Clinical Policy: Lenvatinib (Lenvima)

Reference Number: CP.PHAR.138
Effective Date: 12.01.18
Last Review Date: 11.24
Line of Business: Commercial, HIM, 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 adult 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 adult 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) or not microsatellite instability-high (MSI-H), as determined by an FDA-approved test, 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.

It is the policy of health plans affiliated with Centene Corporation® 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 oncocytic (formerly known as 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. Prescribed as monotherapy;
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 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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

1. Diagnosis of one of the following (a or b):
   a. Medullary thyroid carcinoma (MTC) that is recurrent, progressive, or metastatic;
   b. Anaplastic thyroid carcinoma (ATC) that is metastatic;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For MTC: 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.*
5. For ATC: prescribed in combination with Keytruda®;
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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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 everolimus (Afinitor®), and:
      i. If RCC histology is clear cell, as subsequent therapy;

   **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, 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 everolimus 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Hepatocellular Carcinoma (must meet all)**:**

1. Diagnosis of HCC;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as single agent;
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. For actual body weight ≥ 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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 pMMR or not MSI-H;
6. Disease has progressed following prior platinum-based systemic therapy (e.g., carboplatin, cisplatin);
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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

F. Thymic Carcinomas (off-label) (must meet all):
1. Diagnosis of thymic carcinoma (TC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed as single agent and as subsequent therapy;
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 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

G. Cutaneous Melanoma (off-label) (must meet all):
1. Diagnosis of cutaneous melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is metastatic or unresectable;
5. Prescribed in combination with Keytruda;
   **Prior authorization may be required for Keytruda*
6. Disease has progressed following treatment with an anti-PD-1/PD-L1-based therapy (e.g., Keytruda, Opdivo®);
7. For brand Lenvima requests, member must use generic lenvatinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. 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 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

H. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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, 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 everolimus: 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 ≥ 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, cutaneous melanoma: 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:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ATC: anaplastic thyroid carcinoma
DTC: differentiated thyroid cancer
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
pMMR: mismatch repair proficient

RCC: renal cell carcinoma TC: thymic 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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
everolimus (Afinitor)	RCC: 10 mg PO QD	10 mg/day
Caprelsa® (vandetanib)	MTC: 300 mg PO QD	300 mg/day
Cometriq® (cabozantinib)	MTC: 140 to 180 mg PO QD	180 mg/day
EC systemic therapies:* carboplatin/paclitaxel, cisplatin/docetaxel, carboplatin/docetaxel, cisplatin/doxorubicin, cisplatin/doxorubicin/paclitaxel, cisplatin/gemcitabine carboplatin/paclitaxel/pembrolizumab, carboplatin/paclitaxel/dostarlimab-gxly carboplatin/paclitaxel/bevacizumab, carboplatin/paclitaxel/trastuzumab, cisplatin/ifosfamide, _____ **Monotherapy treatment of combination regimens may also be used (refer to NCCN Uterine Neoplasms Guidelines)*	EC: varies	Varies
Cutaneous Melanoma anti-PD-1/PD-L1-based therapy: Keytruda (pembrolizumab), Opdivo (nivolumab)	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	In combination with Keytruda: 20 mg PO QD	20 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 everolimus: 18 mg PO QD	With Keytruda: 20 mg/day With Afinitor: 18 mg/day

Indication	Dosing Regimen	Maximum Dose
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

VI. Product Availability

Capsules: 4 mg, 10 mg

VII. References

1. Lenvima Prescribing Information. Woodcliff Lake, NJ: Eisai, Inc; January 2025. Available at: http://www.lenvima.com/pdfs/prescribing-information.pdf. Accessed February 13, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 2, 2024.
3. National Comprehensive Cancer Network. Thyroid Carcinoma Version 3.2024. Available at: http://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed August 2, 2024.
4. National Comprehensive Cancer Network. Thymomas and Thymic Carcinomas Version 1.2024. Available at: http://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf. Accessed August 2, 2024.
5. National Comprehensive Cancer Network. Kidney Cancer Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed August 2, 2024.
6. National Comprehensive Cancer Network. Hepatocellular Carcinoma Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf. Accessed July 2, 2024.
7. National Comprehensive Cancer Network. Uterine Neoplasms Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed August 2, 2024.
8. National Comprehensive Cancer Network. Melanoma: Cutaneous Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed August 2, 2024.
9. Arance A, de la Cruz-Merino L, Petrella TM. Phase II LEAP-004 study of Lenvatinib plus pembrolizumab for melanoma with confirmed progression on a programmed cell death protein-1 or programmed death ligand 1 inhibitor given as monotherapy or in combination. J Clin Oncol. 2023 Jan 1; 41(1):75-85.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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, Keytruda for RCC to therapeutic alternatives per NCCN; for brand name requests added requirement for generic alternative if available; HIM.PHAR.21 changed to HIM.PA.154; references reviewed and updated.	07.28.21	11.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
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. Template changes applied to other diagnoses/indications.	08.22.22	11.22
4Q 2023 annual review: for HCC, added prescribed as a single agent per NCCN; added off-label criteria for cutaneous melanoma per NCCN category 2A recommendation; references reviewed and updated.	06.28.23	11.23
4Q 2024 annual review: for DTC, clarified Hurthle cell carcinoma as oncocytic carcinoma and added criteria requiring prescription as monotherapy; for medullary carcinoma, revised section title to include anaplastic carcinoma and added off-label criteria for ATC per NCCN category 2A recommendation; clarified Afinitor as everolimus due to generic availability; for RCC, simplified criteria requiring failure of a prior RCC therapy to "as subsequent therapy"; for EC, clarified systemic therapy as platinum-based systemic therapy; for TC, removed requirement for disease type due to NCCN 2A recommended use in all disease types, simplified criteria requiring members who "have not tolerated or responded to NCCN recommended agents" to "as subsequent therapy"; references reviewed and updated.	08.02.24	11.24
RT4: updated FDA Approved Indication section for EC to require FDA-approved testing for both MSI-H and pMMR (previously required for pMMR only) per PI.	02.13.25	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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 clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.