

Select infliximab Products

Policy # 00217

Original Effective Date: 10/18/2006

Current Effective Date: 02/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

Note: infliximab-dyyb (Zymfentra™) is addressed separately in medical policy 00897.

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.*

Ankylosing Spondylitis

Based on review of available data, the Company may consider the use of infliximab (Remicade®), Infliximab)†, infliximab-dyyb (Inflectra®)†, infliximab-abda (Renflexis®)†, and infliximab-axxq (Avsola®)† for the treatment of ankylosing spondylitis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of ankylosing spondylitis will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of ankylosing spondylitis; AND
- Patient has failed treatment with non-steroidal anti-inflammatory drugs (NSAIDs) or has documented contraindications to NSAIDs; 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.)*
- If the request is for infliximab-abda (Renflexis) or infliximab-axxq (Avsola): Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy, 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.)*
- Patient has a negative tuberculosis (TB) test (e.g., purified protein derivative [PPD], blood test) prior to treatment; AND
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 6 weeks thereafter.

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Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., ASDAS, BASDAI, inflammatory serum markers) or in clinical signs and symptoms such as reduced pain, stiffness, or improved daily functioning; 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.)*
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 6 weeks thereafter.

Crohn's Disease

Based on review of available data, the Company may consider the use of infliximab (Remicade, Infliximab) infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of Crohn's disease to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of Crohn's disease will be considered when the following criteria are met:

Initial

- Patient is an adult or child greater than or equal to 6 years of age with moderately to severely active Crohn's disease; AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- If the request is for infliximab-abda (Renflexis) or infliximab-axxq (Avsola): Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy, 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.)*
- Patient meets EITHER of the following criteria:
 - Adults and children greater than or equal to 6 years of age with moderately to severely active Crohn's disease AND have had an inadequate response to conventional therapy (e.g., mesalamine, corticosteroids, 6-mercaptopurine/azathioprine or azathioprine monotherapy); OR
 - Adult patients with fistulizing Crohn's disease in order to reduce the number of draining enterocutaneous and rectovaginal fistulas and to maintain fistula closure; AND
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 8 weeks thereafter.

Continuation

- Patient has received an initial authorization; AND

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- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or blood in stool; 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.)*
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 8 weeks thereafter.

Note: The recommended maintenance dose of intravenous infliximab is 5 mg/kg every 8 weeks. Members 18 years of age or older who respond to 5 mg/kg every 8 weeks and then lose response may be approved for 10 mg/kg every 8 weeks.

Ulcerative Colitis

Based on review of available data, the Company may consider the use of infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of ulcerative colitis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of ulcerative colitis will be considered when ALL of the following criteria are met:

Initial

- Patient is an adult or child greater than or equal to 6 years of age with moderately to severely active ulcerative colitis; AND
- Patient had an inadequate response to conventional therapy (e.g., corticosteroids, sulfasalazine, mesalamine, balsalazide, azathioprine, cyclosporine, or 6-mercaptopurine); AND
- If the request is for infliximab-abda (Renflexis) or infliximab-axxq (Avsola): Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy, 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.)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 8 weeks thereafter.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or rectal bleeding; AND

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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.)*

- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 8 weeks thereafter.

Rheumatoid Arthritis

Based on review of available data, the Company may consider the use of infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) in combination with methotrexate (MTX) for the treatment of rheumatoid arthritis to be **eligible for coverage**.*

Patient Selection Criteria

Coverage eligibility for infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) in combination with methotrexate for the treatment of rheumatoid arthritis will be considered when ALL of the following criteria are met:

Initial

- Patient has moderately to severely active rheumatoid arthritis; AND
- Patient has failed methotrexate monotherapy; 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.)*
- If the request is for infliximab-abda (Renflexis) or infliximab-axxq (Avsola): Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy, 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.)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- The requested dose will not exceed 3 mg/kg at weeks 0, 2, and 6, followed by 3 mg/kg every 8 weeks thereafter.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; 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.)*
- The requested dose will not exceed 3 mg/kg at weeks 0, 2, and 6, followed by 3 mg/kg every 8 weeks thereafter.

Note: The recommended maintenance dose of intravenous infliximab is 3 mg/kg every 8 weeks. Members who have had an incomplete response to 3 mg/kg every 8 weeks may be approved for a dose of up to 10 mg/kg every 8 weeks.

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Psoriatic Arthritis

Based on review of available data, the Company may consider the use of infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of psoriatic arthritis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of psoriatic arthritis will be considered when ALL of the following criteria are met:

Initial

- Patient has a diagnosis of psoriatic arthritis; AND
- Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs); 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.)*
- If the request is for infliximab-abda (Renflexis) or infliximab-axxq (Avsola): Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy, 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.)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 8 weeks thereafter.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; 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.)*
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 8 weeks thereafter.

Plaque Psoriasis

Based on review of available data, the Company may consider the use of infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of plaque psoriasis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) for the treatment of plaque psoriasis will be considered when ALL of the following criteria are met:

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- Patient is an adult with chronic severe (i.e., extensive and/or disabling) plaque psoriasis; AND
- If the request is for infliximab-abda (Renflexis) or infliximab-axxq (Avsola): Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy, 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.)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- Greater than 10% of body surface area affected OR less than or equal to 10% of body surface area affected involving sensitive areas or areas that would significantly impact daily function (e.g., 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:
 - 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.)*
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 8 weeks thereafter.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as reduced estimated body surface area affected by psoriasis, decreased erythema, induration/thickness, or scaling, and/or improvement in symptoms such as pain, itching, or burning; 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.)*
- The requested dose will not exceed 5 mg/kg at weeks 0, 2, and 6, followed by 5 mg/kg every 8 weeks thereafter.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) when ANY of the following criteria for their respective disease listed below (and denoted in the patient selection criteria above) are not met to be **not medically necessary****:

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- For ankylosing spondylitis:
 - Patient has failed treatment with NSAIDS or has documented contraindications to NSAIDS
 - For infliximab-abda (Renflexis) and infliximab-axxq (Avsola) requests: Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy
 - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., ASDAS, BASDAI, inflammatory serum markers) or in clinical signs and symptoms such as reduced pain, stiffness, or improved daily functioning
- For Crohn's disease:
 - For infliximab-abda (Renflexis) and infliximab-axxq (Avsola) requests: Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy
 - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or blood in stool
- For ulcerative colitis:
 - For infliximab-abda (Renflexis) and infliximab-axxq (Avsola) requests: Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy
 - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or rectal bleeding
- For rheumatoid arthritis:
 - Patient has failed methotrexate monotherapy
 - For infliximab-abda (Renflexis) and infliximab-axxq (Avsola) requests: Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy
 - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths
- For psoriatic arthritis:
 - Patient has failed treatment with one or more DMARDS
 - For infliximab-abda (Renflexis) and infliximab-axxq (Avsola) requests: Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy

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- For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths
- For plaque psoriasis:
 - For infliximab-abda (Renflexis) and infliximab-axxq (Avsola) requests: Patient has failed treatment with infliximab (Remicade, Infliximab) OR infliximab-dyyb (Inflectra) after at least 2 months of therapy.
 - Greater than 10% of body surface area affected OR less than or equal to 10% of body surface area affected involving sensitive areas or areas that would significantly impact daily function (e.g., 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 (e.g., methotrexate, cyclosporine, acitretin)
 - For continuation requests: Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as reduced estimated body surface area affected by psoriasis, decreased erythema, induration/thickness, or scaling, and/or improvement in symptoms such as pain, itching, or burning

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 infliximab (Remicade, Infliximab), infliximab-dyyb (Inflectra), infliximab-abda (Renflexis), and infliximab-axxq (Avsola) when patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****), OR for use in any other indication than those listed above to be **investigational.***

Background/Overview

Remicade is a monoclonal antibody that targets the activity of tumor necrosis factor (TNF) alpha. Remicade is an infused product and the dosing varies based on the indication being treated. Remicade carries approvals for ankylosing spondylitis, Crohn's disease, pediatric Crohn's disease, ulcerative colitis, pediatric ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, and plaque psoriasis. A branded Infliximab product from Janssen is also available on the market. Inflectra, Renflexis, and Avsola are all biosimilars to Remicade. All three of these products carry the same indications as Remicade and branded Infliximab. A biosimilar product is a biological product that is approved based on demonstration that it is highly similar to an already approved biological reference product. The biosimilar must also demonstrate that it has no clinically meaningful differences in

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terms of safety and effectiveness from the reference product. Only minor differences in clinically inactive components are allowable in biosimilar products. Biosimilar products can only be approved by the U.S. Food and Drug Administration (FDA) if they have the same mechanism of action, route of administration, dosage form, and strengths as the reference product as well as only the indications and conditions of use that have been approved by the FDA for the reference product. All infliximab products mentioned in this policy are supplied as 100 mg of infliximab in a 20 ml vial. Anywhere that Remicade is mentioned in this policy, Infliximab can be inferred as well.

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. Nonsteroidal anti-inflammatory drugs 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.

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-MP and Azathioprine are used to treat this condition.

Psoriatic Arthritis

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

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. Treatment is focused on control of the symptoms and prevention of secondary infections. Lesions that cover all or most of the body may be acutely painful and require hospitalization. The body loses vast quantities of fluid and becomes susceptible to severe secondary infections that can involve internal organs and even progress to septic shock. Typical treatments for severe cases of plaque psoriasis include ultraviolet therapy or systemic therapies such as methotrexate or cyclosporine.

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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 DMARDs are used to treat this condition. An example of a DMARD would include methotrexate.

Ulcerative colitis

Ulcerative colitis is a chronic, episodic, inflammatory disease of the large intestine and rectum characterized by bloody diarrhea. This disease usually begins in the rectal area and may eventually extend through the entire large intestine. Repeated episodes of inflammation lead to thickening of the wall of the intestine and rectum with scar tissue. Death of colon tissue or sepsis may occur with severe disease. The goals of treatment are to control the acute attacks, prevent recurrent attacks and promote healing of the colon. Hospitalization is often required for severe attacks. Typically, first line treatments such as corticosteroids, 6-MP and Azathioprine are used to treat this condition.

Disease-Modifying Anti-Rheumatic Drugs

DMARDs are used as a second line defense for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and lupus. These drugs slow the disease process by modifying the immune system.

- methotrexate
- Cyclosporine
- Sulfasalazine
- Mercaptopurine
- Gold Compounds

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Remicade and Infliximab carry FDA approvals for ankylosing spondylitis, Crohn's disease, pediatric Crohn's disease, ulcerative colitis, pediatric ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, and plaque psoriasis.

Inflectra was approved by the FDA in April of 2016. As previously mentioned, Inflectra carries the same indications as Remicade.

Renflexis was approved by the FDA in April of 2017. As previously mentioned, Renflexis carries the same indications as Remicade.

Avsola was approved by the FDA in December of 2019. As previously mentioned Avsola carries the same indications as Remicade.

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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 regulations, other plan medical policies, and accredited national guidelines.

Adult Crohn's Disease

The safety and efficacy of infliximab for active Crohn's Disease were assessed in 2 randomized, double-blind, placebo-controlled clinical studies in 653 patients with moderate to severely active Crohn's Disease with an inadequate response to prior conventional therapies. In the single dose trial, 15% of placebo patients achieved a clinical response at week 4 vs. 81% of patients receiving 5 mg/kg of infliximab. Additionally, 4% of placebo patients and 48% of patients receiving infliximab achieved clinical remission at week 4. In the multidose trial, subjects were randomized to receive placebo at weeks 2 and 6, then every 8 weeks; the 5 mg/kg infliximab maintenance group received 5 mg/kg at weeks 2 and 6, then every 8 weeks. The 10 mg/kg infliximab maintenance group received 5 mg/kg at weeks 2 and 6, then 10 mg/kg ever 8 weeks. At week 2, 57% of patients were in clinical response. At week 30, 25% of subjects in the placebo maintenance group were in clinical remission vs. 39% ($p = 0.022$) in the infliximab 5 mg/kg maintenance group and 46% ($p = 0.001$) in the infliximab 10 mg/kg infliximab maintenance group. In the placebo maintenance group, 11% of subjects in remission were able to discontinue corticosteroid use vs. 25% ($p = 0.059$) and 34% ($p = 0.005$) in the infliximab 5 mg/kg and 10 mg/kg infliximab maintenance groups.

Fistulizing Crohn's Disease

The safety and efficacy of infliximab were assessed in 2 randomized, double-blind, placebo-controlled studies in patients with fistulizing Crohn's disease with fistulas that were of at least 3 months duration.

In the first trial, 94 patients received 3 doses of either placebo or infliximab at weeks 0, 2, and 6. Fistula response was seen in 68% of patients in the 5 mg/kg infliximab group ($p = 0.002$) and 56% of patients in the 10 mg/kg infliximab group ($p = 0.021$) vs. 26% of subjects in the placebo arm. Closure of all fistulas was achieved in 52% of patients treated with infliximab vs. 13% of placebo treated patients ($p < 0.001$). In the second trial, subjects had to have at least 1 draining enterocutaneous fistula. All patients received 5 mg/kg of infliximab at weeks 0, 2, and 6. Patients were randomized to placebo or 5 mg/kg maintenance doses at week 14 and then every 8 weeks through week 46. The primary endpoint was the time from randomization to loss of response among those patients who were in fistula response. At week 14, 65% of patients were in fistula response. Patients randomized to maintenance with infliximab had a longer time to loss of fistula response compared to the placebo maintenance group. At week 54, 38% of patients treated with infliximab had no draining fistulas compared with 22% of placebo treated patients ($p = 0.02$).

Pediatric Crohn's Disease

The safety and efficacy of infliximab were assessed in a randomized, open-label study in 112 pediatric patients aged 6 to 17 years old with moderately to severely active Crohn's disease and an

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inadequate response to conventional therapies. Subjects received 5 mg/kg of infliximab at weeks 0, 2, and 6. At week 10, 103 subjects were randomized to a maintenance regimen of 5 mg/kg of infliximab given either every 8 weeks or every 12 weeks. At week 30, 73% ($p < 0.01$) of subjects in the 8 week group had achieved a clinical response and 60% ($p < 0.05$) had achieved a clinical remission. At week 30, 47% of subjects in the 12 week group had achieved a clinical response and 35% had achieved a clinical remission. At week 54, 64% ($p < 0.01$) of subjects in the 8 week group had achieved a clinical response and 56% ($p < 0.01$) had achieved a clinical remission. At week 54, 33% of subjects in the 12 week group had achieved a clinical response and 24% had achieved a clinical remission. The results demonstrated that there were more responses and remissions in the 8 week group.

Ulcerative Colitis

The safety and efficacy of infliximab were assessed in 2 randomized, double-blind, placebo-controlled clinical studies in 728 subjects with moderately to severely active ulcerative colitis with an inadequate response to conventional oral therapies. Subjects were randomized to either 5 mg/kg or 10 mg/kg of infliximab at weeks 0, 2, 6, and every 8 weeks thereafter. In both ulcerative colitis studies, greater percentages of patients in both infliximab groups achieved clinical response, clinical remission, and mucosal healing than in the placebo group. Each of the effects was maintained through the end of each trial. In addition, a greater proportion of patients in the infliximab groups demonstrated sustained response and sustained remission than in the placebo groups.

Pediatric Ulcerative Colitis

The safety and effectiveness of infliximab in pediatric patients aged 6 years of age and older with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy are supported by evidence from adequate and well controlled studies in adults. Additional safety and pharmacokinetic data were collected in an open label pediatric ulcerative colitis trial in 60 pediatric patients aged 6-17 years of age. All patients received induction dosing of 5 mg/kg of infliximab at weeks 0, 2, and 6. Patients who did not respond to infliximab at week 8 received no further infliximab. At week 8, 45 patients were randomized to a maintenance regimen of 5 mg/kg of infliximab given either every 8 weeks through week 46 or every 12 weeks through week 42. Of the 60 patients treated, 44 were in clinical response at week 8. At week 8, 24 of 60 patients were in clinical remission as measured by the Mayo score and 17 of 51 patients were in remission as measured by the Pediatric Ulcerative Colitis Activity Index (PUCAI) score. At week 54, 8 of 21 patients in the every 8 weeks maintenance group and 4 of 22 patients in the every 12 weeks group achieved remission as measured by the PUCAI score.

Rheumatoid Arthritis

The safety and efficacy of infliximab were assessed in 2 multicenter, randomized, double-blind, pivotal trials which compared placebo plus methotrexate versus one of four various doses/schedules of infliximab plus methotrexate. In the first study, all doses/schedules of infliximab plus methotrexate resulted in improvement in signs and symptoms as measured by the American College of Rheumatology (ACR)20, with a higher percentage of subjects achieving an ACR20, 50, and 70 compared to placebo plus methotrexate. This improvement was noted in week 2 and remained through week 102. Greater effects on each component of ACR20 were observed in all patients

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treated with infliximab plus methotrexate as compared to placebo plus methotrexate. More patients treated with infliximab reached a major clinical response than placebo treated patients. Similar results were noted in the second trial as well.

Ankylosing Spondylitis

The safety and efficacy of infliximab were assessed in a randomized, multicenter, double-blind, placebo-controlled study in 279 patients with active ankylosing spondylitis. At 24 weeks, improvement in the signs and symptoms of ankylosing spondylitis, as measured by the proportion of patients achieving a 20% improvement in Assessment of SpondyloArthritis (ASAS) response criteria (ASAS 20), was seen in 60% of patients in infliximab group vs. 18% of patients in the placebo group ($p < 0.001$). Improvement was observed at week 2 and maintained through week 24. At 24 weeks, the proportions of patients achieving a 50% and a 70% improvement in the signs and symptoms of ankylosing spondylitis, as measured by ASAS response criteria (ASAS 50 and ASAS 70, respectively), were 44% and 28%, respectively, for patients receiving infliximab, compared to 9% and 4%, respectively, for patients receiving placebo ($p < 0.001$, infliximab vs. placebo). A low level of disease activity (defined as a value < 20 [on a scale of 0 -100 mm] in each of the 4 ASAS response parameters) was achieved in 22% of patients treated with infliximab vs. 1% in placebo-treated patients ($p < 0.001$).

Psoriatic Arthritis

The safety and efficacy of infliximab were assessed in a multicenter, double-blind, placebo-controlled study in 200 adult patients with active psoriatic arthritis despite therapy with NSAIDs or DMARDs.

Subjects received either infliximab or placebo. At week 16, placebo patients with $< 10\%$ improvement from baseline in both swollen and tender joint counts were switched to infliximab induction. At week 24, all placebo treated patients crossed over to infliximab induction. Dosing continued for all patients through week 46. Treatment with infliximab resulted in improvement in signs and symptoms, as assessed by the ACR criteria, with 58% of patients treated with infliximab achieving ACR 20 at week 14, compared with 11% of placebo-treated patients ($p < 0.001$). The response was similar regardless of concomitant use of methotrexate. At 6 months, the ACR 20/50/70 responses were achieved by 54%, 41%, and 27%, respectively, of patients receiving infliximab compared to 16%, 4%, and 2%, respectively, of patients receiving placebo. Similar responses were seen in patients with each of the subtypes of psoriatic arthritis, although few patients were enrolled with the arthritis mutilans and spondylitis with peripheral arthritis subtypes.

Plaque Psoriasis

The safety and efficacy of infliximab were assessed in 3 randomized, double-blind, placebo-controlled studies in subjects 18 years of age and older with chronic, stable plaque psoriasis and who were candidates for systemic therapy or phototherapy. The three studies evaluated placebo versus various doses of infliximab. In all three studies, the primary endpoint was the proportion of patients who achieved a reduction in score of at least 75% from baseline at week 10 by the Psoriasis Area and Severity Index (PASI) 75. In study 1, 80% of subjects on 5 mg/kg of infliximab achieved a PASI

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75 at week 10 compared with 3% of patients on placebo. In study 2, 70% and 75% of patients on 3 mg/kg and 5 mg/kg infliximab achieved a PASI 75 at week 10, respectively, compared with 2% on placebo. In study 3, 72% and 88% of patients on 3 mg/kg and 5 mg/kg infliximab achieved a PASI 75 at week 10, respectively, compared with 6% on placebo.

References

1. Remicade [package insert]. Janssen Biotech, Inc. Horsham, Pennsylvania. Updated October 2021.
2. Infliximab [package insert]. Janssen Biotech, Inc. Horsham, Pennsylvania. Updated October 2021.
3. Inflectra [package insert]. Celltrion, Inc. Republic of Korea. Updated June 2021.
4. Renflexis [package insert]. Organon and Company. Jersey City, New Jersey. June 2021.
5. Avsola [package insert]. Amgen, Inc. Thousand Oaks, California. Updated September 2021.

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10/04/2006	Medical Director Review
10/18/2006	Medical Policy Committee approval
10/10/2007	Medical Director Review
10/17/2007	Medical Policy Committee approval No change to policy statements.
11/05/2008	Medical Director Review
11/18/2008	Medical Policy Committee approval. No change to coverage eligibility.
03/04/2009	Medical Director Review
03/18/2009	Medical Policy Committee approval. Added Investigational statement to coverage section. Added FDA Black Box Warning to FDA section. Removed criteria bullet for plaque psoriasis requiring a dermatologist or a physician with expertise when prescribing infliximab. Removed the entire section, "When Services Are Considered Not Medically Necessary", that required a dermatologist or other specialist when prescribing infliximab.
03/05/2010	Medical Policy Committee approval
03/19/2010	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/03/2011	Medical Policy Committee review
03/16/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/01/2012	Medical Policy Committee review
03/21/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/07/2013	Medical Policy Committee review
03/20/2013	Medical Policy Implementation Committee approval. Clarified with notes those requirements that are not medically necessary. Added headings for each indication. Ensured that all indications had a requirement for a PPD (plaque psoriasis was

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	missing one). Removed the requirement from all indications that the patient must have a negative cancer history or history of CHF. Removed notes regarding dosing of the drugs and various notes throughout the patient selection criteria. Under Crohn's disease, expanded the fistulizing Crohn's indication as it is only for adults per the package insert. Under ulcerative colitis, expanded to include that children ages 6 and up are eligible. Made the When Services are Considered Investigational Section a bit cleaner. Created a When Services Are Considered Not Medically Necessary section to differentiate between the two.
05/02/2013	Medical Policy Committee review
05/22/2013	Medical Policy Implementation Committee approval. Removed severely restricted movement or immobilization from ankylosing spondylitis criteria. Removed failure of NSAIDs for psoriatic arthritis. Removed presence of plaque psoriasis for over one year from plaque psoriasis criteria. Clarified criteria to match other similar policies with similar indications.
03/06/2014	Medical Policy Committee review
03/19/2014	Medical Policy Implementation Committee approval. No change to coverage.
03/05/2015	Medical Policy Committee review
03/20/2015	Medical Policy Implementation Committee approval. No change to coverage.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
03/03/2016	Medical Policy Committee review
03/16/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
03/02/2017	Medical Policy Committee review
03/15/2017	Medical Policy Implementation Committee approval. No change to coverage. Updated all of the background, rationale and FDA approval sections.
03/01/2018	Medical Policy Committee review
03/21/2018	Medical Policy Implementation Committee approval. No coverage changes. Updated TB test statement.
03/07/2019	Medical Policy Committee review
03/20/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/05/2020	Medical Policy Committee review
03/11/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/14/2020	Coding update
03/04/2021	Medical Policy Committee review
03/10/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/03/2021	Coding update
10/01/2021	Coding update
03/03/2022	Medical Policy Committee review
03/09/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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11/03/2022	Medical Policy Committee review
11/09/2022	Medical Policy Implementation Committee approval. Added the Janssen Infliximab to the policy.
11/02/2023	Medical Policy Committee review
11/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/02/2025	Medical Policy Committee review
01/08/2025	Medical Policy Implementation Committee approval. Changed title from “infliximab (Remicade, Infliximab)” to “Select infliximab Products.” Added Inflectra, Renflexis, and Avsola to policy, combining this policy as one to target the IV infliximab products. Updated eligibility criteria for Renflexis and Avsola to require a trial and failure of Remicade, Infliximab or Inflectra.
01/05/2026	Medical Policy Committee review
01/07/2026	Medical Policy Implementation Committee approval. Added criteria for continuation requests. Updated criteria to clarify that doses above the labeled maximum dose are considered investigational.

Next Scheduled Review Date: 01/2027

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2025 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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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	J1745, Q5103, Q5104, Q5121
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.

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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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.