BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

LENVIMA™ (lenvatinib) oral
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/or 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.

Medical Necessity Requirements for LENVIMA (lenvatinib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist

Indication
- Locally recurrent or metastatic, progressive, radioactive iodine refractory differentiated thyroid cancer (DTC)

- Advanced renal cell carcinoma (RCC) used with everolimus following one prior anti angiogenic therapy or used with pembrolizumab as a first line treatment
- Unresectable hepatocellular carcinoma (HCC) as a first line treatment
- Endometrial carcinoma used in combination with pembrolizumab for advanced disease that is mismatch repair proficient (pMMR) or not microsatellite instability high (MSI H), with disease progression following prior systemic therapy and not candidates for curative surgery or radiation
- Other oncologic direct treatment uses listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement

- 18 years of age or older

Baseline Clinical Evaluation

- Negative pregnancy test (if applicable)
- Blood pressure measurement and initiation or adjustment of blood pressure medication if abnormal
- Liver enzymes
- Urine dipstick for proteinuria
- 24 hour urine protein if urine dipstick for proteinuria is greater than or equal to 2 plus
- Thyroid function tests
- Serum electrolytes with correction of any abnormalities prior to starting treatment
- Oral examination for individuals at risk for osteonecrosis of the jaw (e.g., use of denosumab, bisphosphonates such as alendronate, etidronate, zoledronic acid, dental disease, or invasive dental procedures)

Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety

- Does not have end stage renal disease
- For hepatocellular carcinoma: does not have moderate or severe hepatic impairment (Child Pugh Class B or C)
- No concomitant drug use that may cause QT prolongation (see Definitions section)

Documentation Requirements

- A completed request form must be submitted, including:
  - Chart notes
  - Lab results (include all related lab values from above criteria)
  - Supporting clinical documentation

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Initial Therapy Criteria Approval Duration:
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications
- Continues to be seen by a physician specializing in the diagnosis or is in consultation with an Oncologist

Clinical Response
- Documentation of positive clinical response to therapy defined as no evidence of disease progression or unacceptable toxicity

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication, or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- Has not developed any significant adverse drug effects that may exclude continued use, including:
  - Uncontrolled or life threatening hypertension
  - Severe and persistent cardiac dysfunction (e.g., decreased ventricular function, cardiac failure, pulmonary edema)
  - Arterial thromboembolic event
  - Hepatic failure or severe and persistent hepatotoxicity
  - Nephrotic syndrome
  - Severe and persistent renal impairment or renal failure
  - Severe and persistent vomiting and/or diarrhea despite medical management
  - Gastrointestinal perforation or life threatening fistula
  - QT interval prolongation
  - Severe hypocalcemia despite dose reduction and calcium supplementation
  - Reversible posterior leukoencephalopathy syndrome (RPLS) that does not resolve or recurs
  - Severe and persistent hemorrhage
  - Wound healing complications
  - Any life threatening adverse reaction
- Does not have end stage renal disease

- For hepatocellular carcinoma: does not have moderate or severe hepatic impairment (Child Pugh Class B or C)
- No concomitant drug use that may cause QT prolongation (see Definitions section)

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration:

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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:

Lenvima (lenvatinib) is a kinase inhibitor indicated for the treatment of: a) patients with locally recurrent or metastatic, progressive, radioactive iodine (RAI)-refractory differentiated thyroid cancer (DTC); b) used in combination with everolimus in patients with advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy; c) used as first-line treatment of patients with unresectable hepatocellular carcinoma (HCC); and d) used in combination with pembrolizumab, in patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation. (This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trial.)

Lenvima (lenvatinib) is a receptor tyrosine kinase (RTK) inhibitor of VEGF receptors VEGFR1 (FLT1), VEGFR2 (KDR), VEGFR3 (FLT4); and other RTK involved in pathogenic angiogenesis, tumor growth, and cancer progressions such as fibroblast growth factor receptors (FGFR-) 1, 2, 3, and 4, platelet derived growth factor receptor alpha (PDGFR-alfa), KIT, and rearranged during transfection (RET) proto-oncogene that encodes for tyrosine kinase receptor. Inhibition of these receptor tyrosine kinases leads to decreased tumor growth and slowing of cancer progression. The combination of lenvatinib and everolimus showed increased anti-angiogenic and antitumor activity in models of human renal cell cancer greater than each drug alone. Many of the anti-angiogenesis drugs used attack the VEGF pathway.

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Definitions:

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

Drugs that prolong QT-interval: (*not an all-inclusive list*)

Amiodarone	Dolasetron
Disopyramide	Erythromycin
Sotalol	Clarithromycin
Quinidine	Ketoconazole
Chloroquine	Itraconazole
Dofetilide	Fluoxetine
Ibutilide	Sertraline
Procainamide	Haloperidol
Levofloxacin	Quetiapine
Ciprofloxacin	Ziprasidone
Moxifloxacin	Pimozide
Granisetron	Methadone

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

Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

Resources:

Lenvima (lenvatinib) product information, revised by Eisai, Inc. 01-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 08, 2025.

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National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Hepatocellular Carcinoma Version 1.2025 – Updated March 20, 2025. Available at https://www.nccn.org. Accessed May 08, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer Version 3.2025 – Updated January 09, 2025. Available at https://www.nccn.org. Accessed May 08, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma Version 1.2025 – Updated March 27, 2025. Available at https://www.nccn.org. Accessed May 08, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Uterine Neoplasms Version 3.2025 – Updated March 07, 2025. Available at https://www.nccn.org. Accessed May 08, 2025.

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.