BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**7/16/15**
LAST REVIEW DATE:	**8/02/18**
LAST CRITERIA REVISION DATE:	**8/02/18**
ARCHIVE DATE:	

FARYDAK® (panobinostat) oral capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

FARYDAK® (panobinostat) oral capsule (cont.)

Criteria:

- **Criteria for initial therapy:** Farydak (panobinostat) is considered ***medically necessary*** when of **ALL** the following criteria are met:

1. Prescriber is an Oncologist
2. Individual is 18 years of age or older
3. A confirmed diagnosis of multiple myeloma (MM) in an individual who has received at least 2 prior regimens, including bortezomib and an immunomodulatory agent (lenalidomide, pomalidomide, or thalidomide)
4. When approved for MM, Farydak (panobinostat) will be used in combination with bortezomib and dexamethasone
5. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
   - Pregnancy test in a woman of child bearing potential
   - Complete blood count with differential to verify **BOTH**:
     - Platelet count is at least at least 100 x 10^9/L
     - Absolute neutrophil count (ANC) is at least 1.5 x 10^9/L
   - Electrocardiogram to verify QT_cF is < 450 msec
   - Comprehensive metabolic panel to verify:
     - Potassium, magnesium, and phosphate are within normal limits
     - Liver enzymes
6. Individual does not have an active infection
7. Will not be used in an individual with severe hepatic impairment
8. Will not be used in an individual with end stage renal disease or individual on dialysis
9. Will not be administered with drug(s) that elevate gastric pH
10. Will not be used with strong CYP3A inducers
11. Will not be used with drugs that prolong QT interval such as amiodarone, bepridil, chloroquine, clarithromycin, disopyramide, methadone, moxifloxacin, pimozide, procainamide, quinidine, and sotalol
12. Woman patient of child bearing potential should use effective contraceptive method during and for at least 3 months after therapy
13. Woman patient who is breast feeding an infant or child should stop breast feeding during therapy

FARYDAK® (panobinostat) oral capsule (cont.)

14. Male patient with a female partner of reproductive potential should use condoms during treatment and for 6 months after therapy

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Farydak (panobinostat) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by an Oncologist

2. Individual's condition responded while on therapy
   - Response is defined as:
     - No evidence of disease progression
     - No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
     - Dose is greater than 10 mg 3 times per week

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
   - Significant adverse effect such as:
     - Severe or life-threatening diarrhea despite use of anti-diarrheal treatment
     - Gastrointestinal hemorrhage
     - Pulmonary hemorrhage
     - Liver toxicity
     - Thrombocytopenia that does not improve despite the recommended treatment modifications
     - Requires repeated platelet transfusions
     - Neutropenia that does not improve despite dose modifications and use of colony-stimulating factors
     - QTcF greater than 480 msec or has clinically significant baseline ST-segment or T-wave abnormalities that do not resolve

5. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Farydak® (panobinostat), a histone deacetylase inhibitor, used in combination with Velcade (bortezomib) and Dexamethasone, is indicated for the treatment of patients with multiple myeloma (MM) who have received at least 2 prior regimens, including Velcade (bortezomib) and an immunomodulatory agent [such as Thalomid

FARYDAK® (panobinostat) oral capsule (cont.)

(thalidomide), Revlimid (lenalidomide), Pomalyst (pomalidomide)]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

MM is a malignancy of plasma cells in the bone marrow. Malignant monoclonal plasma cells accumulate in the bone marrow and produce a monoclonal protein (usually IgG or IgA which are often referred to as M or myeloma proteins) that causes disruption of normal bone marrow function, destruction and invasion of bone surrounding the bone marrow cavity, production and release of M-proteins from the myeloma cells into the blood stream and/or into the urine, and a reduction of normal immune function. MM makes up 10-15% of all hematologic malignancies.

MM is a genetically complex disease that develops through several steps over time and as a result has various clinical presentations or phases. The earliest phase is monoclonal gammopathy of undetermined significance (MGUS), is an indolent, asymptomatic premalignant phase with a small clonal population of plasma cells within the bone marrow of 〈10%. MGUS is considered the initial event in the pathogenesis of MM. Progression to myeloma is approximately 1% per year. The next phase is smoldering multiple myeloma (SMM), another asymptomatic phase distinguished from MGUS by a greater tumor cell content of 〉10% and an average risk of progression to myeloma of 10% per year for the first five years. The myeloma phase is recognized when malignant clones cause clinically relevant end-organ damage such as the features known as CRAB (hypercalcemia, renal dysfunction, anemia, and bone lesions, including bone pain and fractures). Other manifestations include infection, neurologic symptoms (lethargy, headaches, confusion, depression and other), clotting abnormalities and hyperviscosity. The final phase is plasma cell leukemia (PCL).

MM is characterized by multiple relapses and progressive refractoriness to available therapies. There is no cure. The choice of primary therapy is based on whether a patient is a candidate for a stem cell transplant. Drug therapy is used to bridge eligible patients to an autologous stem cell transplant (ASCT).

Agents from four different classes are combined with one another or with corticosteroids and/or various generic chemotherapy medications to make up a MM drug regimen. Medication drug classes include: *Chemotherapy:* liposomal doxorubicin (Doxil), melphalan, cyclophosphamide, vincristine, etoposide, cisplatin, others; *HDAC inhibitor:* panobinostat (Farydak); *Immunomodulators:* lenalidomide (Revlimid), pomalidomide (Pomalyst), thalidomide (Thalomid); *Proteasome inhibitors:* bortezomib (Velcade) and carfilzomib (Kyprolis).

Farydak® (panobinostat) is a histone deacetylase (HDAC) inhibitor that blocks the enzymatic activity of HDAC. HDAC inhibitors act by increasing the productions of proteins that slow cell division and cause cell death. They have shown limited efficacy when used alone. HDAC catalyzes the removal of acetyl groups from the lysine residues of histones and some non-histone proteins. Inhibition of HDAC activity results in increased acetylation of histone proteins, an epigenetic alteration that results in a relaxing of chromatin, leading to transcriptional activation. *In vitro*, panobinostat caused the accumulation of acetylated histones and other proteins, inducing cell cycle arrest and/or apoptosis of some transformed cells. Panobinostat shows more cytotoxicity towards tumor cells compared to normal cells.

FARYDAK® (panobinostat) oral capsule (cont.)

Definitions:

QT interval correction Fridericia method
QT interval divided by the cube root of the RR interval:

$$QTcF = \frac{QT}{\sqrt[3]{RR}}$$

Resources:

Farydak. Package Insert. Revised by manufacturer 6/2016. Accessed 06-24-2017.

Farydak. Package Insert. Revised by manufacturer 2/2016. Accessed 05-23-2016.

Farydak. Package Insert. Revised by manufacturer 2/2015. Accessed 05-08-2015.

Farydak (panobinstat) product information accessed 07-14-18 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7774972a-eeaa-4b9a-9e56-3fc1b968e86a

Gupta M, Pal, RAGK, Tikoo D. Multiple myeloma: The disease and its treatment. Int J Basic Clin Pharmacol 2013 March-April; 2(2):103-121

Rajkumar SV. Multiple myeloma: 2013 update on diagnosis, risk-stratification, and management. Am J Hematol. 2013; 88:226–235

Chou T. Multiple myeloma: Recent progress in diagnosis and treatment. J Clin Exp Hematopathol 2012; 52(3):149-159

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.