Blue Cross Blue Shield Blue Care Network of Michigan

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Retired
Effective Date: 02/02/2023

Unituxin® (dinutuximab)

HCPCS: J9999, J3490, J3590, C9399

Policy:

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

A. Criteria:
   a. FDA approved age
   b. FDA approved indication
   c. High risk is defined as any of the following
      i. Any child who is stage 2A or 2B, older than 1 year, whose cancer has extra copies of the MYCN gene and unfavorable histology
      ii. Any child who is stage 3, not yet 1 year old, whose cancer has extra copies of the MYCN gene
      iii. Any child who is stage 3, older than 1 year, whose cancer has extra copies of the MYCN gene
      iv. Any child who is stage 3, older than 18 months, whose cancer has unfavorable histology
      v. Any child who is stage 4, whose cancer has extra copies of the MYCN gene regardless of age
      vi. Any child who is stage 4 and older than 18 months
      vii. Any child who is stage 4 and between 12 and 18 months old whose cancer has extra copies of the MYCN gene, unfavorable histology, and/or normal DNA ploidy (a DNA index of 1)
      viii. Any child who is stage 4S (not yet 1 year old), whose cancer has extra copies of the MYCN gene
   d. Must be used in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retionoic acid (RA)
   e. Must have achieved at least a partial response to prior first-line multiagent, multimodality therapy (i.e., cytotoxic chemotherapy (e.g., doxorubicin, cyclophosphamide, and vincristine), surgery, radiation, and stem cell transplant)

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 up to 6 months at a time

***Note: Coverage 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:

- Unituxin is a GD2-binding monoclonal antibody indicated, in combination with granulocyte colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the treatment of pediatric patients with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy.

- High-risk neuroblastoma is defined by the Childrens Oncology Group as one of the following:

    - Any child who is stage 2A or 2B, older than 1 year, whose cancer has extra copies of the MYCN gene and unfavorable histology

    - Any child who is stage 3, not yet 1 year old, whose cancer has extra copies of the MYCN gene

    - Any child who is stage 3, older than 1 year, whose cancer has extra copies of the MYCN gene

    - Any child who is stage 3, older than 18 months, whose cancer has unfavorable histology

    - Any child who is stage 4, whose cancer has extra copies of the MYCN gene regardless of age

    - Any child who is stage 4 and older than 18 months

    - Any child who is stage 4 and between 12 and 18 months old whose cancer has extra copies of the MYCN gene, unfavorable histology, and/or normal DNA ploidy (a DNA index of 1)

    - Any child who is stage 4S (not yet 1 year old), whose cancer has extra copies of the MYCN gene

- Safety and efficacy were evaluated in a randomized, open-label, multicenter trial conducted in 226 pediatric patients with high-risk neuroblastoma. All patients had received prior therapy consisting of induction combination chemotherapy, maximum feasible surgical resection, myeloablative consolidation chemotherapy followed by autologous stem cell transplant, and radiation therapy to residual soft tissue disease. Patients were required to have at least a partial response to their first-line multiagent, multimodality therapy. Patients were randomized to receive up to five cycles of Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF) or interleukin-2 (IL-2) plus 13-cis-retinoic acid followed by one cycle of retinoic acid alone or to six cycles of 13-cis-retinoic acid arm. Unituxin was administered at a dose of 17.5 mg/m^2/day on four consecutive days. The primary outcome was event-free survival (EFS), defined as the time from randomization to the first occurrence of relapse, progressive disease, secondary malignancy, or death. The Unituxin arm experienced events in 29% of patients compared to 44% in the retinoic acid arm (p-value = 0.01).

- Use of Unituxin past 5 cycles has not been studied and therefore the medication should not be given once the 5 month treatment duration has concluded.

References:

1. Unituxin [prescribing information]. Silver Spring, MD: United Therapeutics Corp.; September 2020.
2. Parihk N, Howard S, Chantada G, et al. Clinical Practice Guidelines – SIOP-PODC Adapted Risk Stratification and Treatment Guidelines: Recommendations for Neuroblastoma in Low- and Middle-Income Settings. *Pediatric Blood & Cancer.* Wiley Online Library, 2015.
3. Graham DK, Craddock JA, Quinones RR, Keating AK, Maloney K, Foreman NK, Giller RH, Greffe BS. Neoplastic Disease. In: Hay WW, Jr., Levin MJ, Deterding RR, Abzug MJ. eds. *CURRENT Diagnosis & Treatment: Pediatrics, 22e*. New York, NY: McGraw-Hill; 2013. http://accessmedicine.mhmedical.com.proxy.lib.umich.edu/content.aspx?bookid=1016&Sectionid=61604063. Accessed May 07, 2015.
4. Akram A. Highmark Preliminary Medication Review: New Molecular Entity – Antineoplastics: Monoclonal Antibody, dinutuximab (Unituxin®) [United Therapeutics Corporation]. March 2015.
5. Saliba C. OmedaRx Preliminary Medication Assessments: Cancer: dinutuximab (Unituxin™) [United Therapeutics]. March 2015.
6. Saliba C. InsightsRx Comprehensive Medication Assessments: Cancer / Pediatric High-Risk Neuroblastoma. Focus on dinutuximab (Unituxin™). May 2015.

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<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.1</td><td>Effective Date: 02/02/2023</td><td>Retiring policy as drug will no longer be part of the prior authorization program</td></tr>
<tr><td>2.0</td><td>Effective Date: 10/06/2022</td><td>Updated approval length to allow for FDA recommended dosing or up to 6 months at a time</td></tr>
<tr><td>1.9</td><td>Effective Date: 10/07/2021</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.8</td><td>Effective Date: 12/01/2020</td><td>UM medical management system update for BCBS
<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>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.7</td><td>Effective Date: 10/08/2020</td><td>Annual Review</td></tr>
<tr><td>1.6</td><td>Effective Date: 01/01/2020</td><td>UM medical management system update for BCNA and MAPPO
<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>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.5</td><td>Effective Date: 11/07/2019</td><td>Annual Review of Medical Policy</td></tr>
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<tr><td>1.4</td><td>Effective Date: 08/01/2019</td><td>UM medical management system update for BCN
<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>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.3</td><td>Effective Date: 11/01/2018</td><td>Criteria updated per oncology vendor</td></tr>
<tr><td>1.2</td><td>Effective Date: 11/09/2017</td><td>Annual Review of Medical Policy</td></tr>
<tr><td>1.1</td><td>Effective Date: 11/10/2016</td><td>Annual Review of Medical Policy
No criteria changes</td></tr>
<tr><td>1.0</td><td>Effective Date: 08/13/2015</td><td>New Drug Review
<table><tr><th>Line of Business</th><th>PA Required (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.*