

## Clinical Policy: Lenvatinib (Lenvima)

Reference Number: ERX.SPA.296

Effective Date: 12.01.18

Last Review Date: 11.22

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<sup>®</sup>) 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 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.

### 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<sup>™</sup> 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  $\geq$  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 both of the following (i and ii):
    - i. 24 mg per day;
    - ii. 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 Thyroid Carcinoma (off-label) (must meet all):**

1. Diagnosis of medullary thyroid carcinoma (MTC), and both a and b:
  - a. Disease is recurrent, progressive, or metastatic;
  - b. Failure of Cometriq® or Caprelsa®, unless clinically significant adverse effects are experienced or both are contraindicated;\*
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 both of the following (i and ii):
    - i. 24 mg per day;
    - ii. 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;
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, b, or c):\*
  - a. If prescribed in combination with Keytruda, dose does not exceed both of the following (i and ii):
    - i. 20 mg per day;
    - ii. 2 capsules per day;
  - b. If prescribed in combination with Afinitor, dose does not exceed both of the following (i and ii):
    - i. 18 mg per day;
    - ii. 3 capsules per day;
  - c. 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, b, or c):\*
  - a. For actual body weight  $\geq$  60 kg, dose does not exceed both of the following (i and ii):
    - i. 12 mg per day;
    - ii. 3 capsules per day;
  - b. For actual body weight  $<$  60 kg, dose does not exceed both of the following (i and ii):
    - i. 8 mg per day;
    - ii. 2 capsules per day;
  - c. 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  $\geq$  18 years;
4. Prescribed in combination with Keytruda;  
*\*Prior authorization may be required for Keytruda*
5. Disease is pMMR or not MSI-H;
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 both of the following (i and ii):
    - i. 20 mg per day;
    - ii. 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. Thymic Carcinomas** (must meet all):

1. Diagnosis of thymic carcinoma (TC);
2. Prescribed by or in consultation with an oncologist;
3. Age  $\geq$  18 years;
4. Disease is unresectable, locally advanced, or metastatic;
5. Prescribed as single agent therapy for members who have not tolerated or responded to NCCN recommended agents (*see Appendix B*);
6. For brand Lenvima requests, member must use generic lenvatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):\*
  - a. Dose does not exceed both of the following (i and ii):
    - i. 24 mg per day;
    - ii. 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

**G. 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, TC: New dose does not exceed both of the following (i and ii):
    - i. 24 mg per day;
    - ii. 3 capsules per day;
  - b. RCC in combination with Afinitor: New dose does not exceed both of the following (i and ii):
    - i. 18 mg per day;
    - ii. 3 capsules per day;
  - c. HCC: New dose does not exceed one of the following (i or ii):
    - i. For actual body weight  $\geq$  60 kg (1 and 2):
      - 1) 12 mg per day;
      - 2) 3 capsules per day;
    - ii. For actual body weight < 60 kg (1 and 2):
      - 1) 8 mg per day;
      - 2) 2 capsules per day;
  - d. RCC in combination with Keytruda\*\*, EC: New dose does not exceed both of the following (i and ii):
    - i. 20 mg per day;
    - ii. 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*

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

*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
<b>RCC therapeutic agents:</b> 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
<b>EC systemic therapies:*</b> carboplatin/paclitaxel, cisplatin/docetaxel, cisplatin/doxorubicin, carboplatin/paclitaxel/bevacizumab, carboplatin/paclitaxel/trastuzumab, ifosfamide/paclitaxel, cisplatin/ifosfamide, everolimus/letrozole, temsirolimus, Keytruda (pembrolizumab)	EC: varies	Varies
<i>*Monotherapy treatment of combination regimens may also be used (refer to NCCN Uterine Neoplasms Guidelines)</i>		
<b>TC systemic therapies:</b> Carboplatin/paclitaxel	carboplatin AUC 6 mg/mL/min + paclitaxel 200 mg/m <sup>2</sup> IV every 3 weeks	See dosing regimen

*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

Indication	Dosing Regimen	Maximum Dose
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 2022. Available at: <http://www.lenvima.com/pdfs/prescribing-information.pdf>. Accessed August 22, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed July 20, 2022.
3. National Comprehensive Cancer Network. Hepatobiliary Cancers Version 2.2022. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/hepatobiliary.pdf](https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf) Accessed July 21, 2022.
4. National Comprehensive Cancer Network. Thyroid Carcinoma Version 4.2023. Available at: [http://www.nccn.org/professionals/physician\\_gls/pdf/thyroid.pdf](http://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf). Accessed July 21, 2022.
5. National Comprehensive Cancer Network. Kidney Cancer Version 2.2022. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/kidney.pdf](https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf). Accessed July 21, 2022.
6. National Comprehensive Cancer Network. Uterine Neoplasms Version 1.2022. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/uterine.pdf](https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf). Accessed July 21, 2022.

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 of business with 6/12 month approval durations; references reviewed and updated.	10.15.19	11.19
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
4Q 2022 annual review: added off-label criteria for TC per NCCN category 2A recommendation; removed off-label criteria for ATC as use is no longer supported by NCCN; RT4: for EC, revised dMMR to pMMR per updated FDA approved indication; references reviewed and updated.	08.22.22	11.22

**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.

This policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2018 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.