Utilization Review Policy 252

POLICY: Oncology (Injectable) – Pepaxto Utilization Review Medical Policy
- Pepaxto® (melphalan flufenamide intravenous infusion – Oncopeptides)

EFFECTIVE DATE: 07/01/2021
LAST REVISION DATE: 03/10/2021 selected revision 10/27/2021

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW

Pepaxto, an alkylating drug, is indicated in combination with dexamethasone, for treatment of adults with relapsed or refractory **multiple myeloma**, who have received at least four prior lines of therapy, and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody. Pepaxto is not recommended for use as a conditioning regimen for transplant.

The FDA granted accelerated approval to Pepaxto in February 2021 with the condition that the OCEAN trial is conducted as a confirmatory trial.[4] OCEAN showed an increased risk of death with Pepaxto + low-dose dexamethasone in patients with relapsed or refractory multiple myeloma following two to four lines of prior therapy and in patients who were resistant to Revlimid in the last line of therapy. Thus, FDA has suspended enrollment in OCEAN and other ongoing Pepaxto clinical trials.[5] Based on dialogue with FDA, the manufacturer has withdrawn Pepaxto from the market. Pepaxto will continue to be available to patients currently taking it who have achieved benefit with the drug.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Pepaxto. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the criteria and dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Pepaxto, as well as the monitoring required for adverse events and long-term efficacy, approval requires Pepaxto to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Pepaxto is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Multiple Myeloma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):
   - **A)** The patient is currently receiving Pepaxto; AND
   - **B)** Patient is ≥ 18 years of age; AND
   - **C)** The medication will be used in combination with dexamethasone; AND

D) Patient has tried at least four regimens for multiple myeloma; AND

E) Among the previous therapies tried, the patient has received at least one drug from each of the following classes (i, ii, and iii):

i. Proteasome inhibitor; AND
Note: Examples include Velcade (bortezomib injection), Kyprolis (carfilzomib infusion), Ninlaro (ixazomib capsules).

ii. Immunomodulatory drug; AND
Note: Examples include Revlimid (lenalidomide capsules), Pomalyst (pomalidomide capsules), Thalomid (thalidomide capsules).

iii. Anti-CD38 monoclonal antibody; AND
Note: For example, Darzalex (daratumumab infusion), Darzalex Faspro (daratumumab and hyaluronidase-fihj subcutaneous injection), or Sarclisa (isatuximab-irfc infusion).

F) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 40 mg intravenously administered not more frequently than once per 28-day cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Pepaxto is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Pepaxto [prescribing information]. Waltham, MA: Oncopeptides; February 2020.
2. The NCCN Drugs and Biologics Compendium. © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 4, 2021. Search term: Pepaxto, melphalan.
3. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (Version 3.2020 – March 10, 2020). © 2020 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 18, 2020.
4. FDA alerts patients and health care professionals about clinical trial results showing an increased risk of death associated with Pepaxto (melphalan flufenamide) [press release]. Food and Drug Administration; July 28, 2021. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-patients-and-health-care-professionals-about-clinical-trial-results-showing-increased. Accessed on October 27, 2021.
5. Oncopeptides withdraws Pepaxto in US, scale down organization and focus on R&D [press release]. Oncopeptides; October 22, 2021. Available at: https://www.oncopeptides.com/en/media/press-releases/oncopeptides-withdraws-pepaxto-in-us-scale-down-organization-and-focus-on-rd. Accessed on October 27, 2021.

HISTORY

Type of Revision	Summary of Changes	Review Date
New policy	--	03/10/2021
Selected Revision	**Multiple Myeloma:** Due to withdrawal from the market, a requirement was added to limit approval to a patient who is currently receiving Pepaxto.	10/27/2021