09-J2000-42

Original Effective Date: 08/15/15

Reviewed: 09/10/25

Revised: 10/15/25

Subject: Dinutuximab (Unituxin™)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Dinutuximab (Unituxin™) is a chimeric monoclonal antibody that binds to the glycolipid disialoganglioside (GD2). This glycolipid is expressed on neuroblastoma cells and on normal cells of neuroectodermal origin, including the central nervous system and peripheral nerves. GD2 binding induces cell lysis of GD2-expressing cells through antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).

Dinutuximab (Unituxin™) is indicated, in combination with granulocyte-macrophage 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.

Neuroblastoma is the most common extracranial solid tumor in childhood with 90% of cases diagnosed at younger than 5 years of age. The yearly incidence is approximately 10.54 cases per 1 million in children younger than 15 years and prevalence about 1 case per 7,000 live births. The neuroblastoma originates in the adrenal medulla or the paraspinal sites where sympathetic nervous system tissue resides. Patients commonly present with an abdominal mass and up to 70% have metastatic disease at diagnosis. Prognosis depends on patient age, site of the primary tumor, tumor histology, regional lymph node involvement, stage of disease, response to treatment, and biological features.

The Children's Oncology Group (COG) Neuroblastoma Risk Grouping is one of the risk stratification systems used to determine treatment. The risk system is based on the patient age at diagnosis, biological characteristics of the tumor (*MYCN* oncogene status, histopathology classification, tumor DNA index), and stage of the tumor based on the International Neuroblastoma Stage System (INSS). Patients are classified as low, intermediate, or high risk. For patients determined to have high-risk neuroblastoma, treatment is generally divided into three phases: induction, consolidation, and

maintenance. Induction therapy includes chemotherapy followed by surgical resection of the primary tumor. The consolidation phase is characterized by myeloablative chemotherapy and hematopoietic stem cell transplantation (HSCT). Radiation therapy is also performed in the consolidation phase before, during or after myeloablative therapy. Agents used in the maintenance phase include differentiating therapy (oral isotretinoin) and immunotherapy (anti-GD2 monoclonal antibody, interleukin-2/GM-CSF).

POSITION STATEMENT:

Initiation of dinutuximab (Unituxin™) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. High-risk neuroblastoma
    a. When used for **ONE** of the following:
        i. When used with isotretinoin (with or without interleukin-2 (aldesleukin))
        ii. When used with irinotecan (with or without temozolomide)
    b. Therapy includes a granulocyte-macrophage colony-stimulating factor (sargramostim)
    c. Dose does not exceed **ONE** of the following:
        i. 70 mg/m^2 (17.5 mcg/m^2/day) every 24 days for a maximum of 5 cycles
        ii. Dose and frequency for the indication is supported by NCCN Compendium or standard reference compendia (Table 1 or Table 2)
2. Other FDA-approved or NCCN supported diagnosis (Table 1)
    a. When **ONE** of the following is met:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
        ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation (Table 1)
    b. Dose and frequency for the indication is supported by NCCN Compendium or standard reference compendia (Table 1 or Table 2)

Duration of Approval: 6 months

Table 1

NCCN Categories of Evidence Consensus	
Category 1	Based upon high-level evidence; there is uniform NCCN consensus that the intervention is appropriate
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate
Category 2B	Based upon lower-level evidence, there NCCN consensus that the intervention is appropriate
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Table 2

Other compendia	
Compendium	Covered Uses†
AHFS-DI	Narrative text is supportive
Clinical Pharmacology	Narrative text is supportive
Lexicomp	Evidence rating A, B or G
Thomson Micromedex DrugDex	Meets requirements for **BOTH** of the following: • Strength of recommendation: Class I (Recommended) or IIa (Recommended, In Most Cases) • Efficacy: Class I (Effective) or IIa (Evidence Favors Efficacy)
†If covered use criteria are not met, the request should be denied. AHFS-DI, American Hospital Formulary Service Drug Information; For additional information regarding designated compendia, please refer to the "Definitions" section.	

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- The recommended dose of dinutuximab (Unituxin™) is 17.5 mg/m^2/day administered as an infusion intravenously over 10- 20 hours for 4 consecutive days for a maximum of 5 cycles. Cycles 1, 3, and 5 are each 24 days in duration and cycles 2 and 4 are each 32 days in duration. Initiate at an infusion rate of 0.875 mg/m^2/hour for 30 minutes and then gradually increase as tolerated to a maximum of 1.75 m/m^2/hour.
- Verify that patients have adequate hematologic, respiratory, hepatic, and renal function prior to initiating each course of dinutuximab (Unituxin™).
- Administer required premedication and hydration prior to initiation of each infusion.

Dose Adjustments

- Manage adverse reactions by infusion interruption, infusion rate reduction (50%), dose reduction, or permanent discontinuation of dinutuximab (Unituxin™).
- Permanent discontinuation of dinutuximab (Unituxin™) is recommended for the following adverse reactions:
    - Grade 3 or 4 anaphylaxis
    - Grade 3 or 4 serum sickness
    - Grade 3 pain unresponsive to maximum support measures
    - Grade 4 sensory neuropathy or Grade 3 sensory neuropathy that interferes with daily activities for more than 2 weeks
    - Grade 2 peripheral motor neuropathy
    - Subtotal or total vision loss

- Grade 4 hyponatremia despite appropriate fluid management

Drug Availability

- 17.5 mg/5 mL (3.5 mg/mL) solution in a single-use vial.

PRECAUTIONS:

Boxed Warning

- SERIOUS INFUSION REACTIONS AND NEUROPATHY

  Life-threatening infusion adverse reactions may occur and IV prehydration (0.9% Sodium Chloride) and premedication with antihistamines and antipyretics should be administered. Immediately interrupt for severe infusion reactions and permanently discontinue for anaphylaxis.

  Severe neuropathic pain may occur and opioids should be administered prior to, during and for 2 hours following completion of the infusion. Severe peripheral sensory neuropathy ranged from 2-9% in patients with neuroblastoma, and severe motor neuropathy was observed in adults. Discontinue use for severe unresponsive pain, severe sensory neuropathy, or moderate to severe peripheral neuropathy.

Contraindications

- History of anaphylaxis to dinutuximab (Unituxin™).

Precautions/Warnings

- Capillary leak syndrome and hypotension: Administer prehydration with 0.9% Sodium Chloride IV infusion one hour prior to initiation of therapy and monitor patients closely. The infusion may require interruption, modification, or discontinuation.
- Infection: Interrupt until resolution of systemic infection.
- Neurological disorders of the Eye: Interrupt for dilated pupil with sluggish light reflex or other visual disturbances and permanently discontinue for recurrent eye disorders or loss of vision.
- Bone marrow suppression: Monitor peripheral blood counts during therapy.
- Electrolyte abnormalities: Monitor serum electrolytes closely.
- Atypical hemolytic uremic syndrome: Permanently discontinue and institute supportive management.
- Embryo-Fetal toxicity: May cause fetal harm. Advise females of reproductive potential of potential risk to a fetus and to use effective contraception.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J1246	Injection, dinutuximab, 0.1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C49.0 – C49.9	Malignant neoplasm of connective and soft tissue
C72.9	Malignant neoplasm of central nervous system, unspecified
C74.0 – C74.9	Malignant neoplasm of adrenal gland
C80.0	Disseminated malignant neoplasm without specification of site
C80.1	Other malignant neoplasm without specification of site

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the guideline creation.

DEFINITIONS:

Partial Response in Neuroblastoma: 50 to 90% reduction of primary tumor; 50% or greater reduction in measureable sites of metastases; 0-1 bone marrow samples with tumor; number of positive bone sites decreased by greater than 50%.

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.;2025. URL www.clinicalpharmacilogy-ip.com. Accessed 08/28/25.
2. Dinutuximab. In McEvoy GK, editor. AHFS drug information 2016 [monograph on the internet]. Bethesda (MD): American Society of Health-System Pharmacists; 2016 [cited 2016 June 16].
3. Micromedex® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 08/28/25.

4. National Cancer Institute: Neuroblastoma. http://www.cancer.gov/types/neuroblastoma/hp/neuroblastoma-treatment-pdq#section/_1 Accessed 08/28/25.
5. National Cancer Institute: Partial response in neuroblastoma. http://nciterms.nci.nih.gov/ncitbrowser/ConceptReport.jsp?dictionary=NCI_Thesaurus&version=15.05d&code=C103313&ns=NCI_Thesaurus&key=n1442942250&b=1&n=null. Accessed 6/26/2015.
6. Unituxin (dinutuximab) Injection. Silver Spring, MD: United Therapeutics Corp; Sept 2020.
7. Yu AL, Gilman AL, Ozkaynak MF et al. Anti-GD2 Antibody with GM-CSF, Interleukin-2, and Isotretinoin for Neuroblastoma. *N Engl J Med*. 2010; 363: 1324-1334.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 09/10/25.

GUIDELINE UPDATE INFORMATION:

08/15/15	New Medical Coverage Guideline.
11/01/15	Revision: ICD-9 Codes deleted.
08/15/16	Review and revision to guideline; consisting of updating position statement, coding and references.
01/01/24	Revision: Added HCPCS code J1246 and deleted codes C9399 and J9999.
10/15/25	Review and revision to guideline; consisting of updating the position statement to include FDA-label or NCCN supported diagnosis.