certolizumab pegol (Cimzia®)

Policy # 00200
Original Effective Date: 06/18/2008
Current Effective Date: 04/10/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Crohn's Disease

Based on review of available data, the Company may consider certolizumab pegol (Cimzia®)‡ for the treatment of Crohn's disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of certolizumab pegol (Cimzia) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has moderately to severely active Crohn's disease; AND
- Patient has failed treatment with conventional therapies such as corticosteroids, 6-mercaptopurine (6 MP) and azathioprine unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient; AND
- The requested drug is NOT used in combination with other biologic disease-modifying anti-rheumatic drugs (DMARDs), such as adalimumab (Humira®)‡ or etanercept (Enbrel®)‡ OR other drugs such as apremilast (Otezla®)‡ or tofacitinib (Xeljanz®/XR)‡; AND
- Patient has a negative TB (tuberculosis) test (e.g., purified protein derivative [PPD], blood test) prior to treatment; AND
- For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with adalimumab (Humira) after at least TWO months of therapy (unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient).

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*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary ** if not met.)*

Rheumatoid Arthritis

Based on review of available data, the Company may consider certolizumab pegol (Cimzia) for the treatment of rheumatoid arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of certolizumab pegol (Cimzia) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has moderately to severely active rheumatoid arthritis; AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Cimzia is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira) or etanercept (Enbrel) OR other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Humira), tofacitinib (Xeljanz/XR), upadacitinib (Rinvoq™)‡, or subcutaneous tocilizumab (Actemra®)‡ unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

Psoriatic Arthritis

Based on review of available data, the Company may consider the use of certolizumab pegol (Cimzia) for the treatment of psoriatic arthritis to be **eligible for coverage.****

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Current Effective Date: 04/10/2023

Patient Selection Criteria
Coverage eligibility for the use of certolizumab pegol (Cimzia) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has active psoriatic arthritis; AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Cimzia is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira) or etanercept (Enbrel) OR other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Humira), ustekinumab (Stelara®)‡, secukinumab (Cosentyx®‡), tofacitinib (Xeljanz/XR), guselkumab (Tremfya®)‡, apremilast (Otezla), upadacitinib (Rinvoq), or risankizumab-rzaa (Skyrizi®)‡ unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

Ankylosing Spondylitis
Based on review of available data, the Company may consider the use of certolizumab pegol (Cimzia) for the treatment of active ankylosing spondylitis to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for the use of certolizumab pegol (Cimzia) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has active ankylosing spondylitis; AND

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Policy # 00200
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Current Effective Date: 04/10/2023

- Patient has failed treatment with non-steroidal anti-inflammatory drugs (NSAIDs) unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Cimzia is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira) or etanercept (Enbrel) OR other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Humira), secukinumab (Cosentyx), tofacitinib (Xeljanz/XR), or upadacitinib (Rinvoq) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

Plaque Psoriasis

Based on review of available data, the Company may consider the use of certolizumab pegol (Cimzia) for the treatment of moderate to severe plaque psoriasis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of certolizumab pegol (Cimzia) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has moderate to severe plaque psoriasis; AND
- Patient is a candidate for phototherapy or systemic therapy; AND
- Cimzia is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira) or etanercept (Enbrel) OR other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND

certolizumab pegol (Cimzia®)

Policy # 00200
Original Effective Date: 06/18/2008
Current Effective Date: 04/10/2023

- Patient has greater than 10% of body surface area or less than or equal to 10% body surface area with plaque psoriasis involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck or genitalia); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has failed to respond to an adequate trial of one of the following treatment modalities unless there is clinical evidence or patient history that suggests these will be ineffective or cause an adverse reaction to the patient:
  - Ultraviolet B; OR
  - Psoralen positive Ultraviolet A; OR
  - Systemic therapy (e.g., methotrexate, cyclosporine, acitretin); AND

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: adalimumab (Humira), etanercept (Enbrel), apremilast (Otezla), ustekinumab (Stelara), secukinumab (Cosentyx), guselkumab (Tremfya), or risankizumab (Skyrizi) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient: AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- For maintenance dose requests (both formulations) of 400 mg every other week for patients ≤ 90 kilograms: Patient must have tried and failed (e.g., intolerance, inadequate response) the 200 mg every other week dosage regimen after at least 2 months of therapy.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

Non-Radiographic Axial Spondyloarthritis

Based on review of available data, the Company may consider the use of certolizumab pegol (Cimzia) for the treatment of non-radiographic axial spondyloarthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of certolizumab pegol (Cimzia) will be considered when all of the following criteria are met:

- Patient has active non-radiographic axial spondyloarthritis as confirmed by the presence of sacroiliitis on magnetic resonance imaging (MRI); AND
- Patient has failed at least TWO months of current continuous therapy with at least TWO different oral NSAIDs (at prescription strength dosages) unless there is clinical evidence or patient history that suggests these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient is 18 years of age or older; AND
- Cimzia is NOT used in combination with other biologic DMARDs, such as adalimumab (Humira) or etanercept (Enbrel) OR other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of certolizumab pegol (Cimzia) when any of the following criteria for their respective disease state listed below (and denoted in the patient selection criteria above) are not met to be **not medically necessary**:**

- For Crohn's disease:
  - For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with adalimumab (Humira) after at least TWO months of therapy.
- For rheumatoid arthritis:
  - Patient has failed treatment with one or more traditional DMARDs
  - For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Humira), tofacitinib (Xeljanz/XR), upadacitinib (Rinvoq), or subcutaneous tocilizumab (Actemra).
- For psoriatic arthritis:
  - Patient has failed treatment with one or more traditional DMARDs
  - For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Humira), ustekinumab (Stelara),

secukinumab (Cosentyx), tofacitinib (Xeljanz/XR), guselkumab (Tremfya), apremilast (Otezla), upadacitinib (Rinvoq), or risankizumab-rzaa (Skyrizi).

- For active ankylosing spondylitis:
  - Patient has failed treatment with NSAIDs
  - For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Humira), secukinumab (Cosentyx), tofacitinib (Xeljanz/XR), or upadacitinib (Rinvoq).
- For moderate to severe plaque psoriasis:
  - Patient has greater than 10% of body surface area or less than or equal to 10% body surface area with plaque psoriasis involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck or genitalia)
  - Patient has failed to respond to an adequate trial of one of the following treatment modalities:
    - Ultraviolet B; OR
    - Psoralen positive Ultraviolet A; OR
    - Systemic therapy (i.e. methotrexate, cyclosporine, acitretin); AND
  - For NON-lyophilized (prefilled syringe) requests ONLY: Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: adalimumab (Humira), etanercept (Enbrel), apremilast (Otezla), ustekinumab (Stelara), secukinumab (Cosentyx), guselkumab (Tremfya), or risankizumab (Skyrizi)
  - For maintenance dose requests (both formulations) of 400 mg every other week for patients ≤ 90 kilograms: Patient must have tried and failed (e.g. intolerance, inadequate response) the 200 mg every other week dosage regimen after at least 2 months of therapy.
- For active non-radiographic axial spondyloarthritis:
  - Patient has failed at least TWO months of current continuous therapy with at least TWO different oral NSAIDs (at prescription strength dosages).

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of certolizumab pegol (Cimzia) when patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as **not medically necessary**).**

Based on review of available data, the Company considers the use of certolizumab pegol (Cimzia) for indications or dosages (EXCEPT the plaque psoriasis dosage requirement noted as **not medically necessary**)** other than those listed above to be **investigational.***

Background/Overview

Cimzia is a tumor necrosis factor (TNF) blocker 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. Cimzia also carries indications for the treatment of adults with moderately to severely active rheumatoid arthritis, treatment of adults with psoriatic arthritis, treatment of adults with ankylosing spondylitis, treatment of adults with moderate to severe plaque psoriasis, and treatment of adults with active non-radiographic axial spondyloarthritis. Cimzia is supplied as a sterile, white, lyophilized powder for reconstitution in a single use vial for subcutaneous injection. Cimzia is also available in a 200 mg/mL solution in a single-use prefilled syringe. Cimzia lyophilized powder should be prepared and administered by a health care professional.

For Crohn's disease, the recommended adult dose of Cimzia is 400 mg initially, and at weeks 2 and 4. In patients who obtain a clinical response, the recommended maintenance regimen is 400 mg every four weeks. The recommended dose of Cimzia for adult patients with rheumatoid arthritis is 400 mg initially and at weeks 2 and 4, followed by 200 mg every other week. For maintenance dosing, Cimzia 400 mg every 4 weeks can be considered. The recommended dose of Cimzia for adult patients with psoriatic arthritis is 400 mg initially and at week 2 and 4, followed by 200 mg every other week. For maintenance dosing, Cimzia 400 mg every 4 weeks can be considered. The recommended dose of Cimzia for adult patients with ankylosing spondylitis is 400 mg initially and at weeks 2 and 4, followed by 200 mg every 2 weeks or 400 mg every 4 weeks. For plaque psoriasis

in adults, the dose is 400 mg every other week. For some patients (with body weight ≤ 90 kg), a dose of 400 mg initially and at weeks 2 and 4, followed by 200 mg every other week may be considered. The recommended dose of Cimzia for adult patients with active non-radiographic axial spondyloarthritis is 400 mg initially and at weeks 2 and 4, followed by 200 mg every 2 weeks or 400 mg every 4 weeks.

Crohn's Disease
Crohn's disease is a chronic autoimmune disease that can affect any part of the gastrointestinal tract but most commonly occurs in the ileum. As a result of the immune attack, the intestinal wall becomes thick, and deep ulcers may form. In addition to the bowel abnormalities, Crohn's disease can also affect other organs in the body. Typically, first line treatments such as corticosteroids, 6-mercaptopurine, and azathioprine are used to treat this condition prior to using biologic products.

Rheumatoid Arthritis
Rheumatoid arthritis is a chronic (long-term) disease that causes inflammation of the joints and surrounding tissues. It can also affect other organs. It is considered an autoimmune disease. In an autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Psoriatic Arthritis
Psoriatic arthritis is an arthritis that is often associated with psoriasis of the skin. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Ankylosing Spondylitis
Ankylosing spondylitis is a chronic inflammatory disease that affects the joints between the vertebrae of the spine, and the joints between the spine and the pelvis. It eventually causes the affected vertebrae to fuse or grow together. NSAIDs, such as aspirin, are used to reduce inflammation and pain associated with the condition. Corticosteroid therapy or medications to suppress the immune system may be prescribed to control various symptoms.

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Plaque Psoriasis
Psoriasis is a common skin condition that is caused by an increase in production of skin cells. It is characterized by frequent episodes of redness, itching and thick, dry silvery scales on the skin. It is most commonly seen on the trunk, elbows, knees, scalp, skin folds and fingernails. This condition can appear suddenly or gradually and may affect people of any age; it most commonly begins between the ages of 15 and 35. Psoriasis is not contagious. It is an inherited disorder related to an inflammatory response in which the immune system produces too much TNF-alpha. It may be severe in immunosuppressed people or those who have other autoimmune disorders such as rheumatoid arthritis. Typical treatments for severe cases of plaque psoriasis include ultraviolet therapy or systemic therapies such as methotrexate or cyclosporine. Newer biologic therapies are also approved for the treatment of plaque psoriasis.

Traditional Disease-Modifying Anti-Rheumatic Drugs
Traditional disease-modifying anti-rheumatic drugs are used for the treatment of conditions such as rheumatoid arthritis, psoriatic arthritis and plaque psoriasis. These drugs slow the disease process by modifying the immune system.

- methotrexate
- cyclosporine
- sulfasalazine
- mercaptopurine
- gold compounds

Non-Radiographic Axial Spondyloarthritis.
Axial spondyloarthritis is an inflammatory arthritis of the spine. It often presents as chronic back pain, typically before the age of 45 and is often associated with one or more articular features (e.g., synovitis, enthesitis, and dactylitis) and/or non-articular features (e.g., uveitis, psoriasis, and inflammatory bowel diseases). Patients with this condition are classified as having one of two types of axial spondyloarthritis: either radiographic or non-radiographic. As supported by the name, the non-radiographic variety isn't evident on plain radiography and instead the diagnosis is supported by evidence of active inflammation of the sacroiliac joints via magnetic resonance imaging (MRI). Traditional pharmacologic therapy for the treatment of non-radiographic axial spondyloarthritis includes oral NSAIDs. Approximately 70-80% of patients with this condition report substantial relief with NSAID therapy. The effect of an NSAID is typically seen within two to four weeks and multiple

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NSAIDs need to be tried as patient response to a particular NSAID isn't predictable. Currently Cimzia is the only TNF inhibitor product that is approved for non-radiographic axial spondyloarthritis. Most recently, Taltz®‡ and Cosentyx, both interleukin blockers, have gained approval for this indication. If a response to two NSAIDs has not proven beneficial, a tumor necrosis factor (TNF) alpha inhibitor, such as Cimzia, or an interleukin blocker, such as Taltz or Cosentyx, would be the next treatment option.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In April of 2008, The FDA granted approval to Cimzia to treat adults with moderate to severe Crohn's disease who have not responded to conventional therapies. In May 2009, Cimzia was granted approval for the treatment of adults with moderately to severely active rheumatoid arthritis. In September and October 2013, Cimzia was given approval to treat adults with psoriatic arthritis and ankylosing spondylitis, respectively. In June of 2018, Cimzia gained an indication for the treatment of adults with moderate to severe plaque psoriasis. In April of 2019, Cimzia gained an indication for the treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Crohn's Disease

The efficacy and safety of Cimzia were assessed in two double-blind, randomized, placebo-controlled studies (CD1 and CD2) in patients aged 18 years and older with moderately to severely active Crohn's disease, as defined by a Crohn's Disease Activity Index (CDAI1) of 220 to 450 points. Cimzia was administered subcutaneously at a dose of 400 mg in both studies. Stable concomitant medications for Crohn's disease were permitted.

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. 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.

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 intention to treat analysis. 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.

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. Cimzia was administered subcutaneously in combination with methotrexate 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 methotrexate for at least 6 months prior to study medication but had an incomplete response to methotrexate 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 methotrexate 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 methotrexate 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 rheumatoid arthritis 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 rheumatoid arthritis using the ACR20 at week 24.

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. Among patients receiving Cimzia, clinical responses were seen in some patients within one to two weeks after initiation of therapy.

In Study RA-I, inhibition of progression of structural damage was assessed radiographically and expressed as the change in mTSS and its components, the Erosion Score (ES) and Joint Space Narrowing (JSN) score, at week 52, compared to baseline. 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. 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).

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 $\geq$ 3 swollen and tender joints and adult-onset psoriatic arthritis 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 mTSS at week 24.

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 400mg minus placebo at weeks 12 and 24 of (17%, 39%) and (22%, 44%), respectively]. 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 psoriatic arthritis. However, the safety and efficacy of Cimzia in the treatment of patients with plaque psoriasis has not been established. 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. In Study PsA001, Cimzia-treated patients showed improvement in physical function as assessed by the 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)].

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 ankylosing spondylitis. Patients had active disease as defined by the Bath Ankylosing Spondylitis Disease

Activity Index (BASDAI). 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 ankylosing spondylitis patients. The primary efficacy variable was the proportion of patients achieving an Assessment in Ankylosing Spondylitis-20 (ASAS20) response at week 12. In study AS-1, at week 12, a greater proportion of ankylosing spondylitis patients treated with Cimzia 200 mg every 2 weeks or 400 mg every 4 weeks achieved ASAS 20 response compared to ankylosing spondylitis patients treated with placebo. Responses were similar in patients receiving Cimzia 200 mg every 2 weeks and Cimzia 400 mg every 4 weeks.

Plaque Psoriasis
Three multicenter, randomized, double-blind studies (Study PS-1, Study PS-2, and Study PS-3) enrolled subjects 18 years of age or older with moderate-to-severe plaque psoriasis who were eligible for systemic therapy or phototherapy. 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 Psoriasis Area and Severity Index-75 (PASI 75) and Physician Global Assessment (PGA) of "clear" or "almost clear" with at least a 2-point improvement at week 16. 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. In PS-1, the PASI 75 at week 16 was 7% in the placebo group, 65% in the Cimzia 200 mg every 2 week group, and 75% in the Cimzia 400 mg every 2 weeks group. In PS-2, the PASI 75 at week 16 was 13% in the placebo group, 81% in the Cimzia 200 mg every 2 week group, and 82% in the Cimzia 400 mg every 2 weeks group. In PS-3, the PASI 75 at week 16 was 4% in the placebo group, 69% in the Cimzia 200 mg every 2 week group, and 75% in the Cimzia 400 mg every 2 weeks group.

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-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).

Non-Radiographic Axial Spondyloarthritis.
The efficacy and safety of Cimzia were assessed in a multicenter, randomized, double-blind, placebo controlled study (nr-axSpA-1) in 317 subjects ≥18 years of age with adult-onset active axial spondyloarthritis (nr-axSpA) for at least 12 months. 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 400 mg at weeks 0, 2 and 4 or placebo followed by 200 mg of Cimzia every 2 weeks or placebo. 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 c-reactive protein (CRP) levels. A response in ASDAS-MI is indicated by a change from baseline of ≥2.0 in the ASDAS and/or reaching the lowest possible ASDAS value. At week 52, a greater proportion of nr-axSpA patients treated with Cimzia had ASDAS-MI response as compared to patients treated with placebo (47% vs. 7%). At both weeks 12 and 52, ASAS-40 (40% response) responses were greater for patients treated with Cimzia compared to patients treated with placebo (48% vs. 11% and 57% vs. 16%, respectively).

References

1. Cimzia [package insert]. UCB, Inc. Smyrna, Georgia. Updated December 2022.
2. Song IG, Pddunbnyy DA, Redwaleit M, et al. Benefits and risks of ankylosing spondylitis treatment with non-steroidal anti-inflammatory drugs. Arthritis Rheum. 2008;58(4):929.
3. Treatment of axial spondyloarthritis (ankylosing spondylitis and nonradiographic axial spondyloarthritis in adults. UpToDate. Updated through May 2019.
4. Diagnosis and differential diagnosis of axial spondyloarthritis (ankylosing spondylitis and nonradiographic axial spondyloarthritis) in adults. UpToDate. Updated through May 2019.

certolizumab pegol (Cimzia®)

Policy # 00200
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Policy History

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06/04/2008	Medical Director review
06/18/2008	Medical Policy Committee approval. New FDA approved drug for Crohn's disease. New policy.
06/04/2009	Medical Director review
06/17/2009	Medical Policy Committee approval. FDA prescribing information added to policy criteria.
07/01/2010	Medical Policy Committee approval
07/21/2010	Medical Policy Implementation Committee approval. Negative cancer screening changed to negative cancer history in the coverage section Note. No change to coverage.
11/03/2011	Medical Policy Committee approval
11/16/2011	Medical Policy Implementation Committee approval. Added an additional company requirement to the patient selection criteria. Added a Not Medically Necessary section to the policy.
11/01/2012	Medical Policy Committee approval
11/28/2012	Medical Policy Implementation Committee approval. No change to coverage eligibility.
10/10/2013	Medical Policy Committee approval
10/16/2013	Medical Policy Implementation Committee approval. Added the new indication for psoriatic arthritis. Changed to requirement to try both Humira AND Enbrel prior to Cimzia for Rheumatoid Arthritis and Psoriatic Arthritis. Modified the not medically necessary section to reflect changes.
03/06/2014	Medical Policy Committee approval
03/19/2014	Medical Policy Implementation Committee approval. Added indication for Ankylosing Spondylitis to match FDA package insert. Humira and Enbrel will need to be used prior. Reworded background, FDA approval, and rationale sections.
03/05/2015	Medical Policy Committee approval
03/20/2015	Medical Policy Implementation Committee approval. No change to coverage eligibility.

certolizumab pegol (Cimzia®)

Policy # 00200
Original Effective Date: 06/18/2008
Current Effective Date: 04/10/2023

03/03/2016	Medical Policy Committee approval
03/16/2016	Medical Policy Implementation Committee approval. No change to coverage eligibility.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
03/02/2017	Medical Policy Committee approval
03/15/2017	Medical Policy Implementation Committee approval. No change to coverage.
10/05/2017	Medical Policy Committee approval
10/18/2017	Medical Policy Implementation Committee approval. Adjusted the two products that need to be tried and failed prior to Cimzia for rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis. Added a second product, Stelara, to try and fail prior to Cimzia in Crohn's disease
05/03/2018	Medical Policy Committee review
05/16/2018	Medical Policy Implementation Committee approval. Clarified that for the lyophilized vial, there are no requirements for use of other biologics. Updated background information. Lyophilized is considered healthcare professional administered.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. Added the indication of plaque psoriasis. Updated background information, rationale/source.
12/06/2018	Medical Policy Committee review
12/19/2018	Medical Policy Implementation Committee approval. Added Xeljanz/XR as an option for use in psoriatic arthritis prior to Cimzia.
07/03/2019	Medical Policy Committee review
07/18/2019	Medical Policy Implementation Committee approval. Added Skyrizi and Tremfya as first line options in psoriasis. Added a new FDA approved indication (active non-radiographic axial spondyloarthritis) and associated criteria and background/rationale information.
12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. Added Rinvoq as a preferred option for rheumatoid arthritis.
07/02/2020	Medical Policy Committee review
07/08/2020	Medical Policy Implementation Committee approval. Added Otezla as a preferred option for psoriatic arthritis. Added dosing to the investigational statement.
09/11/2020	Coding update

certolizumab pegol (Cimzia®)

Policy # 00200
Original Effective Date: 06/18/2008
Current Effective Date: 04/10/2023

11/05/2020	Medical Policy Committee review
11/11/2020	Medical Policy Implementation Committee approval. Removed Actemra®‡ SubQ as an option prior to use of Cimzia prefilled syringe in rheumatoid arthritis. Added Tremfya as an option prior to use of Cimzia prefilled syringe in psoriatic arthritis. Added Enbrel as an option prior to use of Cimzia prefilled syringe in plaque psoriasis.
11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. No change to coverage.
01/06/2022	Medical Policy Committee review
01/12/2022	Medical Policy Implementation Committee approval. Added subcutaneous Actemra to the list of products than can be tried and failed prior to use of NON-lyophilized (prefilled syringe) Cimzia in rheumatoid arthritis. Added Xeljanz/XR to the list of products that can be tried and failed prior to the use of NON-lyophilized (prefilled syringe) Cimzia in ankylosing spondylitis. Added Rinvoq to the list of products that can be tried and failed prior to the use of NON-lyophilized (prefilled syringe) Cimzia in psoriatic arthritis.
03/03/2022	Medical Policy Committee review
03/09/2022	Medical Policy Implementation Committee approval. Added Skyrizi to the list of products than can be tried and failed prior to use of NON-lyophilized (prefilled syringe) Cimzia in psoriatic arthritis.
08/04/2022	Medical Policy Committee review
08/10/2022	Medical Policy Implementation Committee approval. Removed the requirement for the use of Stelara prior to NON-lyophilized (prefilled syringe) Cimzia requests for Crohn's disease.
03/02/2023	Medical Policy Committee review
03/08/2023	Medical Policy Implementation Committee approval. Added Rinvoq as an option prior to use of NON-lyophilized (prefilled syringe) Cimzia requests in ankylosing spondylitis.

Next Scheduled Review Date: 03/2024

certolizumab pegol (Cimzia®)

Policy # 00200
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Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0717
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into

standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.