Clinical Policy: Panobinostat (Farydak)

Reference Number: CP.PHAR.382
Effective Date: 11.16.16
Last Review Date: 08.22
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Panobinostat (Farydak®) is a histone deacetylase inhibitor.

FDA Approved Indication(s)*

Farydak is indicated in combination with bortezomib and dexamethasone, for the treatment of patients with multiple myeloma (MM) who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.

***Secura Bio, Inc., manufacturer of Farydak, requested withdrawal of approval for the NDA for Farydak because the required post-marketing clinical trial was not feasible for them to complete** (*see Appendix D*)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Farydak is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of MM;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥18 years;
4. Failure of at least 2 prior regimens for MM including bortezomib and an immunomodulatory agent (e.g., dexamethasone), unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for the 2 prior regimens*
5. Farydak is prescribed in combination with bortezomib 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*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Farydak for a covered indication 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. 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MM: multiple myeloma
NCCN: National Comprehensive Cancer Network
NDA: new drug application
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 3 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). For cycle 13 and beyond omit doses on days 8 and 9. Dexamethasone premedication is required for each Kyprolis dose in cycle 1. 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 QD on days 1-21 of repeated 28-day cycles in combination with dixamethasone until disease progression.	4 mg/day
Revlimid® (lenalidomide)	25 mg PO QD on days 1-21 of repeated 28 day cycles 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; then once weekly for 6 weeks (on days 1, 8, 22, and 29) for cycles 5 through 9.	Varies

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.
**Examples*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): severe diarrhea and cardiac toxicities
  - Because of these risks, Farydak has a risk evaluation and mitigation strategy (REMS) program that consists of a Medication Guide and a Dear Healthcare Professional Letter. Patient and physician enrollment in the manufacturer's REMS program is required.

Appendix D: General Information

- Part of the initial accelerated approval of Farydak included a required post-marketing trial intended to verify the clinical benefit of Farydak. On November 22, 2021, Secura Bio, Inc. submitted a letter to the FDA requesting withdrawal of approval of the NDA for Farydak because it was not feasible for them to complete the required post-marketing clinical trials. On November 26, 2021, FDA acknowledged Secura Bio, Inc.'s request for withdrawal of approval of the NDA. As of March 24, 2022 the approval of Farydak is withdrawn.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	20 mg PO every other week 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 up to 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]). The recommended dose of bortezomib is 1.3 mg/m^2 given as an injection. The recommended dose of dexamethasone is 20 mg PO per scheduled day, on a full stomach. See Farydak Prescribing Information for cycle schedules.	20 mg/dose

VI. Product Availability

Capsules: 10 mg, 15 mg, 20 mg

VII. References

1. Farydak Prescribing Information. East Hanover, MJ: Novartis Pharmaceuticals; September 2019. Available at: https://www.pharma.us.novartis.com/files/farydak.pdf. Accessed April 28, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at http://www.nccn.org/professionals/drug_compendium. Accessed April 28, 2022.

3. National Comprehensive Cancer Network. Multiple Myeloma Version 5.2022. Available at: http://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed April 28, 2022.
4. Clinical Pharmacology [database online]. Tampa, FL. Available at: https://www.clinicalkey.com/pharmacology/. Accessed April 28, 2022.
5. National Archives Federal Register: Secura Bio, Inc.; Withdrawal of Approval of New Drug Application for Farydak (Panobinostat) Capsules, 10 Milligrams, 15 Milligrams, and 20 Milligrams. March 24, 2022. Available at: https://www.federalregister.gov/documents/2022/03/24/2022-06182/secura-bio-inc-withdrawal-of-approval-of-new-drug-application-for-farydak-panobinostat-capsules-10#:~:text=stated%20they%20are%20requesting%20withdrawal,of%20its%20opportunity%20for%20hearing. Accessed May 16, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2018 annual review: policies combined for Centene Medicaid (new) and Commercial lines of business; specialist requirement added; added hematologist; references reviewed and updated.	04.26.18	08.18
3Q 2019 annual review: limited number of cycles to 16 per PI; references reviewed and updated.	05.14.19	08.19
3Q 2020 annual review: no significant changes; HIM line of business added; references reviewed and updated.	05.12.20	08.20
3Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	04.02.21	08.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
3Q 2022 annual review: revised to limit approved MM uses to FDA-labeled indication as NCCN no longer includes recommendations for regimens including panobinostat due to recent market withdrawal; added Appendix D with additional information regarding the discontinuation of Farydak; references reviewed and updated.	04.28.22	08.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health

plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.