BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

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LENVIMA™ (lenvatinib) 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.**

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Criteria:

- **Criteria for initial therapy:** Lenvima (lenvatinib) is considered ***medically necessary*** with medical record documentation of **ALL** of the following:

  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. A confirmed diagnosis of **ONE** of the following:
     a. Locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC)
     b. Advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy, when used with Afinitor (everolimus)
     c. Unresectable hepatocellular carcinoma (HCC) as first line treatment
     d. Endometrial carcinoma used in combination with Keytruda (pembrolizumab) for advanced or recurrent disease that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) in patients who are not candidates for curative surgery or radiation and have progressed on prior systemic therapy
     e. 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. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     a. Negative pregnancy test in a woman of child bearing potential
     b. Measurement of blood pressure **AND** initiate **OR** adjust blood pressure medication if abnormal
     c. Liver enzymes
     d. Urine dipstick for proteinuria
     e. 24-hour urine protein if urine dipstick for proteinuria is $\geq$ 2+
     f. Thyroid function tests
     g. Serum electrolytes with correction of any abnormalities prior to starting treatment

  5. Will not be used in a patient with end-stage renal disease

  6. There are no significant interacting drugs

  Initial approval duration: 6 months

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

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

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2. Individual's condition responded while on therapy
    a. Response is defined as:
        i. No evidence of disease progression
        ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. Individual has not developed any significant adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Uncontrolled or life-threatening hypertension
        ii. Severe and persistent cardiac dysfunction such as decreased left or right ventricular function, cardiac failure, or pulmonary edema
        iii. Arterial thromboembolic event
        iv. Hepatic failure or severe and persistent hepatotoxicity
        v. Nephrotic syndrome
        vi. Severe and persistent renal impairment or renal failure
        vii. Severe and persistent vomiting and/or diarrhea despite medical management
        viii. Gastrointestinal perforation or life-threatening fistula
        ix. Reversible posterior leukoencephalopathy syndrome that does not resolve or recurs
        x. Severe and persistent hemorrhage
        xi. Patient with wound healing complications

5. Will not be used in a patient with end-stage renal disease

6. There are no significant interacting drugs

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 a Non-cancer Medications**

    2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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

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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.

Resources:

Lenvima (lenvatinib) product information, revised byEisai, Inc. 12-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on June 23, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Hepatobiliary Cancers Version 3.2021 – Updated June 15, 2021. Available at https://www.nccn.org. Accessed on June 23, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer Version 4.2021 – Updated April 19, 2021. Available at https://www.nccn.org. Accessed on June 23, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma Version 1.2021 – Updated April 09, 2021. Available at https://www.nccn.org. Accessed on June 23, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Uterine Neoplasms Version 3.2021 – Updated June 03, 2021. Available at https://www.nccn.org. Accessed on June 23, 2021.

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.