Evolent Clinical Guideline 3145 for Unituxin™ (dinutuximab)

Guideline Number:	Applicable Codes	
Evolent_CG_3145		
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Original Date:	**Last Revised Date:**	**Implementation Date:**
February 2020	July 2025	July 2025

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STATEMENT

Purpose

To define and describe the accepted indications for Unituxin (dinutuximab) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Neuroblastoma

- The member has unresectable high-risk neuroblastoma AND
- High risk is defined as members who are older than 18 months of age and have disseminated disease, or localized disease with unfavorable markers such as MYCN amplification (*see Attachment A*) AND
- The member is in a hospital/acute care setting to mitigate potential risks of serious infusion reactions, capillary leak syndrome, and hypotension AND
- Unituxin (dinutuximab) may be used in combination with chemotherapy or 13-cis-retinoic acid (isotretinoin), with or without granulocyte-macrophage colony-stimulating factor (sargramostim).

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - History of anaphylaxis to dinutuximab or any component of the formulation.
- US Boxed Warning
  - Infusion reactions
    - Serious and potentially life-threatening infusion reactions occurred in 26% of patients treated with dinutuximab. Administer required prehydration and premedication, including antihistamines, prior to each dinutuximab infusion. Monitor patients closely for signs and symptoms of an infusion reaction during and for at least 4 hours following completion of each dinutuximab infusion. Immediately interrupt dinutuximab for severe infusion reactions and permanently discontinue dinutuximab for anaphylaxis.
  - Neurotoxicity
    - Dinutuximab causes serious neurologic adverse reactions including severe neuropathic pain and peripheral neuropathy.
    - Severe neuropathic pain occurs in the majority of patients. Administer intravenous opioid prior to, during, and for 2 hours following completion of the dinutuximab infusion. In clinical studies of patients with high-risk neuroblastoma, grade 3 peripheral sensory neuropathy occurred in 2% to 9% of patients. In clinical studies of dinutuximab and related GD2-binding antibodies, severe motor neuropathy has occurred. Resolution of motor neuropathy did not occur in all cases. Discontinue dinutuximab for severe unresponsive pain, severe sensory neuropathy, and moderate to severe peripheral motor neuropathy.

EXCLUSION CRITERIA

- Unituxin (dinutuximab) is being used after disease progression with the same regimen or prior anti-disialoganglioside (GD2) antibody therapy [e.g., Danyelza (naxitamab)].
- Dosing exceeds single dose limit of Unituxin (dinutuximab) 17.5 mg/m^2.
- Treatment exceeds the maximum duration limit of 5 cycles.
- Investigational use of Unituxin (dinutuximab) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful

outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.

- Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J9999 - dinutuximab

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
July 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1387 Unituxin (dinutuximab) • Updated references
July 2024	• Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Yu AL, et al. Long-Term Follow-up of a Phase III Study of ch14.18 (Dinutuximab) + Cytokine Immunotherapy in Children with High-Risk Neuroblastoma: COG Study ANBL0032. *Clin Cancer Res*. 2021 Apr 15;27(8):2179-2189. doi: 10.1158/1078-0432.CCR-20-3909.
2. Cicek F, et al. Impact of IL-2 on Treatment Tolerance in Patients With High-Risk Neuroblastoma Treated With Dinutuximab Beta-Based Immunotherapy. *Front Pediatr*. 2020 Dec 16;8:582820. doi: 10.3389/fped.2020.582820.
3. Ladenstein R, et al. Interleukin 2 with anti-GD2 antibody ch14.18/CHO (dinutuximab beta) in patients with high-risk neuroblastoma (HR-NBL1/SIOPEN): a multicentre, randomised, phase 3 trial. *Lancet Oncol*. 2018 Dec;19(12):1617-1629. doi: 10.1016/S1470-2045(18)30578-3..
4. Federico SM, et al. A pilot induction regimen incorporating dinutuximab and sargramostim for the treatment of newly diagnosed high-risk neuroblastoma: A report from the Children's Oncology Group. *Journal of Clinical Oncology*. 2022 June 02;40(16). https://doi.org/10.1200/JCO.2022.40.16_suppl.10003.
5. Mody R, et al. Irinotecan, Temozolomide, and Dinutuximab With GM-CSF in Children With Refractory or Relapsed Neuroblastoma: A Report From the Children's Oncology Group. *J Clin Oncol*. 2020 Jul 1;38(19):2160-2169. doi: 10.1200/JCO.20.00203..
6. Unituxin prescribing information. United Therapeutics Corp. Research Triangle Park, NC 2020.
7. Clinical Pharmacology Elsevier Gold Standard 2025.
8. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
9. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
10. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.

11. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
12. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
13. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.

ATTACHMENT A: CHILDREN'S ONCOLOGY GROUP NEUROBLASTOMA RISK STRATA

Children's Oncology Group neuroblastoma risk strata (version 1)

Risk	Stage	Age	*MYCN* status	DNA ploidy	INPC	Other
Low*	1	Any	Any	Any	Any	
	2a/2b	Any	Not amp	Any	Any	Resection ≥50%
	4s	<365 days	Not amp	DI >1	FH	Asymptomatic
Intermediate¶	2a/2b	0-12 years	Not amp	Any	Any	Biopsy or resection <50%
	3	<547 days	Not amp	Any	Any	
	3	≥547 days - 12 years	Not amp	Any	FH	
	4	<365 days	Not amp	Any	Any	
	4	365 - <547 days	Not amp	DI >1	FH	
	4s	<365 days	Not amp	Any	Any	Symptomatic
	4s	<365 days	Not amp	DI = 1	Any	Asymptomatic or symptomatic
	4s	<365 days	Not amp	Any	UH	Asymptomatic or symptomatic
	4s	<365 days	Missing	Missing	Missing	Too sick for biopsy
High$^{\Delta}$	2a/2b	Any	Amp	Any	Any	Any degree of resection
	3	Any	Amp	Any	Any	
	3	≥547 days	Not amp	Any	UH	
	4	<365 days	Amp	Any	Any	
	4	365 - <547 days	Amp	Any	Any	
	4	365 - <547 days	Any	DI = 1	Any	
	4	365 - <547 days	Any	Any	UH	
	4	≥547 days	Any	Any	Any	
	4s	<365 days	Amp	Any	Any	Asymptomatic or symptomatic

INPC: International Neuroblastoma Pathology Classification; FH: favorable histology; UH: unfavorable histology; Amp: amplified; DI: DNA index.

* Low-risk group as defined in Children's Oncology Group trial ANBL00B1.

¶ Intermediate-risk group as defined in Children's Oncology Group trial ANBL0531.

Δ High-risk group as defined in Children's Oncology Group trial ANBL0532.

UpToDate®

UpToDate accessed on 6/27/2025: https://www.uptodate.com/contents/treatment-and-prognosis-of-neuroblastoma?search=treatment%20of%20neuroblastoma&source=search_result&selectedTitle=1~121&usage_type=default&display_rank=1#H21