BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

VANFLYTA® (quizartinib) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Vanflyta (quizartinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual is 18 years of age or older

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test

   b. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. Vanflyta (quizartinib) will be used in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy

5. Vanflyta (quizartinib) will not be used as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT) as improvement in overall survival with Vanflyta (quizartinib) in this setting has not been demonstrated

6. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
   a. FLT3 internal tandem duplication (ITD)-positive
   b. When used as maintenance therapy after consolidation the absolute neutrophil count is greater than 500/mm^3 and platelet count is greater than 50,000/mm^3
   c. Negative pregnancy test in a woman of childbearing potential
   d. Eastern Cooperative Oncology Group (ECOG) status is 0 or 1

7. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

8. There are **NO** FDA-label contraindications such as:
   a. Severe hypokalemia
   b. Severe hypomagnesemia
   c. Long QT syndrome
   d. History of ventricular arrhythmias or torsades de pointe

9. Individual is currently not taking any other drug(s) which may cause result in a significant drug interaction requiring discontinuation of Vanflyta (quizartinib) such as use with strong or moderate CYP3A Inducers (e.g.., rifampin, rifabutin, phenobarbital, carbamazepine, armodafinil, bexarotene, bosentan, others)

10. Individual does not have severe renal impairment (CrCl <30 mL/min)

11. Individual does not have severe (Child-Pugh Class C or total bilirubin greater than 3 times the upper limit of normal and any value for AST) hepatic impairment

12. QT interval corrected by Fridericia's formula (QTcF) is **NOT** greater than 450 ms

13. Individual does not have any of the following risks for developing torsades de pointes:
   a. Uncontrolled or significant cardiac disease
   b. Recent myocardial infarction
   c. Heart failure
   d. Unstable angina
   e. Bradyarrhythmias
   f. Tachyarrhythmias
   g. Uncontrolled hypertension

h. High-degree atrioventricular block
i. Severe aortic stenosis
j. Uncontrolled hypothyroidism

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Vanflyta (quizartinib) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist

2. Individual's condition has responded while on therapy with response defined as there is no evidence of disease progression and there is no evidence of unacceptable toxicity

3. Individual has been adherent with the medication

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual has not developed any contraindications listed in the Criteria for Initial approval or other significant adverse drug effects that may exclude continued use of Vanflyta (quizartinib) such as:
   a. Recurrent QTcF greater than 500 ms despite appropriate dose reduction and correction or elimination of other risk factors (i.e., correction of electrolyte abnormalities, use of drugs that prolong QT interval)
   b. Torsades de Pointes, polymorphic ventricular tachycardia, signs/symptoms of life-threatening arrhythmia and cardiac arrest
   c. Severe or medically significant or life-threatening non-hematologic adverse reactions the persist beyond 28 days

6. Individual is currently not taking any other drug(s) which may cause a severe adverse reaction(s) or result in a significant drug interaction requiring discontinuation of Vanflyta (quizartinib) such as use of strong or moderate CYP3A Inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, armodafinil, bexarotene, bosentan, others)

7. Individual does not have severe renal impairment (CrCl <30 mL/min)

8. Individual does not have severe (Child-Pugh Class C or total bilirubin greater than 3 times the upper limit of normal and any value for AST) hepatic impairment

9. QT interval corrected by Fridericia's formula (QTcF) is **NOT** greater than 450 ms

10. Individual does not have any of the following risks for developing torsades de pointes:
    a. Uncontrolled or significant cardiac disease
    b. Recent myocardial infarction

c. Heart failure
d. Unstable angina
e. Bradyarrhythmias
f. Tachyarrhythmias
g. Uncontrolled hypertension
h. High-degree atrioventricular block
i. Severe aortic stenosis
j. Uncontrolled hypothyroidism

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Vanflyta (quizartinib) is a kinase inhibitor indicated in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test. Vanflyta (quizartinib)is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT); improvement in overall survival with Vanflyta (quizartinib)in this setting has not been demonstrated.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead

Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Resources:

Vanflyta (quizartinib) product information, revised by Daiichi Sankyo, Inc. 06-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 3.2024 –May 17, 2024. Available at https://www.nccn.org. October 17, 2024.

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.