

Medical Drug Clinical Criteria

Subject:	Pepaxto (melphalan flufenamide; melflufen)		
Document #:	CC-0191	Publish Date:	09/18/2023
Status:	Reviewed	Last Review Date:	08/18/2023

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Overview

This document addresses the use of Pepaxto (melphalan flufenamide). Pepaxto is a peptide-drug conjugate alkylating drug FDA indicated in combination with dexamethasone, for the treatment of adult patients 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 has been removed from the market and will be obsolete on 10/27/2023. This policy will remain active until then.

Dosing and Administration

The recommended dosage of Pepaxto is 40 mg administered intravenously over 30 minutes on Day 1 of each 28-day cycle until disease progression or until unacceptable toxicity. Administer dexamethasone 40 mg orally or intravenously on Days 1, 8, 15 and 22 of each cycle. For patients 75 years of age or older, reduce the dose of dexamethasone to 20 mg. Refer to the prescribing information for dexamethasone for additional dosing information.

Definitions and Measures

CD-38 Monoclonal Antibody: Multiple myeloma (MM) cells have high levels of CD38 expression, which makes CD38 a target for therapeutic antibodies targeting cell surface molecules in MM. Daratumumab (Darzalex) and isatuximab-irfc (Sarclisa) are examples.

Chemotherapy: Medical treatment of a disease, particularly cancer, with drugs or other chemicals.

Immunomodulatory agent: Immunomodulatory drugs (IMiDs) are structural and functional analogs of thalidomide that have potent immunomodulatory properties, antimyeloma activity and better tolerability profile. IMiDs possess antiangiogenic and direct tumoricidal properties and have shown activity against various hematologic malignancies. Lenalidomide is an example.

Multiple Myeloma: Is an infiltration of plasma cells into the bone or other organs producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow and can result in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathologic fractures.

Proteasome inhibitor: Proteasome inhibitors are drugs that block the action of proteasomes, cellular complexes that break down proteins. Bortezomib (Velcade), carfilzomib (Kyprolis), and ixazomib (Ninlaro) are examples.

Refractory disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Pepaxto (melphalan flufenamide)

Requests for Pepaxto (melphalan flufenamide) may be approved if the following criteria are met:

- I. Individual is 18 years of age or older (Label; NCCN 2A); **AND**
- II. Individual has a diagnosis of relapsed or refractory multiple myeloma; **AND**
- III. Individual is using in combination with dexamethasone (IV or oral); **AND**
- IV. Individual has received at least four prior lines of therapy; **AND**
- V. Individual's disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody; **AND**
- VI. Individual has an ECOG status of 0-2.

Requests for Pepaxto may not be approved when the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9247 Injection, melphalan flufenamide, 1 mg [Pepaxto]

ICD-10 Diagnosis

C90.00 Multiple myeloma not having achieved remission

C90.02 Multiple myeloma in relapse

Document History

Revised: 08/18/2023

Document History:

- 08/18/2023 – Annual Review: No changes. Coding Reviewed: No changes.
- 08/19/2022 – Annual Review: No changes. Coding reviewed: Removed ICD-10-CM C90.00-C90.02. Added ICD-10-CM C90.00, C90.02.
- 08/20/2021 - Annual Review: Update criteria with references. Coding reviewed: Added ICD-10-CM codes C90.00-C90.02. Effective 10/1/2021 Added J9247, Removed J34990, J9999, C9080.
- 03/15/2021 – Annual Review: Add new clinical criteria document for Pepaxto. Coding reviewed: Added HCPCS codes J3490, J9999, C9399. All diagnosis pend. Effective 7/1/2021 Added HCPCS C9080, Removed HCPCS C9399. Added ICD-10-CM C90.02.

References

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5. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Accessed on June 21, 2023.
 - a. Multiple Myeloma. V3.2023. Revised December 8, 2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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