PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 03/02/2022; selected revision 06/22/2022

OVERVIEW

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

- **Differentiated thyroid cancer**, for the treatment of patients ≥ 12 years of age with locally advanced or metastatic disease that has progressed following prior vascular endothelial growth factor receptor (VEGFR)-targeted therapy and who are radioactive iodine-refractory or ineligible.
- **Hepatocellular carcinoma,** for the treatment of patients who have been previously treated with Nexavar® (sorafenib tablets).
- **Renal cell carcinoma**, advanced, as monotherapy or in combination with Opdivo® (nivolumab intravenous infusion) as first-line treatment.

Guidelines

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

- **Bone cancer:** NCCN guidelines (version 2.2022 – October 8, 2021) recommend Cabometyx as one of the "other recommended regimens" for second-line (relapsed/refractory or metastatic disease) for Ewing sarcoma and osteosarcoma (category 2A).[3]
- **Gastrointestinal stromal tumors:** NCCN guidelines (version 1.2022 – January 21, 2022) recommend Cabometyx as one of the options after progression on approved therapies, useful in certain circumstances (category 2A).[2,4] The approved therapies are imatinib and Ayvakit® (avapritinib tablets; for *PDGFRA* mutation) as first-line therapy; Sutent® (sunitinib capsules) or Sprycel® (dasatinib tablets; for *PDGFRA* exon 18 mutations that are insensitive to imatinib [including the *PDGFRA D842V* mutation) as second-line therapy; Stivarga® (regorafenib tablets) as third-line therapy; and Qinlock® (ripretinib tablets) as fourth-line therapy.[4]
- **Hepatocellular carcinoma:** NCCN guidelines (version 5.2021 – September 21, 2021) recommend Cabometyx (Child-Pugh Class A only; Category 1) as a subsequent therapy option, along with many other agents.[5]
- **Kidney cancer:** NCCN guidelines (version 4.2022 – December 21, 2021), the preferred regimens for first-line therapy in favorable risk patients with relapsed or Stage IV RCC with predominant clear cell histology are: Inlyta® (axitinib tablets) + Keytruda® (pembrolizumab for injection), Cabometyx + Opdivo, Lenvima® (lenvatinib capsules) + Keytruda (all category 2A). Cabometyx (category 2B) is one of the "other recommended regimens" in this setting.[6] For patients in the poor/intermediate risk grouping, the preferred regimens are Inlyta + Keytruda; Cabometyx + Opdivo; Yervoy (ipilimumab intravenous infusion) + Opdivo; Lenvima + Keytruda (all category 1); Cabometyx monotherapy is also recommended (category 2A). Preferred recommendations for subsequent oral therapies for clear cell histology include Cabometyx, Lenvima + everolimus, and Opdivo (all category 1). Other recommended regimens include Inlyta (category 1), Cabometyx + Opdivo (category 2A) and others. For patients with non-clear cell histology RCC, Sutent, Cabometyx, and enrollment in clinical trials are noted as preferred therapies (category 2A, preferred); Keytruda, Opdivo, and Lenvima + everolimus are other recommended regimens (all category 2A). Many other agents are listed as useful in certain circumstances.
- **Non-small cell lung cancer:** NCCN guidelines (version 1.2022 – December 7, 2021) recommend Cabometyx for *RET* rearrangement positive tumors (category 2A).[7]

- **Uterine neoplasms:** NCCN guidelines (version 1.2022 – November 4, 2021) recommend Cabometyx as biomarker-directed systemic second-line treatment for recurrent or metastatic disease for endometrial carcinoma (category 2A).[8]
- **Thyroid carcinoma**: NCCN guidelines (version 3.2021 – October 15, 2021) state that Cabometyx can be considered if patient has progression after Lenvima or Nexavar for the treatment of locally recurrent, advanced, and/or metastatic disease that is not amendable to radioactive iodine therapy. This recommendation is for follicular, Hürthle cell, and papillary cancer subtypes (all category 1).[9]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Cabometyx. All approvals are provided for 3 years in duration unless otherwise noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Hepatocellular 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 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, Nexavar (sorafenib tablets), Lenvima (lenvatinib capsules), or Opdivo (nivolumab intravenous infusion).

2. **Renal Cell Carcinoma.** Approve for 1 year if the patient meets both of the following criteria (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has relapsed or stage IV disease.

3. **Thyroid Carcinoma, Differentiated.** Approve for 1 year if the patient meets 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 Hürthle cell thyroid carcinoma.
   - **C)** Patient is refractory to radioactive iodine therapy; AND
   - **D)** Patient has tried Lenvima (lenvatinib capsules) or Nexavar (sorafenib tablets).

Other Uses with Supportive Evidence

4. **Bone Cancer.** Approve for 1 year if the patient meets the following criteria (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 at least one previous systemic regimen.

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

6. **Gastrointestinal Stromal Tumors.** Approve for 1 year if the patient meets the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried each of the following (i, ii, iii, and iv):
      i. One of imatinib or Ayvakit (avapritinib tablets); AND
      ii. One of Sutent (sunitinib capsules) or Sprycel (dasatinib tablets); AND
      iii. Stivarga (regorafenib tablets); AND
      iv. Qinlock (ripretinib tablets).

7. **Non-Small Cell Lung 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 a *RET* rearrangement positive tumor.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Cabometyx is not recommended in the following situations:

1. **Metastatic Castration-Resistant Prostate Cancer (mCRPC).** Results from the COMET-1 Phase III pivotal study with Cabometyx 60 mg tablets in men with mCRPC are published.[9] Patients included in the study had disease progression after treatment with docetaxel as well as abiraterone acetate and/or Xtandi® (enzalutamide capsules). The study failed to meet its primary endpoint of demonstrating statistically significant increase in overall survival (OS) compared with prednisone. The median OS with Cabometyx was 11.0 months vs. 9.8 months with prednisone, which was not statistically significant. Based on these results, the second Phase III study, COMET-2 has been discontinued.[10]

2. 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. Cabometyx® tablets [prescribing information]. San Francisco, CA: Exelixis; September 2021.
2. The NCCN Drugs & Biologics Compendium. © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 28, 2022. Search term: cabozantinib.
3. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – October 8, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 28, 2022.
4. The NCCN Gastrointestinal Stromal Tumors (GISTs) Clinical Practice Guidelines in Oncology (version 1.2022 – January 21, 2022). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 28, 2022.
5. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (version 5.2021 – September 21, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 28, 2022.
6. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 4.2022 – December 21, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 28, 2022.
7. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 1.2022 – December 7, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 28, 2022.
8. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 1.2022 – November 4, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 28, 2022.
9. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (version 3.2021 – October 15, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 28, 2022.

10. Smith M, De Bono J, Sternberg C, et al. Phase III study of cabozantinib in previously treated metastatic castration-resistant prostate cancer: COMET-1. *J Clin Oncol.* 2016;34:3005-3013.
11. Exelixis. Study of cabozantinib (XL184) versus mitoxantrone plus prednisone in men with previously treated symptomatic castration-resistant prostate cancer (COMET-2). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2017 April 18]. Available from: http://www.clinicaltrials.gov/ct2/show/NCT01522443?term=NCT01522443&rank=1. NLM identifier: NCT01522443 (terminated).