LOUISIANA BLUE

guselkumab (Tremfya™)

Policy # 00588
Original Effective Date: 01/01/2018
Current Effective Date: 11/25/2024

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.*

Plaque Psoriasis

Based on review of available data, the Company may consider guselkumab (Tremfya™)‡ for the treatment of adult patients with plaque psoriasis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for guselkumab (Tremfya) will be considered when the following criteria are met:

- Patient has a diagnosis of moderate to severe plaque psoriasis; AND
- Patient is 18 years of age or older; AND
- Patient has a negative tuberculosis (TB) test (e.g., purified protein derivative [PPD], blood test) prior to treatment; AND
- Patient is a candidate for phototherapy or systemic therapy; AND
- Tremfya 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 tofacitinib (Xeljanz/XR®)‡ or apremilast (Otezla®)‡; AND
- Patient has greater than 10% of body surface area (BSA) OR less than or equal to 10% BSA 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:
  - Ultraviolet B; OR
  - Psoralen positive Ultraviolet A; OR
  - Systemic therapy (e.g., methotrexate, cyclosporine, acitretin).

  *(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).*

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Psoriatic Arthritis
Based on review of available data, the Company may consider guselkumab (Tremfya) for the treatment of adult patients with active psoriatic arthritis to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for guselkumab (Tremfya) will be considered when all of the following criteria are met:

- Patient has a diagnosis of active psoriatic arthritis; AND
- Patient is 18 years of age or older; AND
- Patient has a negative TB test (e.g. purified protein derivative [PPD], blood test) prior to treatment; AND
- Tremfya is NOT used in combination with other biologic disease-modifying anti-rheumatic drugs (DMARDs), such as Humira or Enbrel OR other drugs such as Otezla or Xeljanz/XR; AND
- Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs).
  *(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).*

Ulcerative Colitis
Based on review of available data, the Company may consider guselkumab (Tremfya) for the treatment of moderately to severely active ulcerative colitis to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for guselkumab (Tremfya) will be considered when all of the following criteria are met:

- Patient has a diagnosis of moderately to severely active ulcerative colitis; AND
- Patient is 18 years of age or older; AND
- Patient has failed or become intolerant to treatment with traditional immunomodulators (e.g., azathioprine, 6-mercaptopurine) or corticosteroids; 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).*
- Tremfya is NOT being used concurrently with other biologic products such as infliximab (Remicade, biosimilars), adalimumab (Humira, biosimilars), or vedolizumab (Entyvio) for the treatment of moderately to severely active ulcerative colitis; AND
- Patient has negative TB test (e.g. purified protein derivative [PPD], blood test) prior to treatment; AND
- For Tremfya intravenous requests only: Dosage is 200 mg at week 0, week 4, and week 8.

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of guselkumab (Tremfya) 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 plaque psoriasis:
  - Patient has greater than 10% BSA OR less than or equal to 10% BSA 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 (e.g., methotrexate, cyclosporine, acitretin)
- For psoriatic arthritis:
  - Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs)
- For ulcerative colitis:
  - Patient has failed or become intolerant to treatment with traditional immunomodulators (e.g., azathioprine, 6-mercaptopurine) or corticosteroids

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 guselkumab (Tremfya) when patient selection criteria are not met (with the exception of those denoted as **not medically necessary****) to be **investigational.***

Background/Overview

Tremfya is an interleukin-23 (IL-23) blocker indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy, for the treatment of adults with active psoriatic arthritis, and for the treatment of adults with moderately to severely active ulcerative colitis. IL-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Tremfya inhibits the release of pro-inflammatory cytokines and chemokines. Tremfya is supplied as 100 mg in a single-dose prefilled syringe or a single dose patient-controlled injector and as 200 mg in a single-dose prefilled pen, single-dose prefilled syringe, or single-dose vial. Tremfya is dosed at 100 mg at weeks 0 and 4 and every 8 weeks thereafter for

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plaque psoriasis and psoriatic arthritis. For ulcerative colitis, an induction dose of 200 mg administered by intravenous infusion at week 0, week 4, and week 8, and a maintenance dose of 100 mg administered by subcutaneous injection beginning at week 16 and every 8 weeks thereafter or 200 mg administered by subcutaneous injection at week 12 and every 4 weeks thereafter is recommended.

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 tumor necrosis factor-alpha (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. Newer biologic therapies are also approved for the treatment of plaque psoriasis.

Psoriatic Arthritis
Psoriatic arthritis is an arthritis that is often associated with psoriasis of the skin. Typically, first line treatments such as DMARDs (disease modifying anti-rheumatic drugs) are used to treat this condition. An example of a DMARD would include methotrexate.

Disease-Modifying Anti-Rheumatic Drugs (DMARDs)
Disease-modifying anti-rheumatic drugs are typically used for the treatment of inflammatory conditions. These drugs slow the disease process by modifying the immune system.

- methotrexate
- cyclosporine
- sulfasalazine
- mercaptopurine
- gold compounds

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

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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-mercaptopurine and azathioprine are used to treat this condition.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Tremfya is an interleukin-23 blocker approved in July of 2017 for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. In July of 2020, Tremfya was approved for the treatment of adult patients with active psoriatic arthritis. Tremfya gained approval for the treatment of adult patients with moderately to severely active ulcerative colitis in September of 2024.

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.

Plaque Psoriasis

The safety and efficacy of Tremfya was assessed in two trials. In these trials, subjects were randomized to either Tremfya (100 mg at weeks 0 and 4, then every 8 weeks) or Humira (80 mg at week 0 and 40 mg at week 1, followed by 40 mg every other week thereafter). These two trials assessed the responses at week 16 compared to placebo for the PASI 90 [proportion of subjects who achieved at least a 90% reduction from baseline in the PASI (Psoriasis Area and Severity Index) composite score]. Comparisons between Tremfya and Humira were made via secondary endpoints at weeks 16 and 24. The PASI 90 response in trial 1 was 73% for the Tremfya group vs. 3% in the placebo group. In trial 2, the PASI 90 response was 70% in the Tremfya group vs. 2% in the placebo group. In regards to secondary endpoints vs. Humira, the Tremfya group had higher PASI 75 and PASI 90 responses at various timepoints.

Psoriatic Arthritis

The safety and efficacy of Tremfya were assessed in two randomized, double-blind, placebo-controlled trials (PsA1 and PsA2) in adult subjects with active psoriatic arthritis who had an inadequate response to standard therapies (e.g., conventional DMARDs, Otezla, or nonsteroidal anti-inflammatory drugs [NSAIDs]). PsA1 evaluated subjects who were treated with placebo, Tremfya 100 mg at weeks 0, 4 and every 8 weeks thereafter, or Tremfya 100 mg every 4 weeks. PsA2 evaluated subjects who were treated with placebo, Tremfya 100 mg at weeks 0, 4 and every 8 weeks thereafter, or Tremfya 100 mg every 4 weeks. The primary endpoint in both trials was the percentage of subjects achieving an ACR20 (20% improvement from baseline in the American College of

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Rheumatology score) response at week 24. In both trials, subjects treated with Tremfya 100 mg every 8 weeks demonstrated a greater clinical response including ACR20, compared to placebo at week 24. In PsA1, 52% of subjects using Tremfya every 8 weeks achieved an ACR20 versus 22% in the placebo group at week 24. In PsA2, 64% of subjects using Tremfya every 8 weeks achieved an ACR20 versus 33% in the placebo group at week 24.

Ulcerative Colitis
The safety and efficacy of Tremfya were assessed in 2 studies, an induction and maintenance study. In the induction trial, UC1, subjects with moderately to severely active ulcerative colitis were randomized 3:2 to receive either Tremfya 200 mg or placebo by intravenous infusion at week 0, week 4, and week 8. The primary endpoint was clinical remission at week 12 defined by the modified Mayo Score (mMS). The mMS is a 3-component Mayo score (0-9) which consists of the following subscores (0 to 3 for each subscore): stool frequency (SFS), rectal bleeding (RBS), and findings on centrally reviewed endoscopy (ES). An ES of 2 was defined by marked erythema, lack of vascular pattern, friability, and/or erosions; an ES of 3 was defined by spontaneous bleeding and ulceration. The primary endpoint in UC1 was achieved by 23% of patients in the Tremfya treatment group compared to 8% of patients in the placebo treatment group. In the maintenance trial, UC2, subjects who demonstrated a clinical response to Tremfya IV induction dosing were re-randomized to receive a subcutaneous maintenance regimen of either Tremfya 100 mg every 8 weeks, Tremfya 200 mg every 4 weeks, or placebo for up to an additional 44 weeks. The primary endpoint for UC2 was clinical remission at week 44 defined by mMS. Secondary endpoints included corticosteroid-free clinical remission, endoscopic improvement, histologic endoscopic mucosal improvement, all at week 44 and maintenance of clinical remission at week 44 in subjects who achieved clinical remission 12 weeks after intravenous Tremfya induction treatment. In UC2, 45% of patients receiving Tremfya 100 mg every 8 weeks, 50% of patients receiving Tremfya 200 mg every 4 weeks, and 19% of patients receiving placebo all met the primary endpoint of clinical remission at week 44.

References

1. Tremfya [package insert]. Jannsen Biotech, Inc. Horsham, Pennsylvania. Updated September 2024.

Policy History

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12/07/2017	Medical Policy Committee review
12/20/2017	Medical Policy Implementation Committee approval. New policy.
04/05/2018	Medical Policy Committee review
04/18/2018	Medical Policy Implementation Committee approval. Changed prerequisite from TWO products to Humira only for plaque psoriasis.
04/04/2019	Medical Policy Committee review
04/24/2019	Medical Policy Implementation Committee approval. No change to coverage.

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07/03/2019	Medical Policy Committee review
07/18/2019	Medical Policy Implementation Committee approval. Removed the requirement for Humira in plaque psoriasis.
07/02/2020	Medical Policy Committee review
07/08/2020	Medical Policy Implementation Committee approval. No change to coverage.
11/05/2020	Medical Policy Committee review
11/11/2020	Medical Policy Implementation Committee approval. Added a new FDA approved indication, psoriatic arthritis. Updated relevant background information.
11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/03/2022	Medical Policy Committee review
11/09/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/02/2023	Medical Policy Committee review
11/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/07/2024	Medical Policy Committee review
11/13/2024	Medical Policy Implementation Committee approval. Added new FDA approved indication, ulcerative colitis, with criteria. Updated relevant background information.

Next Scheduled Review Date: 11/2025

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2023 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 code
HCPCS	J1628
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.

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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.

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.

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