PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Lenvima Prior Authorization Policy
- Lenvima® (lenvatinib capsules – Eisai)

REVIEW DATE: 06/07/2023

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Lenvima, a kinase inhibitor, is indicated for the following uses:[1]

- **Differentiated thyroid cancer** for treatment of locally recurrent or metastatic, progressive, radioactive iodine refractory disease.
- **Endometrial cancer**, in combination with Keytruda® (pembrolizumab intravenous infusion), for advanced disease 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.
- **Hepatocellular carcinoma** for first-line treatment of patients with unresectable disease.
- **Renal cell carcinoma**, advanced in combination with everolimus tablets, following one prior anti-angiogenic therapy.
- **Renal cell carcinoma,** advanced, for first-line treatment of adult patients in combination with Keytruda.

Guidelines

Lenvima is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):[2]

- **Hepatocellular Carcinoma**: NCCN guidelines (version 1.2023 – March 10, 2023) recommend Lenvima as "other recommended regimen" for first-line

systemic therapy (Child-Pugh Class A only) for hepatocellular carcinoma (category 1). It is also recommended as subsequent-line therapy upon disease progression (Child-Pugh Class A only) [category 2A].[3]

- **Kidney Cancer**: NCCN guidelines (version 4.2023 – January 18, 2023) recommend Lenvima + everolimus as a "preferred regimen" as subsequent therapy for relapse or stage IV disease with clear cell histology (category 2A); this combination is also listed as systemic therapy, "other recommended regimens", for relapsed or stage IV disease for non-clear cell histology (category 2A). Lenvima + Keytruda is listed as a "preferred regimen" for first-line therapy for relapsed or stage IV disease for clear cell histology (category 1); this combination is also listed as "other recommended regimen" for subsequent therapy for relapsed or stage IV with clear cell histology (category 2A).[4]
- **Melanoma**: **Cutaneous**: NCCN guidelines (version 2.2023 – March 10, 2023) recommend use of Lenvima + Keytruda (category 2A) for metastatic or unresectable disease, as second-line or subsequent therapy after treatment with anti-programmed death-1 (PD-1)/programmed death-ligand 1 (PD-L1) - based therapy, including in combination with anti-CTL antigen 4 (CTLA-4) for at least two doses.[8]
- **Thymomas and Thymic Carcinomas**: NCCN guidelines (version 1.2023 – December 15, 2022) recommend single-agent Lenvima (category 2A) as second-line systemic therapy for thymic carcinoma.[5]
- **Thyroid Carcinoma**: NCCN guidelines (version 2.2023 – May 18, 2023) indicate that first-line treatment for differentiated thyroid cancer is surgery, whenever possible, followed by radioactive iodine therapy in selected patients, and levothyroxine therapy in all patients.[2] Systemic therapy options include cytotoxic chemotherapy and kinase inhibitors. The guidelines state that for progressive and/or symptomatic disease, Lenvima is a preferred systemic therapy regimen (category 1) for locally recurrent, advanced, and/or metastatic disease not amenable to radioactive iodine therapy. There is a footnote that states that kinase inhibitor therapy may not be appropriate for patients with stable or slowly progressive indolent disease. Lenvima can be considered for treatment of progressive or symptomatic medullary thyroid disease if clinical trials or preferred systemic therapy options are not available or appropriate, or if there is progression on preferred systemic therapy options (category 2A).[6]
- **Uterine Neoplasms**: NCCN guidelines (version 2.2023– April 28, 2023) recommends Lenvima with Keytruda combination therapy for biomarker directed systemic therapy for second-line treatment for recurrent or metastatic endometrial carcinoma for non-MSI-high [MSI-H]/non-MMR-deficient [dMMR] tumors. This combination is a category 1 recommendation as preferred therapy.[7]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Lenvima. All approvals are provided for the duration noted below.

- **Lenvima® (lenvatinib capsules – Eisai)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Endometrial Carcinoma**. Approve for 1 year if the patient meets the following criteria (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR); AND
   - **C)** The medication is used in combination with Keytruda (pembrolizumab intravenous injection); AND
   - **D)** Patient has tried at least one systemic therapy; AND
     Note: Examples of systemic therapy include carboplatin, paclitaxel, docetaxel, cisplatin, doxorubicin, or ifosfamide.
   - **E)** Patient is not a candidate for curative surgery or radiation.

2. **Hepatocellular Cancer**. Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has unresectable or metastatic disease.

3. **Renal Cell Cancer**. Approve for 1 year if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced disease; AND
   - **C)** Patient meets ONE of the following (i or ii):
     - **i.** Lenvima is being used in combination with Keytruda (pembrolizumab intravenous infusion); OR
     - **ii.** Lenvima is being used in combination with everolimus tablets/Afinitor Disperz (everolimus tablets for oral suspension) AND patient meets one of the following (a or b):
       - **a)** Patient has clear cell histology and patient has tried one antiangiogenic therapy; OR
         Note: Examples of antiangiogenic therapy include Inlyta (axitinib tablets), Votrient (pazopanib tablets), sunitinib, or Cabometyx (cabozantinib tablets).
       - **b)** Patient has non-clear cell histology.

4. **Thyroid Carcinoma, Differentiated**. Approve for 1 year if the patient meets the following criteria (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has differentiated thyroid carcinoma.
     Note: Examples of differentiated thyroid carcinoma include papillary, follicular, and oncocytic carcinoma (formerly Hürthle cell carcinoma).

C) The disease is refractory to radioactive iodine therapy.

Other Uses with Supportive Evidence

5. **Melanoma.** Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has unresectable or metastatic melanoma; AND
   C) The medication is used in combination with Keytruda (pembrolizumab intravenous injection); AND
   D) Patient has disease progression on anti-programmed death receptor-1 (PD-1)/programmed death-ligand 1 (PD-L1)-based therapy.
   Note: Examples of anti-PD-1/PD-L1 therapies include Opdivo (nivolumab intravenous infusion) + Yervoy (ipilimumab intravenous infusion), Opdualag (nivolumab and relatlimab-rmbw intravenous infusion), Keytruda, Opdivo.

6. **Thymic Carcinoma**. Approve for 1 year if the patient meets the following criteria (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried at least one chemotherapy regimen.
   Note: Examples of a chemotherapy regimen include carboplatin plus paclitaxel, cisplatin, doxorubicin plus cyclophosphamide, cisplatin plus etoposide.

7. **Thyroid Carcinoma, Medullary**. Approve for 1 year if the patient meets the following criteria (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried at least one systemic therapy.
   Note: Examples of systemic therapy include Caprelsa (vandetanib tablets), Cometriq (cabozantinib capsules), Retevmo (selpercatinib capsules), and Gavreto (pralsetinib capsules).

CONDITIONS NOT COVERED

- **Lenvima® (lenvatinib capsules – Eisai)**

is(are) considered experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Lenvima® capsules [prescribing information]. Woodcliff Lake, NJ: Eisai; November 2022.
2. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 5, 2023. Search term: lenvatinib.
3. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 1.2023 – March 10, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 06, 2023.

4. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 4.2023– January 18, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 5, 2023.
5. The NCCN Thymomas and Thymic Carcinoma Clinical Practice Guidelines in Oncology (version 1.2023 – December 15, 2022). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 5, 2023.
6. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 2.2023 – May 18, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 5, 2023.
7. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 2.2023 – April 28, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 5, 2023.
8. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2023 – March 10, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 6, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Endometrial Carcinoma:** The approval duration was changed from 3 years to 1 year. **Hepatocellular Cancer:** The approval duration was changed from 3 years to 1 year. **Renal Cell Cancer:** The approval duration was changed from 3 years to 1 year. **Thyroid Carcinoma, Differentiated:** The approval duration was changed from 3 years to 1 year. **Thymic Carcinoma:** The approval duration was changed from 3 years to 1 year. **Thyroid Carcinoma, Medullary:** The approval duration was changed from 3 years to 1 year.	06/22/2022
Annual Revision	**Thyroid Carcinoma, Differentiated:** For examples of thyroid carcinoma, changed Hürthle cell carcinoma name to "oncocytic carcinoma (formerly Hürthle cell carcinoma)" based on guideline changes. **Melanoma:** Added new condition of approval for Lenvima use in combination with Keytruda (pembrolizumab for intravenous infusion) for subsequent therapy based on guidelines.	06/07/2023