Clinical Policy: Lenvatinib (Lenvima)

Reference Number: ERX.SPA.296
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Lenvatinib (Lenvima®) is a kinase inhibitor.

FDA Approved Indication(s)
Lenvima is indicated:

- For the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).
- In combination with pembrolizumab, for the first line treatment of adult patients with advanced renal cell carcinoma (RCC).
- In combination with everolimus for the treatment of patients with advanced RCC following one prior anti-angiogenic therapy.
- For the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).
- In combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma (EC) 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Lenvima is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Differentiated Thyroid Cancer (must meet all)**:**

1. Diagnosis of DTC (i.e., papillary, follicular, or Hürthle cell carcinoma);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is radioactive iodine-refractory and recurrent, metastatic, or progressive;
5. For brand Lenvima requests, member must use generic lenvatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 24 mg (3 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

B. Medullary or Anaplastic Thyroid Carcinoma (off-label) (must meet all)**:**

1. Diagnosis of one of the following thyroid carcinomas (a or b):

a. Medullary thyroid carcinoma (MTC), and both i and ii:
   i. Disease is recurrent, progressive, or metastatic;
   ii. Failure of Cometriq® or Caprelsa®, unless clinically significant adverse effects are experienced or both are contraindicated;
   **Prior authorization may be required for Cometriq and Caprelsa.*
b. Anaplastic thyroid carcinoma (ATC), and both i and ii:
   i. Disease is metastatic;
   ii. Prescribed as single agent therapy for members who have not tolerated or responded to NCCN recommended agents (*see Appendix B*);

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For brand Lenvima requests, member must use generic lenvatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 24 mg (3 capsules) per day;
   b. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

C. Renal Cell Carcinoma (must meet all)**:**
1. Diagnosis of advanced RCC (i.e., relapsed, metastatic, or stage IV disease);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Lenvima is prescribed in one of the following ways (a or b):
   a. In combination with Keytruda®;
   b. In combination with Afinitor®, and:
      i. If RCC histology is clear cell or unknown, failure of a prior RCC therapy *(see Appendix B)* unless clinically adverse effects are experienced or all are contraindicated;
      **Prior authorization may be required for prior RCC therapies*

   **Prior authorization may be required for Keytruda and Afinitor*
5. For brand Lenvima requests, member must use generic lenvatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed (i or ii):
      i. If prescribed in combination with Keytruda: 20 mg per day;
      ii. If prescribed in combination with Afinitor: 18 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

D. Hepatocellular Carcinoma (must meet all)**:**
1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For brand Lenvima requests, member must use generic lenvatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 12 mg per day (if actual body weight ≥ 60 kg) or 8 mg (if actual body weight < 60 kg);

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

E. Endometrial Carcinoma (must meet all)**:**

1. Diagnosis of EC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with Keytruda;
   **Prior authorization may be required for Keytruda*
5. Disease is not MSI-H or dMMR (i.e., disease is not indicative of MMR gene mutation or loss of expression);
6. Disease has progressed following prior systemic therapy (e.g., carboplatin/paclitaxel);
7. Member is not a candidate for curative surgery or radiation;
8. For brand Lenvima requests, member must use generic lenvatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
9. Request meets one of the following (a or b):*
   a. Dose does not exceed 20 mg (2 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

F. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Lenvima for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Lenvima requests, member must use generic lenvatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a, b, c, d, or e):*
   a. DTC, MTC, ATC: New dose does not exceed 24 mg per day (3 capsules per day);
   b. RCC in combination with Afinitor: New dose does not exceed 18 mg per day;
   c. HCC: New dose does not exceed 12 mg per day (if actual body weight ≥ 60 kg) or 8 mg (if actual body weight < 60 kg);
   d. RCC in combination with Keytruda**, EC: New dose does not exceed 20 mg (2 capsules) per day;
   e. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*
   ***After completing 2 years of combination therapy with Keytruda, Lenvima may be administered as a single agent until disease progression or until unacceptable toxicity*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ATC: anaplastic thyroid cancer
DTC: differentiated thyroid cancer
dMMR: mismatch repair deficient
EC: endometrial carcinoma
FDA: Food and Drug Administration
HCC: hepatocellular carcinoma
MSI-H: microsatellite instability-high
MTC: medullary thyroid cancer
NCCN: National Comprehensive Cancer Network
RCC: renal cell carcinoma

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Afinitor (everolimus)	RCC: 10 mg PO QD	10 mg per day
RCC therapeutic agents*:* Avastin® (bevacizumab) Cabometyx® (cabozantinib) Keytruda® (pembrolizumab) Inlyta® (axitinib) Nexavar® (sorafenib) Opdivo® (nivolumab) Proleukin® (aldesleukin, rIL-2) Sutent® (sunitinib) Tarceva® (erlotinib) Torisel® (temsirolimus) Votrient® (pazopanib) Yervoy® (ipilimumab)	RCC: varies	Varies
Caprelsa (vandetanib)	MTC: 300 mg PO QD	300 mg per day
Cometriq (cabozantinib)	MTC: 140-180 mg PO QD	180 mg per day
EC systemic therapies:* carboplatin/paclitaxel, cisplatin/docetaxel, cisplatin/doxorubicin, carboplatin/paclitaxel/bevacizumab, carboplatin/paclitaxel/trastuzumab, ifosfamide/paclitaxel, cisplatin/ifosfamide, everolimus/letrozole, temsirolimus, Keytruda (pembrolizumab) **Monotherapy treatment of combination regimens may also be used (refer to NCCN Uterine Neoplasms Guidelines)*	EC: varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
ATC systemic therapies for metastatic disease: dabrafenib/trametinib, larotrectinib, entrectinib, pralsetinib, selpercatinib, paclitaxel/carboplatin, doxetaxel/doxorubicin, paclitaxel, doxorubicin	ATC: varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
DTC	24 mg PO QD	24 mg/day
EC	20 mg PO QD	20 mg/day
HCC	12 mg PO QD (if actual body weight ≥ 60 kg) or 8 mg PO QD (if actual body weight < 60 kg)	12 mg/day
RCC	In combination with Keytruda: 20 mg PO QD. After completing 2 years of combination therapy, Lenvima may be administered as a single agent until disease progression or until unacceptable toxicity In combination with Afinitor: 18 mg PO QD	With Keytruda: 20 mg/day With Afinitor: 18 mg/day

VI. Product Availability
Capsules: 4 mg, 10 mg

VII. References
1. Lenvima Prescribing Information. Woodcliff Lake, NJ: Eisai, Inc; August 2021. Available at: http://www.lenvima.com/pdfs/prescribing-information.pdf. Accessed August 17, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 17, 2021.
3. National Comprehensive Cancer Network. Hepatobiliary Cancers Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf Accessed July 13, 2021.
4. National Comprehensive Cancer Network. Thyroid Carcinoma Version 4.2021. Available at: http://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed July 13, 2021.
5. National Comprehensive Cancer Network. Kidney Cancer Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed August 20, 2021.
6. National Comprehensive Cancer Network. Uterine Neoplasms Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed July 13, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.04.18	11.18
4Q 2019 annual review: NCCN designation of recurrent added to MTC criteria; criteria added for new FDA indication in EC; added Medicaid line	10.15.19	11.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
of business with 6/12 month approval durations; references reviewed and updated.		
4Q 2020 annual review: added off-label criteria for ATC per NCCN category 2A recommendation; references reviewed and updated.	07.13.20	11.20
RT4: updated FDA labeled indication for EC to remove accelerated approval language.	07.28.21	
RT4: criteria added for new FDA approved indication: RCC in combination with pembrolizumab.	08.20.21	
4Q 2021 annual review: no significant changes; added pralsetinib for ATC and Keytruda for RCC to therapeutic alternatives per NCCN; for brand name requests added requirement for generic alternative if available; references reviewed and updated.	07.28.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.