve for 1 year if the patient has had a response, as determined by the prescriber.

Note: Examples of a response include decreased pain or stiffness, improved function or activities of daily living. The patient may not have a full response, but there should have been a recent or past response to Cimzia.

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 400 mg as a subcutaneous injection followed by additional similar doses at 2 and 4 weeks after the first injection, then up to a maximum dose of 400 mg per 28 days.

B) Patients Currently Receiving Cimzia. Do not exceed 400 mg per 28-day period.

---

4. Plaque Psoriasis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i, ii, and iii):

i. The patient is ≥ 18 years of age; AND

ii. The patient meets ONE of the following conditions (a or b):

a) The patient has tried at least at least one traditional systemic agent for psoriasis for at least 3 months, unless intolerant.

Note: Examples of traditional systemic agents for psoriasis include methotrexate (MTX), cyclosporine, acitretin tablets, or psoralen plus ultraviolet A light (PUVA). An exception to the requirement for a trial of one traditional systemic agent for psoriasis can be made if the patient has already has a 3-month trial or previous intolerance to at least one biologic. Refer to Appendix for examples of biologics used for psoriasis. These patients who have already tried a biologic for psoriasis are not required to "step back" and try a traditional systemic agent for psoriasis; OR

b) The patient has a contraindication to methotrexate (MTX), as determined by the prescriber; AND

iii. Cimzia is prescribed by or in consultation with a dermatologist.

B) Patients Currently Receiving Cimzia. Approve for 1 year if the patient has had a response, as determined by the prescriber.

Note: The patient may not have a full response, but there should have been a recent or past response to Cimzia.

Dosing. Approve up to 400 mg as a subcutaneous injection administered subcutaneously no more frequently than once every 2 weeks.

---

5. Psoriatic Arthritis (PsA). Approve Cimzia for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if Cimzia is prescribed by or in consultation with a rheumatologist or a dermatologist.

B) Patients Currently Receiving Cimzia. Approve for 1 year if the patient has had a response, as determined by the prescriber.

Note: Examples of a response include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improvements in acute phase reactants (for example, CRP). The patient may not have a full response, but there should have been a recent or past response to Cimzia.

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 400 mg as a subcutaneous injection followed by additional similar doses at 2 and 4 weeks after the first injection, then up to a maximum dose of 400 mg per 28 days.
B) Patients Currently Receiving Cimzia. Do not exceed 400 mg per 28-day period.

---

6. Rheumatoid Arthritis (RA). Approve Cimzia for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):
- **i.** The patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months.
  Note: Examples of conventional synthetic DMARDs include methotrexate (oral or injectable), leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic. Refer to Appendix for examples of biologics used for RA. These patients who have already tried a biologic for RA are not required to "step back" and try a conventional synthetic DMARD; AND
- **ii.** Cimzia is prescribed by or in consultation with a rheumatologist.

B) Patients Currently Receiving Cimzia. Approve for 1 year if the patient has had a response, as determined by the prescriber.
Note: Examples of a response include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids. The patient may not have a full response, but there should have been a recent or past response to Cimzia.

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 400 mg as a subcutaneous injection followed by additional similar doses at 2 and 4 weeks after the first injection, followed by 200 mg administered no more frequently than once every 4 weeks thereafter.
B) Patients Currently Receiving Cimzia. Do not exceed 400 mg per 28-day period.

Other Uses with Supportive Evidence

---

7. Spondyloarthritis (SpA), Other Subtypes (e.g., undifferentiated arthritis, reactive arthritis [Reiter's disease]) [NOTE: For ankylosing spondylitis, psoriatic arthritis, or non-radiographic axial spondyloarthrits, refer to the respective criteria under FDA-approved indications]. Approve for the duration noted if the patient meets ONE of the following conditions (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following conditions (i, ii, and iii):
- **i.** The patient has arthritis primarily in the knees, ankles, elbows, wrists, hands, and/or feet; AND
- **ii.** The patient has tried at least ONE conventional synthetic disease-modifying antirheumatic drug (DMARD).
  Note: Examples include methotrexate (MTX), leflunomide, and sulfasalazine; AND
- **iii.** Cimzia is prescribed by or in consultation with a rheumatologist.

B) Patients Currently Receiving Cimzia. Approve for 1 year if the patient has had a response, as determined by the prescriber.
Note: Examples of a response include decreased pain or stiffness, improved function or activities of daily living. The patient may not have a full response, but there should have been a recent or past response to Cimzia.

Dosing. Approve the following regimens (A or B):

A) Initial Therapy. Approve up to 400 mg as a subcutaneous injection followed by additional similar doses at 2 and 4 weeks after the first injection, then up to a maximum dose of 400 mg per 28 days.

B) Patients Currently Receiving Cimzia. Do not exceed 400 mg per 28-day period.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Cimzia has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Concurrent Use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drug (DMARD).** Cimzia should not be administered in combination with another biologic or with a targeted synthetic DMARD used for an inflammatory condition (see Appendix for examples). Combination therapy is generally not recommended due to a potentially higher rate of AEs with combinations and lack of data supportive of additional efficacy.[7,8] Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Cimzia.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Cimzia® for injection [prescribing information]. Smyrna, GA: UCB, Inc.; September 2019.
2. Ward MM, Deodhar A, Gensler LS, et al. 2019 update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol*. 2019;71(10):1599-1613.
3. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: management of Crohn's Disease in adults. *Am J Gastroenterol.* 2018:113(4):481-517.
4. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019;80(4):1029-1072.
5. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Care Res (Hoboken).* 2019;71(1):2-29.
6. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.
7. Furst DE, Keystone EC, So AK, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2012. *Ann Rheum Dis*. 2013;72 Suppl 2:ii2-34.
8. Xeljanz® tablets [prescribing information]. New York, NY: Pfizer Inc; February 2016.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New Policy	--	04/22/2020

APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications for Products*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, PJIA, PsO, PsA, RA, SJIA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: PJIA, PSA, RA
		IV formulation: PJIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Ilaris (canakinumab SC injection**)**	Inhibition of IL-1β	SJIA
Kineret® (anakinra SC injection)	Inhibition of IL-1	RA, SJIA^
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx™ (secukinumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzza SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AS – Ankylosing spondylitis; CD – Crohn's disease; PJIA – Polyarticular juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; SJIA – Systemic juvenile idiopathic arthritis; UC – Ulcerative colitis; ^ Off-label use of SJIA supported in guidelines.