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Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	March 6, 2015
Subject:	Lenvima	**Page:**	1 of 7

Last Review Date: March 7, 2025

Lenvima

Description

Lenvima (lenvatinib)

Background
Lenvima (lenvatinib) is used to treat patients with progressive, differentiated thyroid cancer (DTC) whose disease progressed despite receiving radioactive iodine therapy (radioactive iodine refractory disease). DTC is a cancerous growth of the thyroid gland which is located in the neck and helps regulate the body's metabolism. Lenvima is also used to treat patients with renal cell carcinoma, unresectable hepatocellular carcinoma, or endometrial carcinoma. Lenvima is a receptor tyrosine kinase (RTK) inhibitor which works by blocking certain proteins from helping cancer cells grow and divide (1).

Regulatory Status
FDA-approved indications: Lenvima is a kinase inhibitor indicated for (1):

1. Differentiated Thyroid Cancer (DTC): single agent for patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer
2. Renal Cell Cancer (RCC):
    a. In combination with pembrolizumab, for the first-line treatment of adult patients with advanced RCC
    b. In combination with everolimus, for patients with advanced RCC following one prior anti-angiogenic therapy
3. Unresectable Hepatocellular Carcinoma (HCC): as first-line treatment
4. Advanced endometrial carcinoma (EC): in combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma that is mismatch repair

proficient (pMMR), as determined by an FDA-approved test, or not microsatellite instability-high (MSI-H), who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

Off-Label Use: (2)

1. Unresectable HCC: as subsequent-line therapy in disease progression if Child-Pugh Class A

Lenvima may cause serious side effects, including cardiac failure, blood clot formation (arterial thromboembolic events), liver damage (hepatotoxicity), kidney damage (renal failure and impairment), an opening in the wall of the stomach or intestines (gastrointestinal perforation) or an abnormal connection between two parts of the stomach or intestines (fistula formation), changes in the heart's electrical activity (QT interval prolongation), low levels of calcium in the blood (hypocalcemia), the simultaneous occurrence of headache, confusion, seizures and visual changes (reversible posterior leukoencephalopathy syndrome), serious bleeding (hemorrhage), risks to an unborn child if a patient becomes pregnant during treatment, and impairing suppression of the production of thyroid-stimulating hormone (1).

Related policies
Cabometyx, Fotivda, Inlyta, Nexavar, Sutent, Votrient

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Lenvima may be considered **medically necessary** if the conditions indicated below are met.

Lenvima may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Differentiated thyroid cancer (DTC)
    a. Locally recurrent or metastatic disease
    b. Progression after radioactive iodine therapy (radioactive iodine-refractory)

2. Advanced renal cell carcinoma (RCC) **AND ONE** of the following:
    a. Used in combination with pembrolizumab as first-line treatment
    b. Used in combination with everolimus
        i. Progression after one prior anti-angiogenic therapy

3. Unresectable hepatocellular carcinoma (HCC) **AND ONE** of the following:
    a. Used as first-line treatment
    b. Used as subsequent-line therapy
        i. Patient must be Child-Pugh Class A

4. Advanced endometrial carcinoma (EC)
    a. Used in combination with pembrolizumab
    b. Patient is **ONE** of the following:
        i. Mismatch repair proficient (pMMR), as determined by an FDA-approved test
        ii. **NOT** microsatellite instability-high (MSI-H)
    c. Disease progression following prior systemic therapy
    d. **NOT** a candidate for curative surgery or radiation

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Differentiated Thyroid Cancer (DTC)
2. Advanced Renal Cell Carcinoma (RCC)
3. Unresectable hepatocellular carcinoma (HCC)
4. Advanced endometrial carcinoma (EC)
    a. Used in combination with pembrolizumab

AND ALL of the following:

a. **NO** disease progression
b. **NO** unacceptable toxicity. Examples include:
   i. life-threatening hypertension
   ii. severe cardiac dysfunction
   iii. hepatotoxicity
   iv. nephrotic syndrome
   v. renal failure/impairment
   vi. gastrointestinal perforation/fistula formation
   vii. severe QT prolongation (grade 3 or 4)
   viii. Reversible Posterior Leukoencephalopathy Syndrome (RPLS)
   ix. arterial thromboembolic events and severe hemorrhage

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Reference

Diagnosis	Recommended Dosing
Differentiated Thyroid Cancer (DTC)	24 mg once daily
Renal Cell Carcinoma (RCC) - First-Line Treatment of Patients with Advanced RCC	20 mg orally once daily, in combination with 200 mg pembrolizumab administered as IV infusion over 30 minutes every 3 weeks
Renal Cell Carcinoma (RCC) – Previously Treated RCC	18 mg in combination with 5 mg everolimus once daily
Hepatocellular Carcinoma (HCC)	12 mg once daily for patients greater than or equal to 60 kg or 8 mg once daily for patients less than 60 kg
Endometrial carcinoma	20 mg orally once daily, in combination with 200 mg pembrolizumab administered as IV infusion over 30 minutes every 3 weeks

Lenvima comes in cartons of 6 blister cards. Each card contains a 5 day supply of medication. Each carton therefore contains a 30 day supply.

Strength	How Supplied
4 mg	One 4 mg capsule / Five 4 mg capsules per card
8 mg	Two 4 mg capsules / Ten 4 mg capsules per card
10 mg	One 10 mg capsule / Five 10 mg capsules per card
12 mg	Three 4 mg capsules / Fifteen 4 mg capsules per card
14 mg	One 10 mg capsule and one 4 mg capsule / Five 10 mg capsules and five 4 mg capsules per card
18 mg	One 10 mg capsule and two 4 mg capsules / Five 10 mg capsules and ten 4 mg capsules per card
20 mg	Two 10 mg capsules / Ten 10 mg capsules per card
24 mg	Two 10 mg capsules and one 4 mg capsule / Ten 10 mg capsules and five 4 mg capsules per card

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Differentiated thyroid cancer (DTC) is the most common type of thyroid cancer which is a cancerous growth of the thyroid gland which is located in the neck and helps regulate the body's metabolism. Lenvima is also used to treat patients with renal cell carcinoma, unresectable hepatocellular carcinoma, or endometrial carcinoma. Lenvima is a kinase inhibitor, which works by blocking certain proteins from helping cancer cells grow and divide. Lenvima may cause serious side effects, including cardiac failure, blood clot formation, liver damage, and kidney damage. The safety and effectiveness of Lenvima in pediatric patients have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Lenvima while maintaining optimal therapeutic outcomes.

References

1. Lenvima [package insert]. Woodcliff Lake, New Jersey: Eisai Inc.; November 2025.
2. NCCN Drugs & Biologics Compendium® Lenvatinib 2025. National Comprehensive Cancer Network, Inc. Accessed on January 9, 2025.

Policy History

Date	Action
March 2015	Addition to PA
June 2015	Annual review
June 2016	Annual editorial review and reference update Addition of advanced renal cell cancer (RCC) in combination with everolimus, for patients with advanced RCC following one prior anti-angiogenic therapy and renewal requirement of renewal requirement of no disease progression or unacceptable toxicity Policy changed from 5.04.55 to 5.21.55
June 2017	Annual editorial review and reference update
June 2018	Annual editorial review and reference update.
August 2018	Addition of unresectable hepatocellular carcinoma as first-line treatment, changes to regulatory status, addition of examples of unacceptable toxicities, addition of reference dosing and strengths
November 2018	Annual review
June 2019	Annual review and reference update
October 2019	Addition of indication: endometrial carcinoma
December 2019	Annual review
June 2020	Annual review and reference update
June 2021	Annual review and reference update
September 2021	Added option to use in combination with pembrolizumab for first-line treatment of advanced RCC. Removed requirement to use in combination with everolimus for advanced RCC continuation
December 2021	Annual review and reference update
June 2022	Annual review and reference update
September 2022	Per reconsideration review: addition of off-label indication per NCCN guidelines to include subsequent-line therapy for hepatocellular carcinoma (HCC). Per PI update, revised endometrial carcinoma indication so patients can be pMMR or not MSI-H
December 2022	Annual review and reference update
March 2023	Annual review and reference update
March 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.