RXADVANCE
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Clinical Policy Title:	panobinostat
Policy Number:	RxA.127
Drug(s) Applied:	Farydak®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Panobinostat (Farydak®) is a histone deacetylase inhibitor. It is indicated, in combination with bortezomib and dexamethasone, for the treatment of patients with multiple myeloma (MM) who have received at least two (2) prior regimens, including bortezomib and an immunomodulatory agent. This indication is approved under accelerated approval based on progression free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
panobinostat (Farydak®)	Multiple Myeloma	20 mg PO every other day for 3 doses per week (on Days 1, 3, 5, 8, 10, and 12) of Weeks 1 and 2 for each 21-day cycle for 8 cycles. Consider continuing treatment for an additional 8 cycles for patients with clinical benefit who do not experience unresolved severe or medically significant toxicity (total treatment duration: up to 16 cycles [48 weeks]).	20 mg/dose

Dosage Forms

- Capsules: 10 mg, 15 mg, 20 mg

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.

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all)**:**

1. Diagnosis of multiple myeloma;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age 18 years of age or older;
4. Failure of at least two (2) prior regimens for multiple myeloma, including bortezomib and an immunomodulatory agent (e.g., dexamethasone), unless contraindicated or clinically significant

adverse effects are experienced;

5. Used in combination with one of the following (a, b, or c):*
   a. bortezomib and dexamethasone;
   b. carfilzomib (Kyprolis®); or
   c. lenalidomide (Revlimid®) and dexamethasone;

   **Prior authorization may be required for these agents.*
6. Request meets one of the following (a or b):
   a. Dose does not exceed six 20 mg doses per 21-day cycle for 16 cycles total;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy

A. Multiple Myeloma (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy.
2. Member is currently receiving panobinostat for a covered indication and has received this medication for at least 30 days;
3. Member is responding positively to therapy;
4. If used in combination with bortezomib and dexamethasone, member has not received more than 16 cycles (48 weeks) of therapy;
5. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed six 20 mg doses per 21-day cycle for 16 cycles total;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration
Commercial: 12 months
Medicaid: 12 months

Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MM: Multiple Myeloma
REMS: Risk Evaluation and Mitigation Strategy

APPENDIX B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name*	Dosing Regimen	Dose Limit/ Maximum Dose
Darzalex® (daratumumab)	16 mg/kg IV administered: *As monotherapy or in combination with lenalidomide/ dexamethasone*: weekly for weeks 1 to 8, then every 2 weeks for weeks 9 to 24, then every 4 weeks for week 25 onward until disease progression; *In combination with bortezomib/dexamethasone*: weekly for weeks 1 to 9, then every 3 weeks for weeks 10 to 24, then every 4 weeks for week 25 onward until disease progression.	Varies
Doxil® (liposomal doxorubicin)	30 mg/m^2 IV over 1 hour on day 4 repeated every 4 weeks; used in combination with bortezomib.	Varies
Empliciti™ (elotuzumab)	10 mg/kg IV every week for the first two cycles, then every 2 weeks thereafter until disease progression; used in combination with lenalidomide and dexamethasone.	Varies
Kyprolis® (carfilzomib)	20 mg/m^2 IV on two consecutive days each week for 3 weeks (Days 1, 2, 8, 9, 15 and 16) followed by a 12-day rest period (Days 17 to 28). Each 28-day period is considered one treatment cycle. If tolerated in cycle 1, the dose should be escalated to 27 mg/m^2 and in the subsequent cycles.	Varies
Ninlaro® (ixazomib)	4 mg PO on Days 1, 8, and 15 of a 28-day cycle; used in combination with lenalidomide and dexamethasone	4 mg/day
Pomalyst® (pomalidomide)	4 mg PO OD on days 1-21 of repeated 28-day cycles until disease progression; may be given in combination with dexamethasone.	4 mg/day
Revlimid® (lenalidomide)	25 mg PO OD on days 1-21 of repeated 28 day cycles; may be given in combination with dexamethasone.	25 mg/day
bortezomib (Velcade®)	1.3 mg/m^2 IV bolus or SC twice weekly, with at least 72 hours between doses (on days 1, 4, 8, 11, 22, 25, 29, and 32), for cycles 1 to 4;	Varies

	then once weekly for 6 weeks (on days 1, 8, 22, and 29) for cycles 5 through 9.	

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):
  - None reported

- Boxed Warning(s):
  - Severe diarrhea occurred in 25% of panobinostat treated patients. Monitor for symptoms, institute anti-diarrheal treatment, interrupt panobinostat and then reduce dose or discontinue panobinostat.
  - Severe and fatal cardiac ischemic events, severe arrhythmias, and ECG changes have occurred in patients receiving panobinostat . Arrhythmias may be exacerbated by electrolyte abnormalities. Obtain ECG and electrolytes at baseline and periodically during treatment as clinically indicated.

APPENDIX D: General Information

- The NCCN multiple myeloma guidelines panobinostat as a category 1 recommendation in combination with dexamethasone and bortezomib. Panobinostat is a category 2A recommendation in combination with carfilzomib or in combination with dexamethasone and lenalidomide.
- Fatal and serious cases of gastrointestinal and pulmonary hemorrhage have been reported.
- It is recommended to monitor hepatic enzymes during panobinostat therapy due to hepatotoxicity risks.
- Women of childbearing age should be counselled to avoid pregnancy while taking panobinostat due to the potential to cause fetal harm.

References

1. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at http://www.nccn.org/professionals/drug_compendium. Accessed September 7, 2020.
2. National Comprehensive Cancer Network. Multiple Myeloma Version 2.2021. Available at: http://www. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed September 10, 2020.
3. Clinical Pharmacology [database online]. Tampa, FL. Available at: http://clinicalpharmacology-ip.com. Accessed September 7, 2020.
4. Farydak Prescribing Information. Las Vegas, Secura Bio, Inc.; September 2019. Available at: https://farydak.com/assets/pdf/Farydak-SBI-USPI-201909.pdf. Accessed September 10, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	02/2020	03/06/2020
Policy was reviewed Policy changes: 1. Policy title table was updated. 2. Line of business policy applies was updated to All lines of business 3. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 4. Updated the approval length for Commercial line of business from length of benefit to 6 months for initial and 12 months for continuation therapy. 5. Appendix D added. 6. References were reviewed and updated.	09/10/2020	12/07/2020