PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 06/19/2024

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 1.2024 – April 9, 2024) 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 4.2024 – May 30, 2024) recommend Lenvima + everolimus as one of the "Other Recommended Regimens" 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 2.2024 – April 3, 2024) 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 1.2024 – November 21, 2023) recommend single-agent Lenvima (category 2A) as one of the "Preferred" second-line systemic therapy for thymic carcinoma.[5] Lenvima can also be considered as a "preferred" first-line therapy in patients who cannot tolerate first-line combination regimens (category 2A).
- **Thyroid Carcinoma**: NCCN guidelines (version 2.2024 – March 12, 2024) 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] Lenvima, in combination with Keytruda, is recommended as "Useful in Certain Circumstances" (category 2A) for first-line or second-line therapy in anaplastic carcinoma.

- **Uterine Neoplasms**: NCCN guidelines (version 2.2024– March 6, 2024) recommends Lenvima with Keytruda combination therapy as "Useful in Certain Circumstances" for biomarker directed systemic therapy for first-line or second-line treatment for recurrent endometrial carcinoma for pMMR 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Lenvima is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Endometrial Carcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has advanced endometrial carcinoma that is mismatch repair proficient (pMMR); 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 BOTH of the following (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 ALL of the following (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), pazopanib, sunitinib, or Cabometyx (cabozantinib tablets).

b) Patient has non-clear cell histology.

4. **Thyroid Carcinoma, Differentiated**. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has differentiated thyroid carcinoma; AND
   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 ALL of the following (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 BOTH of the following (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 BOTH of the following (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).

8. **Thyroid Carcinoma, Anaplastic.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) The medication is used in combination with Keytruda (pembrolizumab intravenous injection).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Lenvima is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Lenvima® capsules [prescribing information]. Woodcliff Lake, NJ: Eisai; November 2022.
2. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024. Search term: lenvatinib.
3. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 1.2024 – April 9, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024.
4. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 4.2024– May 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024.
5. The NCCN Thymomas and Thymic Carcinoma Clinical Practice Guidelines in Oncology (version 1.2024 – November 21, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024.
6. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 2.2024 – March 12, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024.
7. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 2.2024 – March 6, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024.
8. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2024 – April 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 17, 2024.