axatilimab-csfr (Niktimvo™)

Medicare Advantage Medical Policy #MA-136
Original Effective Date: 11/01/2025
Current Effective Date: 11/01/2025

Applies to all products administered or underwritten by the Health Plan, 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.*

Based on review of available data, the Health Plan may consider axatilimab-csfr (Niktimvo™)‡ for the treatment of chronic graft-versus-host disease (cGVHD) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for axatilimab-csfr (Niktimvo) for the treatment of chronic graft-versus-host disease (cGVHD) will be considered when the patient selection criteria are met:

Initial:

- Patient has a diagnosis of chronic graft-versus-host disease (cGVHD) as defined by ALL of the following:
  - Patient has undergone allogeneic hematopoietic cell transplantation (HCT); AND
  - Patient has clinical symptoms and signs that are components of the National Institutes of Health (NIH) consensus criteria for diagnosis of cGVHD; AND
    (See Policy Guidelines section for NIH consensus criteria)
- cGVHD is classified as moderate or severe based on a clinically appropriate grading scale (e.g., NIH disease grade, CIBMTR score); AND
  (See Policy Guidelines for grading scale descriptions)
- Patient has a history of failure with BOTH of the following:
  - Corticosteroid (e.g., prednisone, methylprednisolone); AND
  - ONE of the following:
    - bortezomib (Velcade®)‡; OR
    - ibrutinib (Imbruvica®)‡; OR
    - Immunosuppressant agent (e.g., hydroxychloroquine, methotrexate, cyclosporine, mycophenolate, tacrolimus); OR
    - ruxolitinib (Jakafi®)‡; OR
    - belumosudil (Rezurock®)‡; OR
    - rituximab (Rituxan®, biosimilars) ‡; AND
- Patient weighs at least 40 kg; AND
- Dose does not exceed 0.3 mg/kg or 35 mg, whichever is lowest, every 2 weeks.

Continuation:

- Patient has received an initial authorization for Niktimvo from the plan OR has provided documentation of authorization from previous Medicare Advantage plan; AND
- According to the prescriber, patient is experiencing improvement while on therapy; AND

- Dose does not exceed 0.3 mg/kg or 35 mg, whichever is lower, every 2 weeks.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of axatilimab-csfr (Niktimvo) when the patient's disease is not classified as moderate to severe to be **not medically necessary.****

Based on review of available data, the Health Plan considers the continued use of axatilimab-csfr (Niktimvo) when the patient is not experiencing improvement while on therapy to be **not medically necessary.****

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 Health Plan considers the use of axatilimab-csfr (Niktimvo) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Policy Guidelines

National Institutes of Health (NIH) Consensus Criteria for Diagnosis of cGVHD

- Presence of at least one diagnostic clinical manifestation; OR
- Presence of at least one distinctive clinical manifestation, confirmed by biopsy or other relevant tests in the same or another organ; OR
- Lung biopsy that demonstrates pathologic evidence of bronchiolitis obliterans

Organ System	***Diagnostic* Clinical Manifestations**
Skin	Poikiloderma, lichen planus-like features, sclerotic features, morphea-like features, lichen sclerosis-like features
Oral Mucosa	Lichen planus-type features
Genitalia	Lichen planus-like features and lichen sclerosus-like features affecting either males or females. For females, vaginal scarring or clitoral/labial agglutination. For males, phimosis or urethral/meatus scarring or stenosis
Gastrointestinal	Esophageal web, strictures or stenosis
Lung	Bronchiolitis obliterans
Musculoskeletal	Fasciitis, joint stiffness or contractures

Organ system	***Distinctive* Findings**
Skin	Depigmentation, papulosquamous lesions
Nails	Dystrophy, longitudinal ridging, onycholysis, pterygium unguis, nail loss

Hair and scalp	Alopecia, loss of body hair, scaling of scalp
Mouth	Xerostomia, mucoceles, mucosal atrophy, ulcers, pseudomembranes
Eyes	Dry, gritty, or painful eye, cicatricial conjunctivitis, keratoconjunctivitis sicca, confluent areas of punctate keratopathy
Lung	Bronchiolitis obliterans syndrome
Musculoskeletal	Myositis or polymyositis

NIH Disease Grades

Grade	Description
Mild	Involves $\geq$ 2 organs/sites with no clinically significant functional impairment
Moderate	Involves 3 organs/sites with no clinically significant functional impairment OR $\leq$ 1 organ/site with clinically significant functional impairment, but no major disability
Severe	Major disability caused by cGVHD

Center for Internation Blood & Marrow Transplant Research (CIBMTR) Score
This score predicts the likelihood of complications after a blood or marrow transplant. Possible scores range from 0 to 13 with a higher score indicating higher risk for mortality.

A scoring calculator and details can be found here: https://www.oncologynewscentral.com/calculators/center-for-international-blood-and-marrow-transplant-research-cibmtr-chronic-graft-versus-host-disease-gvhd-risk-score

Background/Overview

Niktimvo is a monoclonal antibody administered intravenously every 2 weeks that targets the colony-stimulating factor 1 receptor (CSF-1R). The CSF-1R is a cell surface protein that controls the survival and function of monocytes and macrophages. Niktimvo is approved for the treatment of chronic graft-versus-host-disease (cGVHD) in patients who have failed at least 2 prior lines of systemic therapy. It is thought that the inhibition of CSF-1R by this drug reduces the number of disease-mediating macrophages and their monocyte precursors to disrupt the fibrotic disease process present in cGVHD.

Graft-versus-host disease (GVHD) is a condition that may occur after an allogeneic hematopoietic stem cell transplant where the transplanted cells (i.e. graft) from the donor induce an immune response in the recipient (i.e. host), encouraging the host's immune system to attack and reject the newly transplanted cells. GVHD can be categorized as acute (aGVHD) or chronic (cGVHD), with differentiation of the two established by consensus criteria from the National Institutes of Health (NIH). A previous diagnosis of aGVHD is not required for cGVHD diagnosis. Manifestations of

cGVHD may span several organ systems or may be restricted to one site. Common characteristics of cGVHD include skin reactions, dry oral mucosa, gastrointestinal ulcerations, and bronchiolar obstruction.

The selection of specific treatments for cGVHD depends on the severity of disease. The goal of treatment is to eliminate disease activity, limit adverse events, and enable withdrawal of therapy without recurrence of cGVHD. Treatment is usually required for 3-5 years, though some patients may require lifelong therapy. Mild disease is treated with local/topical therapy to the affected organ systems. Moderate disease is treated with systemic steroids, with topical therapy added on if needed. For severe disease, prednisone plus an additional immunosuppressive agent is used as initial therapy. Between 40% and 60% of patients with cGVHD do not respond to initial steroid therapy and require escalation to other therapies.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Niktimvo was approved in August 2024 for the treatment of chronic graft-versus-host disease (cGVHD) in adults and pediatrics weighing at least 40 kg after failure of at least two prior lines of systemic therapy.

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.

The efficacy of Niktimvo was evaluated in AGAVE-201, a randomized, open-label, multicenter study in adult and pediatric patients with recurrent or refractory cGVHD who had received at least 2 lines of systemic therapy and required additional treatment. Patients with platelet count $\geq$ 50 x 10^9/L, absolute neutrophil count $\geq$ 1 x 10^9/L, ALT and AST $\leq$ 2.5 x ULN ($\leq$ 5 x ULN if liver cGVHD was present), total bilirubin $\leq$ 1.5 x ULN, and creatinine clearance $\geq$ 30 mL/min were eligible. Patients with uncontrolled infections were not eligible.

Treatment consisted of Niktimvo 0.3 mg/kg administered intravenously every 2 weeks until disease progression, lack of efficacy by 9 months, or unacceptable toxicity. Continued treatment with GVHD prophylaxis and standard care systemic cGVHD therapies were permitted as long as the patient had been on a stable dose for at least 2 weeks prior to study. Initiation of new systemic cGVHD therapy while on study was not permitted.

The efficacy of Niktimvo was based on overall response rate (ORR) through Cycle 7 Day 1, where overall response included complete response or partial response according to the 2014 NIH

Consensus Development Project on Response Criteria. The ORR for the 79 treated patients was 75% (95% CI, 64, 84) with 0 complete responses and 59 patients exhibiting a partial response. The median time to first response was 1.5 months (range, 0.9 to 5.1 months). The median duration of response, calculated from first response to progression, death, or new systemic therapies for cGVHD, was 1.9 months (95% CI: 1.6, 3.5). In patients who achieved response, no death or new systemic therapy initiation occurred in 60% (95% CI: 43, 74) of patients for at least 12 months since response.

References

1. Niktimvo [package insert]. Incyte Corporation. Wilmington, DE. Updated January 2025.
2. Niktimvo (axatilimab). New Drug Review. IPD Analytics. Updated August 2024.
3. Zieser R. Clinical Manifestations and Diagnosis of Chronic Graft-versus-Host Disease. UpToDate. Updated February 2024.

Policy History

Original Effective Date: 11/01/2025
Current Effective Date: 11/01/2025
08/19/2025 UM Committee review and approval. New policy.
Next Scheduled Review Date: 08/2026

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 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	J9038
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.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan 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 Health Plan 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.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.