PHARMACY COVERAGE GUIDELINE

LENVIMA™ (lenvatinib) oral capsule

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 precertification 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:** Lenvima (lenvatinib) 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. Locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC)

b. Advanced renal cell carcinoma (RCC) used with Afinitor (everolimus) following one prior anti-angiogenic therapy **OR** used with Keytruda (pembrolizumab) as first-line treatment

c. Unresectable hepatocellular carcinoma (HCC) as first line treatment

d. Endometrial carcinoma used in combination with Keytruda (pembrolizumab) for advanced disease that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) in patients who have disease progression following prior systemic therapy in any setting and who are not candidates for curative surgery or radiation

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. The 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. 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 ≥ 2+
   f. Thyroid function tests
   g. Serum electrolytes with correction of any abnormalities prior to starting treatment
   h. Oral examination in an individual at risk for osteonecrosis of the jaw such as uses denosumab, uses bisphosphonates (ex., alendronate, etidronate, zoledronic acid, etc.), has dental disease, or invasive dental procedures

5. Individual does not have end-stage renal disease.

6. Individual does not use drugs that may cause QT prolongation. (see Definitions section)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Lenvima (lenvatinib) 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 **ALL** of the following:
   a. No evidence of disease progression
   b. 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 other significant adverse drug effects that may exclude continued use such as:
    a. Uncontrolled or life-threatening hypertension
    b. Severe and persistent cardiac dysfunction such as decreased left or right ventricular function, cardiac failure, or pulmonary edema
    c. Arterial thromboembolic event
    d. Hepatic failure or severe and persistent hepatotoxicity
    e. Nephrotic syndrome
    f. Severe and persistent renal impairment or renal failure
    g. Severe and persistent vomiting and/or diarrhea despite medical management
    h. Gastrointestinal perforation or life-threatening fistula
    i. QT interval prolongation
    j. Severe hypocalcemia despite dose reduction and calcium supplementation
    k. Reversible posterior leukoencephalopathy syndrome (RPLS) that does not resolve or recurs
    l. Severe and persistent hemorrhage
    m. Patient with wound healing complications

5. Individual does not have end-stage renal disease.

6. Individual does not use drugs that may cause QT prolongation. (see Definitions section)

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:

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.

Definitions:

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

Amiodarone	Dolasetron
Dispyrimide	Erythromycin
Sotalol	Clarithromycin
Quindine	Ketoconazole
Chlororquine	Itraconazole
Dofetilide	Fluoxetine
Ibutilide	Sertaline
Procainamide	Haloperidol
Levofloxacin	Quetiapine
Ciprofloxacin	Ziprasidone
Moxifloxacin	Pimozide
Granisetron	Methadone

Resources:

Lenvima (lenvatinib) product information, revised by Eisai, Inc. 12-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed August 04, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Hepatobiliary Cancers Version 2.2022 – Updated July 15,2022. Available at https://www.nccn.org. Accessed August 04, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer Version 2.2023 – Updated August 03, 2022. Available at https://www.nccn.org. Accessed August 04, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma Version 2.2022 – Updated May 05, 2022. Available at https://www.nccn.org. Accessed August 03, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Uterine Neoplasms Version 1.2021 – Updated November 04,2021. Available at https://www.nccn.org. Accessed August 04, 2022.

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.