PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 06/04/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

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), 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.
- **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 1.2025 – March 20, 2025) recommend Lenvima as "other recommended regimen" for first-line systemic therapy (Child-Pugh Class A only) for hepatocellular carcinoma (category 1).[3] Lenvima is no longer recommended for subsequent therapy.
- **Kidney Cancer**: NCCN guidelines (version 3.2025 – January 9, 2025) 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 2.2025 – January 28, 2025) 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 2.2025 – May 19, 2025) 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 1.2025 – March 27, 2025) 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 papillary or follicular carcinoma, Lenvima is a "preferred" systemic therapy regimen (category 1) for locally recurrent, advanced, and/or metastatic disease not amenable to radioactive iodine therapy. The guidelines note that a majority of oncocytic carcinoma are non-iodine-avid, so "radioactive-iodine refractory" may not be applicable to oncocytic carcinoma. 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 3.2025– March 7, 2025) recommends Lenvima with Keytruda combination therapy as "Useful in Certain Circumstances" for biomarker directed systemic therapy for first-line treatment for pMMR tumors (category 1).[7] Lenvima is recommended under "Other Recommended Regimens" as second-line or subsequent therapy treatment for recurrent endometrial carcinoma (category 2A). Lenvima in combination with Keytruda is also recommended as "Useful in Certain Circumstances (Biomarker-directed therapy)" for pMMR tumors in the second-line or subsequent therapy setting (category 1).

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 ALL of the following (A, B, and C):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient meets ALL of the following (a, b, and c):
       - **a)** Patient has advanced endometrial carcinoma that is mismatch repair proficient (pMMR); AND
       - **b)** The medication is used in combination with Keytruda (pembrolizumab intravenous injection); AND
       - **c)** Patient has tried at least one systemic therapy; OR
         Note: Examples of systemic therapy include carboplatin, paclitaxel, docetaxel, cisplatin, doxorubicin, or ifosfamide.
     - **ii.** Lenvima is used as a single agent for second-line or subsequent therapy; AND
   - **C)** Patient is not a candidate for curative surgery or radiation.

2. **Hepatocellular 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 unresectable or metastatic disease; AND
   - **C)** The medication is used as first-line therapy.

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 and B):
Note: Differentiated thyroid carcinoma include papillary, follicular, and oncocytic carcinoma (formerly Hürthle cell carcinoma).
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
  i. Patient meets BOTH of the following (a and b):
    a. Patient has papillary or follicular thyroid carcinoma; AND
    b. The disease is refractory to radioactive iodine therapy; OR
  ii. Patient has oncocytic (formerly Hürthle cell) carcinoma.

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 COVERED

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

is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Lenvima® capsules [prescribing information]. Woodcliff Lake, NJ: Eisai; January 2025.
2. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed May 21, 2025. Search term: lenvatinib.
3. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 1.2025 – March 20, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed May 30, 2025.
4. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 3.2025– January 9, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed May 21, 2025.
5. The NCCN Thymomas and Thymic Carcinoma Clinical Practice Guidelines in Oncology (version 2.2025 – May 19, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed May 30, 2025.
6. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 1.2025 – March 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed May 30, 2025.
7. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 3.2025 – March 7, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed May 30, 2025.
8. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2025 – January 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed May 21, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
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
Annual Revision	**Endometrial Carcinoma:** Criterion referencing endometrial carcinoma "….is not microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR)" has been simplified to "…endometrial carcinoma that is mismatch repair proficient (pMMR)" as per guideline verbiage. Reference to MSI-H has been deleted from criterion. **Thyroid Carcinoma, Anaplastic:** Added new condition of approval and criteria per guideline recommendation.	06/19/2024
Annual Revision	**Endometrial Carcinoma:** Added criterion that Lenvima can be used as a single agent for second-line or subsequent therapy. **Hepatocellular Carcinoma:** Added criterion that Lenvima is used as first-line therapy. **Thyroid Carcinoma, Differentiated:** Moved Note listing the different types of differentiate thyroid carcinoma to be under the indication. Separated criteria such that radioactive iodine-refractory disease is applicable to only follicular or papillary carcinoma and not for oncocytic carcinoma.	06/04/2025

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