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Policy Number: 022.006

Title: Coverage Determination Policy for Cimzia (Certolizumab)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:

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Doctors helping patients for more than 25 years

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Coverage Policy Number: 022.006

Line of Business: Medicare Part B

Policy Type: Prior Authorization

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Coverage Determination:

The following criteria should be met in addition to any indication-specific criteria:

- Evidence of negative Tuberculosis (TB) screening test **OR** currently receiving treatment or completed treatment for TB
- Evidence of evaluation for Hepatitis B (HBV) infection prior to initiation of Cimzia and monitoring for HBV reactivation during treatment with Cimzia
- Patient does **NOT** have any other contraindications to Cimzia, including but not limited to: active infection, NYHA Class III or IV congestive heart failure, or demyelinating disease (e.g. multiple sclerosis, optic neuritis)
- **This policy refers to Cimzia (certolizumab pegol) powder for injection which should be administered by a healthcare provider. Cimzia (certolizumab pegol) as a prefilled syringe for injection is generally for self-administration and may be obtained under the pharmacy benefit.**

Initial/New Requests

1. Crohn's Disease (CD)

Cimzia will be approved based on **ALL** of the following criteria:

A. Diagnosis of moderately to severely active Crohn's disease

B. **ONE** of the following:

I. History of failure to ONE of the following conventional therapies at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced:
   a. Corticosteroids (e.g., prednisone, methylprednisolone, budesonide)
   b. 6-mercaptopurine (Purinethol)
   c. Azathioprine (Imuran)
   d. Methotrexate (Rheumatrex, Trexall)

II. Patient has been previously treated with a biologic DMARD FDA-approved for the treatment of Crohn's disease [e.g., Humira (adalimumab), Stelara (ustekinumb)

III. Patient is currently on Cimzia

C. Cimzia is initiated and titrated according to US FDA labeled dosing for CD

D. Patient is NOT receiving Cimzia in combination with EITHER of the following:

I. Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)]

II. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib)]

2. Rheumatoid Arthritis (RA)

Cimzia will be approved based on **ALL** of the following criteria:

A. Diagnosis of moderately to severely active rheumatoid arthritis

B. **ONE** of the following:

I. History of failure intolerance to a 3 month trial of ONE non-biologic disease modifying anti-rheumatic drug (DMARD) [e.g., methotrexate, leflunomide, sulfasalazine, hydroxychloroquine] at maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced

II. Patient has been previously treated with a biologic or targeted synthetic DMARD FDA-approved for the treatment of rheumatoid arthritis [e.g., Humira (adalimumab), Simponi (golimumab, Olumiant (baricitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib))

III. Patient is currently on Cimzia

C. Cimzia is initiated and titrated according to US FDA labeled dosing for RA

D. Patient is NOT receiving Cimzia in combination with EITHER of the following:

I. Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)]

II. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib)]

3. Psoriatic Arthritis (PsA)

Cimzia will be approved based on **ALL** of the following criteria:

A. Diagnosis of active psoriatic arthritis

B. **ONE** of the following:

I. History of failure to a 3 month trial of methotrexate at the maximally indicated dose, unless contraindicated or clinically significant adverse effects are experienced

II. Patient has been previously treated with a biologic or targeted synthetic DMARD FDA-approved for the treatment of psoriatic arthritis [e.g., Humira (adalimumab), Simponi (golimumab), Stelara (ustekinumab), Tremfya (guselkumab), Xeljanz (tofacitinib), Otezla (apremilast), Rinvoq (upadacitinib)]

III. Patient is currently on Cimzia

C. Cimzia is initiated and titrated according to US FDA labeled dosing for PsA

D. Patient is NOT receiving Cimzia in combination with EITHER of the following:

I. Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)]

II. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib)]

III. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

4. Ankylosing Spondylitis (AS) and Non-radiographic Axial spondyloarthritis (nr-axSpA)

Cimzia will be approved based on **ALL** of the following criteria:

A. Diagnosis of active ankylosing spondylitis or non-radiographic axial spondyloarthritis

B. **ONE** of the following:

I. History of failure to two NSAIDs (e.g., ibuprofen, naproxen) at the maximally indicated doses, each used for at least 4 weeks, unless contraindicated or clinically significant adverse effects are experienced

II. Patient has been previously treated with a biologic or targeted synthetic DMARD FDA-approved for the treatment of ankylosing spondylitis or nr-axSpA [e.g., Humira (adalimumab), Simponi (golimumab), Rinvoq (upadacitinib), Xeljanz/Xeljanz XR (tofacitinib)]

III. Patient is currently on Cimzia

C. Cimzia is initiated and titrated according to US FDA labeled dosing for AS or nr-axSpA

D. Patient is NOT receiving Cimzia in combination with EITHER of the following:

I. Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)]

II. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib)]

III. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

5. Plaque Psoriasis (PS)

Cimzia will be approved based on **ALL** of the following criteria:

A. Diagnosis of moderate to severe plaque psoriasis

B. **ONE** of the following:

I. **ALL** of the following:

a. Greater than or equal to 3% body surface area involvement, palmoplantar, facial, genital involvement, or severe scalp psoriasis

b. History of failure to one of the following topical therapies, unless contraindicated or clinically significant adverse effects are experienced:

i. Corticosteroids (e.g., betamethasone, clobetasol, desonide)

ii. Vitamin D analogs (e.g., calcitriol, calcipotriene)

iii. Tazarotene

iv. Calcineurin inhibitors (e.g., tacrolimus, pimecrolimus)

v. Anthralin

vi. Coal tar

c. History of failure to a 3 month trial of methotrexate at the maximally indicated dose, unless contraindicated or

clinically significant adverse effects are experienced

II. Patient has been previously treated with a biologic or targeted synthetic DMARD FDA-approved for the treatment of plaque psoriasis [e.g., Humira (adalimumab), Otezla (apremilast), Skyrizi (risankizumab-rzaa), Stelara (ustekinumab), Tremfya (guselkumab)]

III. Patient is currently on Cimzia

C. Cimzia is initiated and titrated according to US FDA labeled dosing for PS

D. Patient is NOT receiving Cimzia in combination with EITHER of the following:

IV. Biologic DMARD [e.g., Actemra (tocilizumab), Enbrel (etanercept), Rituxan (rituximab), Orencia (abatacept)]

V. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (baricitinib)]

VI. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]

Renewal/Continuation of Therapy Requests

Cimzia will be approved for continued used when **ALL** of the following criteria are met:

1. Documentation of positive clinical response to Cimzia therapy
2. The patient still meets indication specific criteria above with the exception of diagnosis of moderate-to-severe/active disease.
3. Cimzia is dosed according to US FDA labeled dosing for the specified indication

FDA Approved Dose and Indication

Indications	Approved Dosing
Ankylosing spondylitis **Non-radiographic axial spondyloarthritis** **Psoriatic arthritis** **Rheumatoid arthritis**	**Initial:** 400 mg subQ (as 2 injections of 200 mg) once and then repeat at weeks 2 and 4 Maintenance (if clinical response is achieved): 200 mg subQ every 2 weeks or 400 mg once every 4 weeks
Crohn's disease	**Initial:** 400 mg subQ (as 2 injections of 200 mg) once and then repeat at weeks 2 and 4 **Maintenance** *(if clinical response is achieved)*: 400 mg subQ once every 4 weeks
Plaque psoriasis	400 mg (given as 2 injections of 200 mg each) subQ every other week. In some patients with body weight 90 kg or less, following initial doses of 400 mg at weeks 0, 2, and 4, the maintenance dose may be reduced to 200 mg subQ every other week

General Background

Cimzia (certolizumab pegol) is a tumor necrosis factor (TNF) blocker which results in an interference in the production of downstream inflammatory mediators, including interleukin-1, prostaglandins, platelet activating factor, and nitric oxide. 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. Examples of conventional therapy include anti-inflammatory drugs, corticosteroids, and oral immunosuppressive agents. Cimzia is also indicated for the treatment of adults with moderately to severely active rheumatoid arthritis, active psoriatic arthritis, and active ankylosing spondylitis who have failed conventional therapy.

Warnings

Cimzia has FDA Black Box safety warnings for serious infections and malignancy. Patients being treated with Cimzia are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were on concomitant immunosuppressants, over 65 years old, or with comorbid conditions. Reported infections include active tuberculosis, invasive fungal infections, and infections due to opportunistic pathogens including Legionella and Listeria. The risks and benefits of treatment with Cimzia should be considered carefully before initiating treatment in patients with chronic or recurrent infections. Patients should be monitored closely for signs and symptoms of infection during and after treatment with Cimzia. Cases of lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers.

Clinical Evidence

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 CDAI of 220 to 450 points, inclusive. 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 4 weeks to week 24. Assessments were done at weeks 0 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. At week 6, the proportion of clinical responders was statistically significantly greater for Cimzia-treated patients compared to controls. 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.

**The CDAI is the sum of the following clinical or laboratory variables after multiplying by their weighting factor given in parentheses:*

- Number of liquid or soft stools each day for seven days (2)
- Abdominal pain graded from 0-3 in severity each day for seven days (5)
- General well-being, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days (7)
- Presence of complications where 1 point is added for each complication (20). Complications include:
    - o the presence of joint pains (arthralgia) or frank arthritis
    - o inflammation of the iris or uveitis
    - o presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers
    - o anal fissures, fistulae or abscesses
    - o other fistulae (e.g., enterocutaneous, vesicle, vaginal)
    - o fever (>37.8° C) during the previous week
- Taking diphenoxylate/atropine [Lomotil®] or opiates for diarrhea (30)
- Presence of an abdominal mass where 0 = none, 2 = questionable, 5 = definite (10);
- Absolute deviation of hematocrit from 47% in males and 42% in females (6)
- Percentage deviation from standard body weight (1)

Rheumatoid Arthritis

The efficacy and safety of Cimzia were assessed in four randomized, placebo-controlled, double blind studies in patients with moderately to severely active rheumatoid arthritis 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. Overall, the Cimzia treated patients achieved greater improvements from baseline than placebo-treated patients in physical function and they achieved a major clinical response, defined as achieving an ACR70 response over a continuous 6-month period, compared to 1% of placebo-treated patients.

The ACR20 is a composite measure defined as both improvement of 20% in the number of tender and number of swollen joints, and a 20% improvement in three of the following five criteria: patient global assessment, physician global assessment, functional ability measure [most often Health Assessment Questionnaire (HAQ)], visual analog pain scale, and erythrocyte sedimentation rate or C-reactive protein (CRP).[5] ACR50 and ACR70 are the same instruments with improvement levels defined as 50% and 70% respectively versus 20% for ACR20.

Psoriatic Arthritis

A multi-center, randomized, double-blind, placebo controlled trial (PsA001) assessed the efficacy and safety of Cimzia in adult patients with active psoriatic arthritis despite DMARD therapy. Patients in this study had at least 3 swollen tender joints and adult-onset PsA of at least 6 months' duration. Patients had failed one or more DMARDs. Patients received a loading dose of Cimzia 400mg at weeks 0, 2 and 4 or placebo followed by either Cimzia 200mg every other week or Cimzia 400mg 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. ACR20 response rates were higher in Cimzia treated patients relative to placebo. Therefore, treatment with Cimzia resulted in improvement in skin manifestations in patients with PsA.

Ankylosing Spondylitis

A multicenter, randomized, double=blind, placebo-controlled study (AS-1) assessed the efficacy and safety of Cimzia in adult patients with adult-onset active axial spondyloarthritis. 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 400mg at weeks 0, 2 and 4 or placebo followed by either 200mg of Cimzia every 2 weeks or 400mg of Cimzia every 4 weeks or placebo. The primary efficacy variable was the proportion of patients achieving an ASAS20 response at Week 12. The percent of AS patients achieving ASAS20 responses was greater than compared to AS patients treated with placebo.

Non-radiographic Axial Spondyloarthritis

In a multicenter, randomized, double-blind, placebo controlled study (nr-axSpA-1) the efficacy and safety of Cimzia was assessed in adult patients with adult-onset nr-axSpA. Patients must have had objective signs of inflammation indicated by C-reactive protein (CRP) levels above the upper limit of normal and/or sacroiliitis on magnetic resonance imaging (MRI), indicative of inflammatory disease [positive CRP (> ULN) and/or positive MRI], but without definitive radiographic evidence of structural damage on sacroiliac joints. 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 two NSAIDs. Patients were treated with a loading dose of Cimzia 400mg at weeks 0, 2 and 4 or placebo followed by 200mg of Cimzia every 2 weeks. The primary endpoint was the proportion of patients achieving an Ankylosing Spondylitis Disease Activity Score-Major Improvement (ASDAS-MI) response at Week 52. The ASDAS is a composite weighted scoring system that assesses disease activity, including patient-reported outcomes and CRP levels. A response in ASDAS-Major Improvement (MI) is indicated by a change from baseline of ≥2.0 in the ASDAS and/or reaching the lowest possible ASDAS value. In study nr-axSpA-1, at week

52, a greater proportion of nr-axSpA patients treated with Cimzia had ASDAS-MI response compared to patients treated with placebo. At both weeks 12 and 52, ASAS40 responses were greater for patients treated with Cimzia compared to patients treated with placebo. In study AS-1, at week 12, patients with nr-axSpA treated with Cimzia 200 mg every 2 weeks and Cimzia 400 mg every 4 weeks had an ASAS 20 response of 42% and 47%, respectively, compared to 20% of patients treated with placebo. The ASAS 40 response in patients treated with Cimzia 200 mg every 2 weeks and 400 mg every 4 weeks was 30% and 37%, respectively, compared to 11% of patients treated with placebo at week 12.

Plaque Psoriasis

Three multicenter, randomized, double-blind studies (PS1, PS2 and PS3) enrolled adults 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%. Patients were randomized to placebo, Cimzia 200mg every other week (following a loading dose of Cimzia 400mg at weeks 0, 2, and 4) or Cimzia 400mg every other week. Studies PS1 and PS2 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. Study PS3 assessed the proportion of patients who achieved a PASI 75 at week 12 as the primary endpoint. Across all studies and treatment groups, the percentage of PSAI 75 responders at week 16 was higher than compared to placebo. In PS1 and PS2, among subjects who were PGA clear or almost clear responders at week 16 and receiving Cimzia 400mg every other week, the PGA response rates were 55% and 65%, respectively.

HCPCS Code

HCPCS Code	Description
J0717	Cimzia (Certolizumab)

Dosage Form, Strength, and Route of Administration
200 mg lyophilized powder in a single-dose vial, administered Sub Q
200 mg/mL solution in a single-dose prefilled syringe, administered Sub Q

Acronyms

TNF = Tumor Necrosis Factor

TB = Tuberculosis

HBV = Hepatitis B

CD =Crohn's Disease

RA = Rheumatoid arthritis

SpA = Ankylosing spondylitis

PS = Plaque psoriasis

nr-axSpA = Non-Radiographic Axial Spondyloarthritis

BASDAI = Bath Ankylosing Spondylitis Disease Activity Index

FDA = Food and Drug Administration

DAS = Disease Activity Score

CDAI = Crohn's Disease Activity Index

DMARDs = Disease-Modifying Antirheumatic Drugs

MTX = Methotrexate

ASAS = Assessment in Ankylosing Spondylitis

PsA = Psoriatic Arthritis

HCQ = hydroxychloroquine

References

1. Cimzia [prescribing information]. Smyrna, GA: UCB, Inc; December 2022
2. Lichtenstein GR, Abreu MT, Cohen R, Tremaine W. American Gastroenterological Association Institute medical position statement on corticosteroids, immunomodulators, and infliximab in inflammatory bowel disease. Gastroenterology 2006 Mar;130(3):935-9.
3. 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.
4. Certolizumab: IBM Micromedex® DRUGDEX® (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/. Accessed July 07, 2023.
5. Siegel JN, Zhen BG. (2005), Use of the American College of Rheumatology N (ACR-N) index of improvement in rheumatoid arthritis: Argument in favor. Arthritis & Rheumatism, 52: 1637-1641.