Lenvima® (lenvatinib)
(Oral)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

LENVIMA capsules are supplied in cartons of 6 cards. Each card is a 5-day blister card as follows:	
Strength	**Quantity Limit**
24 mg (ten 10 mg capsules and five 4 mg capsules per card)	1 carton every 30 days
20 mg (ten 10 mg capsules per card)	1 carton every 30 days
18 mg (five 10 mg capsules and ten 4 mg capsules per card)	1 carton every 30 days
14 mg (five 10 mg capsules and five 4 mg capsules per card)	1 carton every 30 days
12 mg (fifteen 4 mg capsules per card)	1 carton every 30 days
10 mg (five 10 mg capsules per card)	1 carton every 30 days
8 mg (ten 4 mg capsules per card)	1 carton every 30 days
4 mg (five 4 mg capsules per card)	1 carton every 30 days

B. Max Units (per dose and over time) [HCPCS Unit]:

Indication	Max Units	Frequency
Thyroid Carcinoma	24 mg	Daily
Renal Cell Carcinoma	20 mg	Daily
Hepatocellular Carcinoma	– 12 mg if ≥ 60 kg – 8 mg if < 60 kg	Daily
Endometrial Carcinoma	20 mg	Daily
Thymic Carcinoma	24 mg	
Cutaneous Melanoma	20 mg	Daily

III. Initial Approval Criteria[1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient's thyroid function has been assessed prior to initiating therapy and will be monitored at least monthly during treatment; **AND**
- Patient will avoid coadministration with medicinal products that have a known potential to prolong the QT/QTc interval (e.g., Class Ia and III antiarrhythmics, etc.), and if therapy is unavoidable, the patient will be monitored closely for adverse reactions; **AND**

Thyroid Carcinoma (Follicular, Oncocytic, or Papillary) † Φ [1-4]

- Used as single agent therapy; **AND**
- Patient has locally recurrent, unresectable, persistent, or metastatic disease; **AND**
- Disease is progressive and/or symptomatic; **AND**
- Disease is not amenable to radioactive iodine (RAI) therapy

Thyroid Carcinoma (Medullary) ‡ Φ [2,3]

- Used as single agent therapy; **AND**
- Patient has recurrent or persistent distant metastatic disease that is progressive or symptomatic; **AND**
  - Patient has progressed on preferred systemic therapy options (i.e., vandetanib or cabozantinib); **OR**
  - Clinical trials or preferred systemic therapy options (i.e., vandetanib or cabozantinib) are not available or appropriate for the patient

Renal Cell Cancer (RCC) † ‡ [1,2,5,9]

- Patient has advanced, relapsed, or stage IV disease; **AND**
  - Used in combination with everolimus; **AND**
    - Used as subsequent therapy for clear cell histology; **OR**
    - Patient has non-clear cell histology; **OR**
  - Used in combination with pembrolizumab; **AND**
    - Patient has clear cell histology

Hepatocellular Carcinoma (HCC) † ‡ Φ [1,2,6]

- Used as single agent therapy; **AND**
- Patient has Child-Pugh Class A disease; **AND**
  - Patient has unresectable disease and is not a transplant candidate; **OR**
  - Patient has liver-confined disease inoperable by performance status or comorbidity or has minimal or uncertain extrahepatic disease; **OR**
  - Patient has metastatic disease or extensive liver tumor burden

Endometrial Carcinoma (Uterine Neoplasms) † [1,2,7]

- Used in combination with pembrolizumab; **AND**
- Disease is mismatch repair proficient (pMMR) as determined by an FDA-approved or CLIA-compliant test❖ or NOT microsatellite instability-high (MSI-H); **AND**
  - Used as first-line therapy for recurrent disease after prior platinum-based therapy *(excluding use in patients with isolated metastases)*; **OR**
  - Used as subsequent therapy for advanced, recurrent, or metastatic disease

Thymic Carcinoma ‡ [2,8]

- Used as a single agent; **AND**
  - Patient is unable to tolerate first-line combination regimens; **AND**
    - Used as preoperative systemic therapy of surgically resectable disease if R0 resection is considered uncertain; **OR**
    - Used as postoperative treatment after R1 (microscopic residual tumor) or R2 (macroscopic residual tumor) resection; **OR**
    - Used as first-line therapy for recurrent, advanced, or metastatic disease; **OR**
  - Used as second-line therapy; **AND**
    - Patient has unresectable or metastatic disease

Cutaneous Melanoma ‡ [2,10]

- Used as subsequent therapy; **AND**
- Used for metastatic or unresectable disease with progression following treatment with anti-PD-1/PD-L1-based therapy, including in combination with anti-CTLA-4 (e.g., ipilimumab) for ≥2 doses; **AND**
- Used in combination with pembrolizumab

❖*If confirmed using an FDA approved assay - http://www.fda.gov/companiondiagnostics*

† FDA-Labeled Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: life-threatening hypertension, severe cardiac dysfunction (including cardiomyopathy, ventricular dysfunction, congestive heart failure, cardiac failure, ventricular hypokinesia, or decrease in ventricular ejection fraction), hepatotoxicity, proteinuria/nephrotic syndrome,

renal failure/impairment, gastrointestinal perforation/fistula formation, severe/recurrent diarrhea, severe QT interval prolongation, reversible posterior leukoencephalopathy syndrome (RPLS), arterial thromboembolic events, hemorrhagic events, severe hypocalcemia, impairment of thyroid stimulating hormone suppression/thyroid dysfunction, impaired wound healing, osteonecrosis of the jaw (ONJ), etc.

V. Dosage/Administration [1,8,10]

Indication	Dose
Thyroid Carcinoma	24 mg (two 10 mg capsules and one 4 mg capsule) orally once daily until disease progression or unacceptable toxicity
RCC	Combination with everolimus: 18 mg (one 10 mg capsule and two 4 mg capsules) orally once daily (in combination with everolimus 5 mg orally once daily) until disease progression or unacceptable toxicity Combination with pembrolizumab: 20 mg (two 10 mg capsules) orally once daily (in combination with pembrolizumab 200 mg IV every 3 weeks) until disease progression or until unacceptable toxicity for up to 24 months **After completing 24 months of combination therapy with pembrolizumab, LENVIMA may be administered as a single agent until disease progression or until unacceptable toxicity*
HCC	The recommended dose is based on actual body weight and is taken orally once daily until disease progression or unacceptable toxicity: • 12 mg for patients greater than or equal to 60 kg or • 8 mg for patients less than 60 kg
Endometrial Carcinoma	20 mg (two 10 mg capsules) orally once daily (in combination with pembrolizumab 200 mg administered as an intravenous infusion every 3 weeks) until disease progression or unacceptable toxicity
Thymic Carcinoma	24 mg (two 10 mg capsules and one 4 mg capsule) orally once daily until disease progression or unacceptable toxicity
Cutaneous Melanoma	20 mg (two 10 mg capsules) orally once daily (in combination with pembrolizumab 200 mg administered as an intravenous infusion every 3 weeks) until disease progression or unacceptable toxicity
******Refer to the Lenvima full prescribing information for directions on how to use the capsules to prepare a suspension for oral administration or for feeding tube administration.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug, oral, chemotherapeutic, nos

NDC(s):

LENVIMA capsules are supplied in cartons of 6 cards. Each card is a 5-day blister card as follows:	
NDC	**Strength**
62856-0724-xx	24 mg (ten 10 mg capsules and five 4 mg capsules per card)
62856-0720-xx	20 mg (ten 10 mg capsules per card)
62856-0718-xx	18 mg (five 10 mg capsules and ten 4 mg capsules per card)
62856-0714-xx	14 mg (five 10 mg capsules and five 4 mg capsules per card)
62856-0712-xx	12 mg (fifteen 4 mg capsules per card)
62856-0710-xx	10 mg (five 10 mg capsules per card)
62856-0708-xx	8 mg (ten 4 mg capsules per card)
62856-0704-xx	4 mg (five 4 mg capsules per card)

VII. References

1. Lenvima [package insert]. Eisai Inc., Nutley, NJ; October 2023. Accessed December 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for lenvatinib. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed December 2023.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Thyroid Carcinoma. Version 4.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed December 2023.
4. Schlumberger M, Tahara M, Wirth LJ, et al. Lenvatinib versus placebo in radioiodine-refractory thyroid cancer. N Engl J Med. 2015 Feb 12;372(7):621-30.
5. Motzer RJ, Hutson TE, Glen H, et al. Lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma: a randomised, phase 2, open-label, multicentre trial. Lancet Oncol. 2015 Nov;16(15):1473-1482.
6. Kudo M, Finn RS, Qin S, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. Lancet. 2018 Mar 24;391(10126):1163-1173.
7. Makker V, Rasco D, Vogelzang NJ, et al. Lenvatinib plus pembrolizumab in patients with advanced endometrial cancer: an interim analysis of a multicentre, open-label, single-arm, phase 2 trial. Lancet Oncol. 2019 May;20(5):711-718.
8. Sato J, Satouchi M, Itoh S, et al. Lenvatinib in patients with advanced or metastatic thymic carcinoma (REMORA): a multicentre, phase 2 trial. Lancet Oncol. 2020 Jun;21(6):843-850.

9. Motzer R, Alekseev B, Rha S, et al. Lenvatinib plus Pembrolizumab or Everolimus for Advanced Renal Cell Carcinoma. N Engl J Med 2021 Apr 8;384(14):1289-1300
10. Arance A, de la Cruz-Merino, L, Petrella TM, et al. 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. doi: 10.1200/JCO.22.00221.

Appendix 1 – Covered Diagnosis Codes

ICD-10	Description
C22.0	Liver cell carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C37	Malignant neoplasm of thymus
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified

ICD-10	Description
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C73	Malignant neoplasm of thyroid gland
D15.0	Benign neoplasm of thymus
D38.4	Neoplasm of uncertain behavior of thymus
Z85.238	Personal history of other malignant neoplasm of thymus
Z85.820	Personal history of malignant melanoma of skin

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD):

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC