Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 10/03/2024

Niktimvo™ (axatilimab-csfr)

HCPCS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Trial and failure of at least two prior lines of systemic therapy
   d. Trial and failure, intolerance, or a contraindication to the preferred products as specified in the BCBSM/BCN medical utilization management drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Niktimvo is a monoclonal antibody against the colony-stimulating factor 1 (CSF-1) receptor indicated for the treatment of chronic graft-versus-host disease (cGVHD) after failure of at least two prior lines of systemic therapy in adult and pediatric patients weighing at least 40 kg.

- GVHD is a condition that may occur after an aHSCT 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

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established by consensus criteria from the National Institutes of Health (NIH). A previous diagnosis of aGVHD is not required for cGVHD diagnosis. A recent review by Herzog et al reported no prior diagnosis of aGVHD in 39% of patients with cGVHD. 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 (GI) ulcerations, and bronchiolar obstruction. The incidence of cGVHD after aHSCT is about 40%, affecting approximately 140,000 persons in the United States. Analysis from the Chronic GVHD Consortium reported non-relapse mortality rates of 22% after 5 years and 40% (95% confidence interval (CI) 30%–50%) after 12 years. GVHD has been classically divided into acute and chronic variants based on the time of onset using a cutoff of 100 days. However, this conventional division has been challenged by the recognition that signs of acute and chronic GVHD may occur outside of these designated periods. Patients who demonstrate progression of disease by day 5 or nonresponse by day 7 are considered to have corticosteroid resistance.

  - Acute GVHD manifestations include:
    - Classic maculopapular rash
    - Abdominal cramps with diarrhea
    - Rising serum bilirubin concentration
  - Chronic GVHD manifestations include:
    - Skin involvement resembling lichen planus or the cutaneous manifestations of scleroderma
    - Dry oral mucosa with ulcerations and sclerosis of the gastrointestinal tract
    - Rising serum bilirubin concentration
    - Decrease in lung function
    - Joint dysfunction

- Mild disease is treated with local/topical therapy to the affected organ systems. Moderate disease is treated with systemic steroids such as prednisone, 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. Corticosteroids are the primary treatment of cGVHD. Other therapies that may be used include calcineurin inhibitors, an mTOR inhibitor (everolimus or sirolimus), infliximab, rituximab, mycophenolate mofetil and imatinib. The prophylaxis and management of graft versus host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation from 2020 recommend steroids as the first-line treatment for newly diagnosed cGVHD. These guidelines mention that there are no data available allowing the comparison of the efficacy of different second-line treatment options for chronic GVHD, and no indirect comparisons are possible. Therefore, no standard second-line treatment for chronic GVHD exists. The most widely used components of second-line treatment for chronic GVHD, in addition to corticosteroids, are calcineurin inhibitors, extracorporeal photopheresis, ibrutinib (which is approved by the FDA), JAK inhibitors, mycophenolate mofetil, rituximab, mammalian target of rapamycin (mTOR) inhibitors, pentostatin, proteasome inhibitors, and tyrosine kinase inhibitors.

- The National Comprehensive Cancer Network (NCCN) Hematopoietic Cell Transplantation (HCT): Graft-Versus-Host Disease Guidelines version 1.2024 have indicated that Jakafi® is a category 1 recommended agent for steroid-

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refractory GVHD, both acute and chronic. All other agents are a category 2A including Rezurock® and Imbruvica®. Niktimvo has not been included in the NCCN guidelines at this time.

- The efficacy of Niktimvo is supported by the AGAVE-201 trial, a Phase II, open-label, randomized, multicenter study that evaluated the efficacy, safety, and tolerability of Niktimvo at three different doses in patients with allogenic hematopoietic stem cell transplant (aHSCT) with recurrent or refractory active cGVHD who had received at least two lines of systemic therapy. 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 (corticosteroids, calcineurin inhibitors, or sirolimus/everolimus) 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 overall response rate within the first six months of treatment was 75% (95% CI: 64, 84).
        - 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.
    - 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).

References:

1. Niktimvo [prescribing information]. Wilmington, DE. Incyte Corporation. August, 2024
2. National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology for Hematopoietic Cell Transplantation (HCT): Graft-Versus-Host Disease Guidelines version 1.2024. NCCN.org
3. IPD analytics – New Drug Review – Niktimvo (axatilimab). Payer & Provider Insights. IPDAnalytics.com
4. Incyte Press Release Incyte and Syndax Announce U.S. FDA Approval of Niktimvo™ (axatilimab-csfr) for the Treatment of Chronic Graft-Versus-Host Disease (GVHD) | Incyte/ August 14, 2024.

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<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>No</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

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