BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

VORANIGO® (vorasidenib)
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:** Voranigo (vorasidenib) 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 12 years of age or older and weigh at least 40 kg

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Grade 2 astrocytoma or oligodendroglioma with residual or recurrent susceptible isocitrate dehydrogenase-1 (IDH1) or isocitrate dehydrogenase-2 (IDH2) mutation following at least one surgery for glioma including biopsy, sub-total resection, or gross total resection and not be in need of immediate chemotherapy or radiotherapy

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. 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. Documentation of presence of IDH1 or IDH2 mutations in tumor specimens [**Note**: FDA-approved test for detection of IDH1 or IDH2 mutations in Grade 2 astrocytoma or oligodendroglioma for selecting patients for treatment is not available]
   b. Liver function tests aspartate aminotransferase (AST), alanine transaminase (ALT), gamma-glutamyl transferase (GGT), total bilirubin and alkaline phosphatase
   c. Negative pregnancy test in a woman of childbearing potential
   d. Karnofsky Performance Scale (KPS) score (for individuals ≥ 16 years of age) or Lansky Play Performance Scale (LPPS) score (for individuals <16 years of age) of ≥ 60%

5. Individual has not received prior anticancer therapy, including chemotherapy and radiation, other than surgery for treatment of glioma

6. Individual has MRI-evaluable, measurable, non-enhancing disease with at least one target lesion measuring at least 1 centimeter by at least one centimeter

7. Individual does not have high risk features such as brainstem involvement, neurocognitive deficits due to tumor, or uncontrolled or persistent seizures

8. **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)

9. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation such as:
   a. Strong CYP1A2 inhibitors (e.g., fluvoxamine, enoxacin, ciprofloxacin, zafirlukast, others)
   b. Moderate and strong CYP1A2 inducers (e.g., rifampin, carbamazepine, primidone, smoking, others)
   c. CYP3A4 substrates where a minimal concentration changes results in reduced efficacy (e.g., aminophylline, amiodarone, carbamazepine, cyclosporine, everolimus, fosphenytoin, others)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Voranigo (vorasidenib) 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 no disease progression or unacceptable drug toxicity

3. Individual has been adherent with the medication

4. The request is for a dose of at least 10 mg daily

5. **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)

6. Individual has not developed any significant adverse drug effects that may exclude continued use such as hepatotoxicity [may reduce dose, withhold, or permanently discontinue based on severity]

7. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation such as:
    a. CYP1A2 inhibitors (e.g., fluvoxamine, enoxacin, ciprofloxacin, zafirlukast, others)
    b. CYP1A2 moderate and strong inducers (e.g., rifampin, carbamazepine, primidone, smoking, others)
    c. CYP3A4 substrates where a minimal concentration changes results in reduced efficacy (e.g., aminophylline, amiodarone, carbamazepine, cyclosporine, everolimus, fosphenytoin, others)

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:

Voranigo (vorasidenib) is an isocitrate dehydrogenase-1 (IDH1) and isocitrate dehydrogenase-2 (IDH2) inhibitor indicated for the treatment of adult and pediatric individuals 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation following surgery including biopsy, sub-total resection, or gross total resection.

Gliomas are a common malignant primary brain tumor in adults. They can be categorized into two distinct tumor subtypes. Gliomas that have a mutation in IDH1 or IDH2 and an unbalanced translocation between chromosomes 1 and 19 (1p/19q-codeleted) are defined as oligodendrogliomas, while IDH-mutant gliomas without 1p/19q codeletion (1p/19q–non-codeleted) are defined as astrocytomas. Oligodendrogliomas and astrocytomas grow slowly and continuously with invasion of normal brain tissue (so-called low-grade gliomas); they eventually become aggressive tumors with accelerated tumor growth and neovascularization (so-called high-grade gliomas). This transformation can be detected by the appearance of enhancement on magnetic resonance imaging (MRI). The combination of radiation therapy and chemotherapy has become the standard care for the postoperative treatment of individuals with IDH-mutant grade 2 gliomas who are judged to be at high risk for early disease progression. Adjuvant chemoradiotherapy can result in long-lasting disease remission, but treatment is not

curative, and it is associated with radiation-induced neurocognitive dysfunction and chemotherapy-associated toxic effects. To defer these potential long-term toxic effects, many individuals with IDH-mutant grade 2 gliomas do not receive immediate adjuvant chemoradiotherapy after their initial diagnosis and are instead use a watch-and-wait approach by monitoring serial MRI scans of the head.

Definitions:

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

Performance Status/Scores					
Score	**ECOG (or Zubrod)**	**Score**	**Karnofsky**	**Score**	**Lansky**
0	Fully active, able to carry on all pre-disease performance without restriction	100	Normal, no complaints, no evidence of disease	100	Fully active, normal
		90	Able to carry on normal activity, minor signs or symptoms of disease	90	Minor restrictions in physical strenuous activity
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	80	Normal activity with effort, some signs or symptoms of disease	80	Active, but tires more quickly
		70	Cares for self, unable to carry on normal activity or do active work	70	Both greater restriction of and less time spent in play activity
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours	60	Requires occasional assistance, but is able to care for most of his/her needs	60	Up and around, but minimal active play; keeps busy with quieter activities
		50	Requires considerable assistance and frequent medical care	50	Gets dressed but lies around much of the day, no active play but able to participate in all quiet play and activities
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	40	Disabled, requires special care and assistance	40	Mostly in bed; participates in quiet activities
		30	Severely disabled, hospitalization indicated, but death not imminent	30	n bed; needs assistance even for quiet play
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair	20	Very sick, hospitalization indicated, but death not imminent	20	Often sleeping; play entirely limited to very passive activities
		10	Moribund, fatal process progressing rapidly	10	No play; does not get out of bed

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National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines): Central Nervous System Cancers Version 2.2024 –Updated July 25, 2024.

OLIGODENDROGLIOMA (IDH-MUTANT, 1p19q CODELETED): SYSTEMIC THERAPY OPTIONS		
	Preferred Regimens	Other Recommended Regimens
Adjuvant treatment after surgery/biopsy and treatment with RT and chemotherapy is not preferred, WHO grade 2, KPS ≥ 60	IDH inhibitor (if residual disease is present)	None
ASTROCYTOMA (IDH-MUTANT, 1p/19q–NON-CODELETED): SYSTEMIC THERAPY OPTIONS		
	Preferred Regimens	Other Recommended Regimens
Adjuvant treatment after surgery/biopsy and treatment with RT and chemotherapy is not preferred, WHO grade 2, KPS ≥ 60	IDH inhibitor (if residual disease is present)	None

Resources:

Voranigo (vorasidenib) product information, revised by Servier Pharmaceutical LLC 08-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 14, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Central Nervous System Cancers Version 2.2024 –Updated July 25, 2024. Available at https://www.nccn.org. Accessed August 14, 2024.

Mellinghoff IK, van de Bent MJ, Blumenthal DT, et al.: Vorasidenib in IDH1- or IDH2-Mutant Low-Grade Glioma. NEJM 2023 Aug 17;389 (7):589-601. Accessed August 14, 2024.

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04164901: A Phase 3, Multicenter, Randomized, Double-blind, Placebo-Controlled Study of AG-881 in Subjects with Residual or Recurrent Grade 2 Glioma With an IDH1 or IDH2 Mutation. Available from: http://clinicaltrials.gov. Last update posted December 05, 2023. Last verified December 2023. Accessed August 14, 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.