BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

OJEMDA™ (tovorafenib)
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:** Ojemda (tovorafenib) 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 6 months to 25 years of age

3. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Relapsed or refractory low-grade glioma (LGG) harboring a BRAF fusion or rearrangement or BRAF V600 mutation who received at least **one** prior line of systemic therapy

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 does not have **ANY** of the following:
   a. Tumors harboring additional activating alterations (e.g., histone mutation, IDH1/2 mutations, FGFR mutations or fusions, MYBL alterations, etc.)
   b. Known or suspected neurofibromatosis type 1

5. 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. Presence of BRAF fusion or rearrangement or BRAF V600 mutation
   b. There is evidence of radiographic progression
   c. Liver function tests including aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin
   d. Karnofsky (those 16 years of age or older) or Lansky (those younger than 16 years of) performance score of at least 50
   e. Documentation of a negative pregnancy test in a woman of childbearing potential

6. **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)

7. Individual is not currently taking any other drugs which may cause a significant drug interaction requiring discontinuation such as:
   a. Use with moderate and strong CYP2C8 Inhibitors (e.g., gemfibrozil, montelukast)
   b. Use with moderate and strong CYP2C8 Inducers (e.g., paclitaxel, torsemide, repaglinide)
   c. Hormonal contraceptives

8. Individual does not have moderate (bilirubin greater than 1.5 times to 3 times the upper limit of normal (ULN) and any AST) or severe (bilirubin greater than 3 times the ULN and any AST) hepatic impairment

9. Individual does not have severe renal impairment (estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 m^2)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Ojemda (tovorafenib) 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 the following:
   a. There is no evidence of disease progression
   b. There is no evidence of unacceptable drug toxicity

c. The individual is clinically stable

3. Individual does not have **ANY** of the following:
   a. Tumors harboring additional activating alterations (e.g., histone mutation, IDH1/2 mutations, FGFR mutations or fusions, MYBL alterations, etc.)
   b. Known or suspected neurofibromatosis type 1

4. Individual has been adherent with the medication

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:
   a. Major hemorrhagic event such as symptomatic bleeding in a critical area or organ or intratumoral hemorrhage
   b. New or worsening skin reactions
   c. Hepatotoxicity

7. Individual is not currently taking any other drugs which may cause a significant drug interaction requiring discontinuation such as:
   a. Use with moderate and strong CYP2C8 Inhibitors (e.g., gemfibrozil, montelukast)
   b. Use with moderate and strong CYP2C8 Inducers (e.g., paclitaxel, torsemide, repaglinide)
   c. Hormonal contraceptives

8. Individual does not have moderate (bilirubin greater than 1.5 times to 3 times the upper limit of normal (ULN) and any AST) or severe (bilirubin greater than 3 times the ULN and any AST) hepatic impairment

9. Individual does not have severe renal impairment (estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 m^2)

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:

Ojemda (tovorafenib) is a kinase inhibitor indicated for the treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (LGG) harboring a BRAF fusion or rearrangement, or

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BRAF V600 mutation. This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Tovorafenib is a Type II RAF kinase inhibitor of mutant BRAF V600E, wild-type BRAF, and wild-type CRAF kinases.

Pediatric low-grade gliomas are common brain tumors seen in children. They occur anywhere in the central nervous system. Histopathologic classification is determined on which normal cell the tumor resembles (i.e., astrocytes, oligodendrocytes, ependymal cells). Grading is determined by presence of necrosis, giant cells, mitosis, endothelial proliferation, hyperchromatic nuclei, and pleomorphic cells. The World Health Organization classifies Grade I and Grade II tumors as low-grade gliomas. Low-grade gliomas are slow growing and chronic.

Treatment of pediatric low-grade gliomas can include surgery, radiation, and multiagent chemotherapy. Surgery is associated with a high overall survival rate but not all individuals are able to undergo complete surgical resection due to tumor location. Incomplete or unresectable low-grade glioma is associated with a high rate of disease progression and recurrence. There is currently no standard of care for patients who progress after initial therapy. Tovorafenib is FDA-approved for pediatric low-grade gliomas.

Definitions:

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

Karnofsky Performance Score (≥ 16 years old)

Karnofsky Performance Score:	
100%	Able to carry on normal activity, no evidence of disease
90%	Able to carry on normal activity, minor signs or symptoms of disease
80%	Normal activity with effort, some signs and symptoms of disease
70%	Cares for self, unable to carry on normal activity or to work
60%	Requires occasional assistance from others but able to care for most needs
50%	Requires considerable assistance from others and frequent medical care
40%	Disabled, requires special care and assistance
30%	Severely disabled, hospitalization indicated, though death not imminent
20%	Very sick, hospitalization indicated, active support treatment necessary
10%	Moribund
0%	Dead

Lansky Performance Score (< 16 years old)

Score	Description
100	Fully active, normal
90	Minor restrictions in physical strenuous activity

80	Active, but tires more quickly
70	Both greater restriction of, and less time spent in, play activity
60	Up and around, but minimal active play; keeps busy with quieter activities
50	Gets dressed, but lies around much of the day; no active play; able to participate in all quiet play and activities
40	Mostly in bed, participates in quiet activities
30	In bed, needs assistance even for quiet play
20	Often sleeping, play entirely limited to very passive activities
10	No play, does not get out of bed
0	Dead

Resources:

Ojemda (tovorafenib) product information, revised by Day One Biopharmaceuticals, Inc. 04-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 15, 2024.

Louis DN, Schiff D, Batchelor T. Classification, and pathologic diagnosis of gliomas, glioneuronal tumors, and neuronal tumors. In: UpToDate, Wen PY, Eichler AF (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through April 2024. Topic last updated on April 11, 2024. Accessed May 16, 2024.

Batchelor T, Louis DN. Molecular pathogenesis of diffuse gliomas. In: UpToDate, Wen PY, Eichler AF. (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through April 2024. Topic last updated on May 16, 2023. Accessed May 16, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Central Nervous System Cancers. Version 1.2023 –March 24, 2023. Available at https://www.nccn.org. Accessed May 15, 2024.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Pediatric Central Nervous System Cancers Version 1.2024 –Updated February 26, 2024. Available at https://www.nccn.org. Accessed May 16, 2024.

Kilburn LB, Khuong-Quang DA, Hansford JR, et al: The type II RAF inhibitor tovorafenib in relapsed/refractory pediatric low-grade glioma: the phase 2 FIREFLY-1 trial. Nature Medicine 2023 April; Available at https://doi.org/10.1038/s41591-023-02668-y. Accessed May 15, 2024.

Kilburn LB, Khuong-Quang DA, Hansford JR, et al: The type II RAF inhibitor tovorafenib in relapsed/refractory pediatric low-grade glioma: the phase 2 FIREFLY-1 trial. Nature Medicine 2023 April; Available at https://doi.org/10.1038/s41591-023-02668-y. Accessed May 15, 2024. PROTOCOL

ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). Identifier NCT04775485: FIREFLY-1: A Phase 2, Open-Label, Multicenter Study to Evaluate the Safety and Effi cacy of the Oral Pan-RAF Inhibitor DAY101 in Pediatric Patients With RAF-Altered, Recurrent or Progressive Low-Grade Glioma and Advanced Solid Tumors. Available from: http://clinicaltrials.gov. Last update posted December 27, 2023. Last verified December 2023. Accessed May 15, 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.