PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Oral) – Cabometyx Prior Authorization Policy
- Cabometyx® (cabozantinib tablets – Exelixis)

REVIEW DATE: 03/25/2026; selected revision 04/21/2026

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

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

- **Differentiated thyroid cancer**, for the treatment of locally advanced or metastatic disease that has progressed following prior vascular endothelial growth factor receptor (VEGFR)-targeted therapy in patients ≥ 12 years of age who are radioactive iodine-refractory or ineligible.
- **Hepatocellular carcinoma,** for the treatment of patients who have been previously treated with sorafenib.
- **Neuroendocrine tumors,** for the treatment of previously treated, unresectable, locally advanced or metastatic, well-differentiated **pancreatic** neuroendocrine tumors (pNET) in adults and pediatric patients ≥ 12 years of age.
- **Neuroendocrine tumors,** for the treatment of previously treated, unresectable, locally advanced or metastatic, well-differentiated **extra-**

pancreatic neuroendocrine tumors (epNET) in adult and pediatric patients ≥ 12 years of age.
- **Renal cell carcinoma**, advanced, as monotherapy or in combination with Opdivo® (nivolumab intravenous infusion) as first-line treatment.

Guidelines

The use of Cabometyx is recommended across multiple National Comprehensive Cancer Network (NCCN) guidelines and the NCCN Compendium.[2-11] Recommendations with a category of evidence of 2B or higher support the approval criteria outlined below.

POLICY STATEMENT

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

Cabometyx® (cabozantinib tablets - Exelixis) 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. **Hepatocellular 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 been previously treated with at least one systemic regimen.
   Note: Examples of a systemic regimen include one of the following drugs: Tecentriq (atezolizumab intravenous infusion), bevacizumab, Imjudo (tremelimumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), sorafenib, Lenvima (lenvatinib capsules), or Opdivo (nivolumab intravenous infusion).

2. **Neuroendocrine Tumors.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   A) Patient is ≥ 12 years of age; AND
   B) Patient has locally advanced, unresectable, or metastatic disease; AND
   C) Patient has well-differentiated neuroendocrine tumors; AND
   D) Patient has ONE of the following tumor types (a or b):
      a) Pancreatic neuroendocrine tumors; OR
      b) Extra-pancreatic neuroendocrine tumors; AND
      Note: Examples of tumor sites could be in the small bowel, lung, thymus, rectum, cecum, non-cecum colon, stomach, appendix.
   E) The medication will be used as subsequent therapy.

3. **Renal Cell 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 relapsed or Stage IV disease.

4. **Thyroid Carcinoma, Differentiated.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 12 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) Patient is refractory to radioactive iodine therapy; AND
   D) Patient has tried Lenvima (lenvatinib capsules) or sorafenib.

Other Uses with Supportive Evidence

5. **Adrenal Gland Tumor.** 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 locoregional unresectable or metastatic adrenocortical carcinoma.

6. **Bone Cancer.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient meets ONE of the following (i or ii):
      i. Patient has Ewing sarcoma; OR
      ii. Patient has osteosarcoma; AND
   B) Patient has tried at least one previous systemic regimen.
   Note: Examples of a systemic regimen include one of the following: vincristine, doxorubicin, cyclophosphamide, topotecan, irinotecan, cisplatin, ifosfamide, Stivarga (regorafenib tablets), sorafenib.

7. **Endometrial 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 one systemic regimen.
   Note: Examples of a systemic regimen include one of the following: carboplatin, paclitaxel, trastuzumab, docetaxel, doxorubicin, cisplatin, and topotecan.

8. **Gastrointestinal Stromal Tumors.** 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 ALL of the following (i, ii, iii, and iv):
      i. One of imatinib or Ayvakit (avapritinib tablets); AND
      ii. One of sunitinib or Sprycel (dasatinib tablets); AND
      iii. Stivarga (regorafenib tablets); AND
      iv. Qinlock (ripretinib tablets).

9. **Non-Small Cell Lung 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 a *RET* rearrangement positive tumor; AND
C) Patient has progressed on one of the first-line therapies, Gavreto (pralsetinib capsules) or Retevmo (selpercatinib capsules or tablets).

10. Pheochromocytoma/Paraganglioma. 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 locally unresectable disease or distant metastases.

11. Soft Tissue Sarcoma. 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 advanced, metastatic, or unresectable disease; AND
C) Patient has been previously treated with at least one systemic therapy; AND
Note: Examples of a systemic regimen include pazopanib tablets, eribulin mesylate intravenous infusion, Yondelis (trabectedin intravenous infusion), temozolomide capsules, and Stivarga (regorafenib tablets).
D) Patient has ONE of the following (i, ii, iii, iv, v, vi, or vii):
i. Extremity/body wall, head/neck soft tissue sarcoma; OR
ii. Retroperitoneal/intra-abdominal soft tissue sarcoma; OR
iii. Rhabdomyosarcoma; OR
iv. Borderline/malignant phyllodes tumor of the breast; OR
v. Alveolar soft part sarcoma; OR
vi. Extraskeletal myxoid chondrosarcoma; OR
vii. Epitheloid hemangioendothelioma.

CONDITIONS NOT COVERED

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

REFERENCES

1. Cabometyx® tablets [prescribing information]. San Francisco, CA: Exelixis; March 2025.
2. The NCCN Drugs & Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 20, 2025. Search term: cabozantinib.
3. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2026 – December 19, 2025). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 20, 2026.
4. The NCCN Gastrointestinal Stromal Tumors (GISTs) Clinical Practice Guidelines in Oncology (version 1.2026 – January 13, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 20, 2026.
5. The NCCN Hepatocellular Carcinoma Clinical Practice Guidelines in Oncology (version 1.2026 – March 10, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 20, 2026.
6. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 1.2026– July 24, 2025). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 20, 2026.

7. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 5.2026 – March 13, 2026 © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 20, 2026.
8. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 2.2026 – November 14, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 20, 2026.
9. 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 March 20, 2026.
10. The NCCN Neuroendocrine and Adrenal Tumors Clinical Practice Guidelines in Oncology (version 3.2025 – October 1, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March20, 2026.
11. The NCCN Soft Tissue Sarcoma Clinical Practice Guidelines in Oncology (version 3.2026 – March 12, 2026). © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 20, 2026.

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.	03/20/2024
Annual Revision	**Neuroendocrine Tumors:** Added new approval condition and criteria. **Non-Small Cell Lung Cancer:** Cabometyx is no longer recommended as first-line therapy for RET rearrangement positive disease. Added criterion that patient has progressed on Gavreto or Retevmo (first-line therapies).	03/12/2025
Selected Revision	**Neuroendocrine Tumors:** Moved indication from Other Uses with Supportive Evidence to FDA-Approved use. Changed age criteria to ≥ 12 years of age based on prescribing information. Removed "lung or thymus tumors and gastrointestinal tract tumors" and replaced it with "extra-pancreatic tumors" based on labeling. **Adrenal Gland Tumor:** New condition of approval and criteria were added under Other Uses with Supportive Evidence. **Pheochromocytoma/Paraganglioma:** New condition of approval and criteria were added under Other Uses with Supportive Evidence.	04/09/2025
Annual Revision	**Pheochromocytoma/Paraganglioma:** The requirement for a patient to have locally unresectable disease was updated to include distant metastases. **Soft Tissue Sarcoma:** New condition of approval and criteria were added under Other Uses with Supportive Evidence. **Conditions Not Covered:** The condition of Metastatic Castration Resistant Prostate Cancer was removed.	03/25/2026
Selected Revision	The policy name was changed to as listed. Previously, it was Oncology – Cabometyx Prior Authorization policy.	04/22/2026