

Pepaxto® (melphalan flufenamide) (Intravenous)

Document Number: IC-0595

Last Review Date: 10/01/2021

Date of Origin: 04/06/2021

Dates Reviewed: 04/2021, 07/2021, 08/2021, 10/2021

I. Length of Authorization

Coverage is provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Pepaxto 20 mg single-dose vial: 2 vials every 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 40 mg (billable units) on Day 1 of each 28-day treatment cycle

III. Initial Approval Criteria¹

Coverage is provided in the following conditions:

- Patient is at least 18 years or older; **AND**

Universal Criteria

- Patient does not have a history of serious allergic reactions to melphalan; **AND**
- Therapy will NOT be used as a conditioning regimen for transplant; **AND**

Multiple Myeloma (MM) †¹⁻⁵

- Patient has relapsed, refractory, or progressive disease; **AND**
- Used in combination with dexamethasone; **AND**
- Patient received at least four prior lines of therapy and is refractory to a proteasome inhibitor (e.g., bortezomib, carfilzomib, etc.) an immunomodulatory agent (e.g., lenalidomide, pomalidomide, etc.) and a CD38-directed antibody (e.g., daratumumab, isatuximab, etc.); **AND**
- Provider attests to discussing with patient the possible risks and benefits of therapy with Pepaxto in the context of other treatments and will monitor therapy accordingly*

***Note:** On July 27, 2021, the FDA issued a CDER alert to patients and health care professionals that the pivotal study OCEAN, Study OP-103 evaluating Pepaxto (melphalan flufenamide) with dexamethasone to treat patients with multiple myeloma showed an increased risk of death. As a result, the FDA encouraged health care professionals to review patients' progress on Pepaxto and discuss the risks of continued administration with each patient in the context of other treatments. Also, patients currently receiving Pepaxto were advised to discuss with their health care professional the risks and benefits of receiving Pepaxto.

† FDA indication(s); ‡ Compendia recommended indication(s); Φ Orphan Drug

IV. Renewal Criteria^{1,5}

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include severe thrombocytopenia, severe neutropenia, severe anemia, clinically significant infections, secondary malignancies, etc.; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Provider attests to discussing with the patient the risks and benefits of continued therapy with Pepaxto in the context of other treatments*

***Note:** On July 27, 2021, the FDA issued a CDER alert to patients and health care professionals that the pivotal study OCEAN, Study OP-103 evaluating Pepaxto (melphalan flufenamide) with dexamethasone to treat patients with multiple myeloma showed an increased risk of death. As a result, the FDA encouraged health care professionals to review patients' progress on Pepaxto and discuss the risks of continued administration with each patient in the context of other treatments. Also, patients currently receiving Pepaxto were advised to discuss with their health care professional the risks and benefits of receiving Pepaxto.

V. Dosage/Administration

Indication	Dose
Multiple Myeloma	The recommended dose of Pepaxto is 40 mg administered as a single intravenous infusion over 30 minutes on day 1 of each 28-day treatment cycle, in combination with dexamethasone, until disease progression or until unacceptable toxicity.

VI. Billing Code/Availability Information

HCPCS Code:

- J9999 – Not otherwise classified, antineoplastic drug (*Discontinue use on 10/01/2021*)
- J9247 – Injection, melphalan flufenamide, 1mg; 1 billable unit = 1 mg (*Effective 10/01/2021*)

- C9080 – Injection, melphalan flufenamide hydrochloride, 1 mg; 1 billable unit = 1 mg
(hospital outpatient use only) (Discontinue use on 10/01/2021)

NDC:

- Pepaxto 20 mg lyophilized powder in a single-dose vial for reconstitution: 73657-0020-xx

VII. References

1. Pepaxto [package insert]. Waltham, MA; Oncopeptides, Inc.; February 2021. Accessed May 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for melphalan flufenamide. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed May 2021
3. Mateos MV, Oriol A, Larocca A, et al. Clinical Activity of Melflufen in Patients with Triple-Class Refractory Multiple Myeloma and Poor-Risk Features in an Updated Analysis of HORIZON (OP-106), a Phase 2 Study in Patients with Relapsed/Refractory Multiple Myeloma Refractory to Pomalidomide and/or Daratumumab. Blood. 2019 Nov 134;suppl(1):1883. <https://doi.org/10.1182/blood-2019-124825>.
4. Delforouh M, Strese S, Wickström M, et al. In vitro and in vivo activity of melflufen (J1) in lymphoma. BMC Cancer. 2016; 16: 263.
5. Schjesvold F, Robak P, Pour L, Aschan J, Sonneveld P. OCEAN: a randomized Phase III study of melflufen + dexamethasone to treat relapsed refractory multiple myeloma. Future Oncol. 2020 Apr;16(11):631-641. doi: 10.2217/fon-2020-0024. Epub 2020 Mar 6. PMID: 32141766.
6. Richardson PG, Oriol A, Larocca A, et al. Melflufen and Dexamethasone in Heavily Pretreated Relapsed and Refractory Multiple Myeloma. Journal of Clinical Oncology 2021 39:7, 757-767.
7. Ocio EM, Efebera YA, Hájek R, et al. ANCHOR (OP-104): Melflufen Plus Dexamethasone (dex) and Daratumumab (dara) or Bortezomib (BTZ) in Relapsed/Refractory Multiple Myeloma (RRMM) Refractory to an IMiD and/or a Proteasome Inhibitor (PI) - Updated Efficacy and Safety. Blood (2020) 136 (Supplement 1): 9–10.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse

C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
D47.2	Monoclonal gammopathy
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC