# Pepaxto® (melphalan flufenamide)
## (Intravenous)

Document Number: IC-0595

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**Dates Reviewed: 04/2021, 07/2021, 08/2021, 10/2021, 07/2022**

## I. Length of Authorization

Coverage is provided for 6 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 billable units (40 mg) on Day 1 of each 28-day treatment cycle

## III. Initial Approval Criteria[1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

**Universal Criteria** [1]

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

**Multiple Myeloma (MM) † Φ** [1-4]

- Patient has relapsed or refractory 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.*

❖***Note from the manufacturer: As of 10/22/21, Pepaxto was withdrawn from the US market, and is no longer available for new prescriptions.***

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

## IV. Renewal Criteria [1,4]

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.*

❖***Note from the manufacturer: As of 10/22/21, Pepaxto was withdrawn from the US market, and is no longer available for new prescriptions.***

## V. Dosage/Administration [1]

| 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:

- J9247 – Injection, melphalan flufenamide, 1mg; 1 billable unit = 1 mg

NDC:

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

❖*Note from the manufacturer: As of 10/22/21, Pepaxto was withdrawn from the US market, and is no longer available for new prescriptions.*

## VII. References


1. Pepaxto [package insert]. Waltham, MA; Oncopeptides, Inc.; February 2021. Accessed June 2022.
2. 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.
3. Delforoush M, Strese S, Wickström M, et al. In vitro and in vivo activity of melflufen (J1)in lymphoma. BMC Cancer. 2016; 16: 263.
4. 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.
5. 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.
6. 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 |
| 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), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/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/LCA): 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 |