Clinical Policy Title:	panobinostat
Policy Number:	RxA.127
Drug(s) Applied:	Farydak®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
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 orally 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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered 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 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®) (off-label), or
   c. lenalidomide (Revlimid®) and dexamethasone (off-label);
   *Prior authorization may be required for these agents.
6. Dose does not exceed six 20 mg doses per 21-day cycle for 16 cycles total.
7. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use; (prescriber must submit supporting evidence).
   *Prescribed regimen must be FDA-approved or recommended by NCCN

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 for the covered indications and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If used in combination with bortezomib and dexamethasone, member has not received more than 16 cycles (48 weeks) of therapy;
4. New dose does not exceed six 20 mg doses per 21-day cycle for 16 cycles total.
5. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use; (prescriber must submit supporting evidence).
   *Prescribed regimen must be FDA-approved or recommended by NCCN

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

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

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

Darzalex® (daratumumab)	**16 mg/kg intravenously 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 intravenously over 1 hour on day 4 repeated every 4 weeks; used in combination with bortezomib.	Varies
Empliciti™(elotuzumab)	10 mg/kg intravenously 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 intravenously 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 orally 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 orally once daily 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 orally once daily 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 intravenously bolus or subcutaneously 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; then once weekly for 6 weeks (on days 1, 8, 22, and 29) for cycles 5 through 9.	Varies

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

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. Farydak Prescribing Information. Las Vegas, Secura Bio, Inc.; September 2019. Available at: https://farydak.com/assets/pdf/Farydak-SBI-USPI-201909.pdf. Accessed May 28, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia . Accessed May 28, 2021.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 7.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed May 28, 2021.
4. Clinical Pharmacology [database online]. Elsevier; Gold Standard, Inc.; 2021. Available at: https://www.clinicalkey.com/pharmacology/ . Accessed May 28, 2021

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	09/10/2020	12/07/2020

months for continuation therapy. 5. Appendix D added. 6. References were reviewed and updated.		
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Initial Approval Criteria I.A.5.b, I.A.5.c, and I.A.7 were updated to include “off-label...” 3. Continued Therapy Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 4. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 5. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 6. References were reviewed and updated. 7.	05/28/2021	09/14/2021