Clinical Policy Title:	lenvatinib
Policy Number:	RxA.198
Drug(s) Applied:	Lenvima®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Lenvatinib (Lenvima®) is a kinase inhibitor. It is indicated:

- For the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).
- In combination with everolimus for the treatment of patients with advanced renal cell carcinoma (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. 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
lenvatinib (Lenvima®)	DTC	24 mg by mouth once daily	24 mg/day
	EC	20 mg by mouth once daily in combination with pembrolizumab 200 mg administered as an intravenous infusion over 30 minutes every 3 weeks	20 mg/day
	RCC	18 mg by mouth once daily with everolimus 5 mg orally once daily.	18 mg/day
	HCC	12 mg by mouth once daily (if actual body weight ≥ 60 kg) or 8 mg by mouth once daily (if actual body weight < 60 kg)	12 mg/day

Dosage Forms

- Capsules: 4 mg, 10 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 locally recurrent, metastatic, or progressive;
5. 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: 6 months

Medicaid: 6 months

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

1. Diagnosis of medullary or anaplastic thyroid carcinoma (MTC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For medullary carcinoma, must meet all of the following:
   a. disease is recurrent, or persistent distant metastases if symptomatic or progressive;
   b. Failure of Cometriq® or Caprelsa®, unless contraindicated or clinically significant adverse effects are experienced or there is progression despite treatment;

   **Prior authorization may be required for Cometriq and Caprelsa.*
5. For anaplastic carcinoma, must meet all of the following:
   a. Disease is metastatic;
   b. Prescribed a first-line or second-line single agent therapy for members who are not tolerating or had no response to recommended agents (See Appendix B) without curative option (useful in certain circumstances)
6. 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: 6 months

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. Will be used in combination with Afinitor®;
   **Prior authorization may be required for Afinitor*
5. If RCC histology is clear cell, failure of a prior first-line RCC therapy *(see Appendix B)* unless contraindicated or clinically adverse effects are experienced;

**Prior authorizatio n may be required for prior RCC therapies*

6. If RCC histology is non-clear cell, used as systemic therapy
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 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: 6 months
Medicaid: 6 months

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

1. Diagnosis of unresectable hepatocellular carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member must meet the following:
   a. Liver function is classified as Child-Pugh Class A
   b. Have unresectable disease and are not a transplant candidate
   c. Have liver-confined disease, inoperable by performance status, comorbidity or with minimal or uncertain extrahepatic disease
   d. Have metastatic disease or extensive liver tumor burden
5. Prescribed as single agent therapy;
6. 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 per day (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: 6 months
Medicaid: 6 months

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

1. Diagnosis of advanced endometrial carcinoma;
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. 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: 6 months

Medicaid: 6 months

F. Thymomas and Thymic Carcinomas (off-label):

1. Diagnosis of thymic carcinoma
2. Used as single agent for one of the following:
   a. Prescribed as first line therapy for members who cannot tolerate combination regimens for any of the following:
      i. Unresectable locally advanced disease in combination with radiation therapy;
      ii. Potentially resectable locally advanced disease;
      iii. Potentially resectable solitary metastasis or ipsilateral pleural metastasis;
      iv. Consideration following surgery for solitary metastasis or ipsilateral pleural metastasis;
      v. Extrathoracic metastatic disease.
   b. Prescribed for postoperative treatment for members who are unable to tolerate first-line combination regimens after R1 or R2 resection;
   c. Prescribed as second-line therapy for one of the following:
      i. Unresectable disease following first-line chemotherapy for potentially resectable locally advanced disease, solitary metastasis, or ipsilateral pleural metastasis;
      ii. Extrathoracic metastatic disease.
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
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: 6 months

Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance ordocumentation supports that member has
   met initial approval criteria for the covered indications and has received medication for at least 30 days;
2. Member is responding positively to therapy;
3. 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 (3 capsules) per day;
   b. RCC: New dose does not exceed 18 mg per day;
   c. HCC: New dose does not exceed 12 mg per day (actual body weight ≥ 60 kg) or 8

mg (actual body weight < 60 kg);

d. 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

Approval Duration

Commercial: 12 months

Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

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 carcinoma
NCCN: National Comprehensive Cancer Network
RCC: Renal cell carcinoma
ATC: Anaplastic Thyroid Carcinoma

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
RCC therapeutic agents		
Afinitor® (everolimus)	RCC: 10 mg by mouth once daily	10 mg/day
Keytruda® (embrolizumab), Avastin® (bevacizumab), Cabometyx® (cabozantinib), Inlyta® (axitinib), Nexavar® (sorafenib), Opdivo® (nivolumab), Proleukin® (aldesleukin, rIL-2), Sutent® (sunitinib), Tarceva® (erlotinib), Torisel® (temsirolimus), Votrient® (pazopanib), Yervoy® (ipilimumab)	RCC: regimens vary	Varies
Anaplastic carcinoma- recommended regimens		
Taflinar® (dabrafenib) and Mekinist® (trametinib),	dabrafenib 150 mg twice daily and trametinib 2 mg once daily	See dosing
Vitrakvi® (Larotrectinib)	100 mg twice daily	
Rozlytrek® (entrectinib)	600 mg once daily	
Gavreto™ (pralsetinib)	400 mg once daily	
Retevmo™ (selpercatinib)	120 mg twice daily (<50	

	kg) or 160 mg twice daily (≥50 kg)	

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

- Contraindication(s):
  - None

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Targeted therapy is about identifying other features of cancer cells. There are different types of targeted therapies, defined in three broad categories. Some targeted therapies focus on the internal components and function of the cancer cell. The targeted therapies use small molecules that can get into the cell and disrupt the function of the cells, causing them to die. There are several types of targeted therapy that focus on the inner parts of the cells. Other targeted therapies target receptors that are on the outside of the cell. Therapies that target receptors are also known as monoclonal antibodies.
- Lenvatinib is a targeted therapy that targets and binds to the tyrosine kinase receptors.

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1) Policy title was updated. 2) Dosing information updated. 3) Continued Therapy Approval criteria II.A.1 was rephrased. 4) Appendices were updated. 5) References were updated.	06/15/2020	09/14/2020
Policy was reviewed: 1) Dosing information updated for indication EC & HCC. 2) Replaced abbreviated form PO, QD to "by mouth" "Once daily" respectively. 3) Clinical policy Initial Approval Criteria (2) off label indications added for Thymomas and Thymic Carcinomas & Thyroid Carcinoma - Anaplastic Carcinoma. 4) Therapeutic alternative verbiage updated "Below are sugg...". 5) References were revised and added.Updated initial criteria in section I.B to include criteria for anaplastic carcinoma (NCCN 2A recommendation) 6) Updated section I.C initial approval criteria for RCC for non-clear cell histology 7) Updated section I.D.4 initial approval criteria for HCC to elaborate on who is eligible for therapy. Added I.D.5 8) Added initial approval criteria for NCCN 2A recommendation – thymomas and thymic carcinomas in section I.F	03/03/2021	06/10/2021