PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 02/17/2021; selected revision 09/29/2021

OVERVIEW

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

- **Differentiated thyroid cancer**, for the treatment of adults and pediatric 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 (RCC)**, as monotherapy or in combination with Opdivo® (nivolumab intravenous infusion) for the first-line treatment of patients with advanced disease.

Guidelines

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

- **Bone cancer:** The NCCN bone cancer guidelines (version 1.2021 – November 20, 2020) recommend Cabometyx as one of the "other recommended regimens" for second-line (relapsed/refractory or metastatic disease) Ewing sarcoma (category 2A).[2-3]
- **Gastrointestinal stromal tumors:** The NCCN guidelines (version 1.2021 – October 30, 2020) recommend Cabometyx as one of the options after failure on approved therapies ("useful in certain circumstances", category 2A).[2,4] The approved therapies are imatinib and Ayvakit® (avapritinib tablets; for *PDGFRA* mutation) first-line; Sutent® (sunitinib capsules) as second-line therapy; Stivarga® (regorafenib tablets) as third-line therapy; and Qinlock® (ripretinib tablets) as fourth-line therapy.[2,4]
- **Hepatocellular carcinoma:** The NCCN guidelines (version 5.2020 – August 4, 2020) recommend Cabometyx (Child-Pugh Class A only; Category 1) as a subsequent therapy option, along with many other agents.[5]
- **Kidney cancer:** According to the NCCN clinical practice guidelines for kidney cancer (version 2.2021 – February 3, 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, Sutent, and Votrient® (pazopanib tablets) [all category 2A]. Cabometyx (category 2B) is one of the "other recommended regimens" for favorable risk patients.[2] For patients in the poor/intermediate risk grouping, the preferred regimens are Inlyta + Keytruda; Yervoy (ipilimumab for injection) + Opdivo (both category 1); Cabometyx; and Cabometyx + Opdivo (both category 2A). Recommendations for subsequent oral therapies include Cabometyx (category 1, preferred), Inlyta (category 1), Lenvima™ (lenvatinib capsules) + everolimus [category 1]; everolimus, Sutent, or Votrient are all category 2A recommended therapies. For patients with non-clear cell histology RCC, Sutent and enrollment in clinical trials are noted as preferred therapies (category 2A, preferred); Cabometyx, everolimus, and Lenvima + everolimus are other recommended regimens (both category 2A). Many other agents are listed as useful in certain circumstances.

- **Non-small cell lung cancer:** The NCCN guidelines (version 3.2021 – February 16, 2021) recommend Cabometyx as "useful in certain circumstances" for *RET* rearrangements (category 2A).[4,5]
- **Thyroid carcinoma**: NCCN guidelines (version 2.2021 – September 1, 2021) state that Cabometyx can be considered if clinical trials or other systemic therapies are not available or appropriate 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 2A).

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 3 years if the patient has been previously treated with at least one tyrosine kinase inhibitor therapy.
   Note: Examples are Nexavar (sorafenib tablets), Lenvima (lenvatinib capsules).

2. **Renal Cell Carcinoma.** Approve for 3 years if the patient has relapsed or stage IV disease.

3. **Thyroid Carcinoma.** Approve for 3 years 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 a vascular endothelial growth factor receptor (VEGFR)-targeted therapy.
   Note: Examples of VEGFR-targeted therapy include Lenvima (lenvatinib capsules), Nexavar (sorafenib tablets), Votrient (pazopanib tablets), Sutent (sunitinib capsules), Inlyta (axitinib tablets).

Other Uses with Supportive Evidence

4. **Bone Cancer.** Approve for 3 years 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 tried at least one previous systemic regimen.

5. **Gastrointestinal Stromal Tumors.** Approve for 3 years if the patient meets the following (A and B):
   A) Patient has previously tried one of imatinib (Gleevec tablets, generic) or Ayvakit (avapritinib tablets); AND

B) Patient has previously tried each of Sutent (sunitinib capsules), Stivarga (regorafinib tablets), and Qinlock (ripretinib tablets).

6. Non-Small Cell Lung Cancer. Approve for 3 years if the tumor is positive for *RET* rearrangements.

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.[8] Patients included in the study had disease progression after treatment with docetaxel as well as Zytiga® (abiraterone acetate tablets) 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.[9]

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

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3. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 1.2021 – November 20, 2020). © 2020 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 17, 2021.
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5. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (version 5.2020 – August 4, 2020). © 2020 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 17, 2021.
6. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 2.2021 – February 3, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 8, 2021.
7. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2021 – February 16, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 17, 2021.
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