Clinical Policy Title:	melphalan flufenamide; melflufen
Policy Number:	RxA.679
Drug(s) Applied:	Pepaxto®
Original Policy Date:	04/15/2021
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Pepaxto® is an alkylating drug 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.
This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Limitations of Use:

- Pepaxto® is not indicated and is not recommended for use as a conditioning regimen for transplant outside of controlled clinical trials

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
melphalan flufenamide; melflufen (Pepaxto®)	relapsed or refractory multiple myeloma (RRMM)	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.	40 mg IV every 28 days.

Dosage Forms

- Injection: 20 mg lyophilized powder in single-dose vial.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the provisions of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all):

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM);
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an oncologist;
4. Member 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;
5. Pepaxto® is prescribed in combination with dexamethasone;
6. Dose does not exceed 40 mg IV every 28 days;

Approval Duration
Commercial: 3 months
Medicaid: 3 months

II. Continued Therapy Approval

A. Multiple Myeloma (must meet all):

1. Member is currently receiving the medication that has been authorized by RxAdvance or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Dose does not exceed 40 mg IV every 28 days;

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
RRMM: Relapsed or Refractory Multiple Myeloma
IV: Intra Venous
CD38: Cluster of Differentiation 38

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug name	Dosing Regimen	Dose Limit/Maximum Dose
Blenrep® (belantamab mafodotin-blmf))	The recommended dosage is 2.5 mg/kg as an intravenous infusion over approximately 30 minutes once every 3 weeks	2.5 mg/kg (actual body weight) IV every 3 weeks.
Ninlaro® (ixazomib)	Recommended starting dose of 4 mg taken orally on Days 1, 8, and 15	4 mg/dose PO
Pomalyst® (pomalidomide)	4 mg per day taken orally on days 1-21 of repeated 28-day cycles until disease progression	4 mg/day PO
Farydak® (panobinostat)	20 mg, taken orally once every other day for 3 doses per week (on Days 1,3, 5, 8, 10, and 12) of Weeks 1 and 2 of each 21-day cycle for 8 cycles	20 mg/dose PO; 10 mg/dose PO if taking a strong CYP3A4 inhibitor

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Pepaxto® is contraindicated in patients with a history of serious hypersensitivity reaction to melphalan flufenamide or melphalan.

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Thrombocytopenia: Monitor platelets counts at baseline, during treatment, and as clinically indicated. Dose delay or dose reduction may be required to allow recovery of platelets.
- Neutropenia: Monitor neutrophil counts at baseline, during treatment and as clinically indicated. Monitor patients with neutropenia for signs of infection. Dose delay or dose reduction may be required to allow recovery of neutrophils.
- Anemia: Monitor red blood cell counts at baseline, during treatment, and as clinically indicated.

References

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11. Farydak® prescribing information Las Vegas, NV: Secura Bio, Inc; September 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/205353s000lbl.pdf. Accessed April 15, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	04/15/2021	06/10/2021