PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 02/17/2021

OVERVIEW

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

- **Renal cell carcinoma (RCC)**, as monotherapy or in combination with Opdivo (nivolumab for injection) for the first-line treatment of patients with advanced disease.
- **Hepatocellular carcinoma,** for the treatment of patients who have been previously treated with Nexavar® (sorafenib tablets).

Guidelines

- **Renal cell carcinoma (RCC):** In the National Comprehensive Cancer Network (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 (nivolumab for injection), Sutent® (sunitinib malate capsules), 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.
- **Hepatocellular carcinoma:** The NCCN hepatobiliary cancers (version 5.2020 – August 4, 2020) recommends Cabometyx (Child-Pugh Class A only; Category 1) as a subsequent therapy option, along with many other agents.[3]
- **Non-small cell lung cancer:** The NCCN Non-Small Cell Lung Cancer guidelines (version 3.2021 – February 16, 2021) recommend cabozantinib as "useful in certain circumstances" for *RET* rearrangements (category 2A).[4,5]
- **Gastrointestinal stromal tumors (GIST):** The NCCN GISTs 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).[4,6] 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 Gavreto (ripretinib tablets) as fourth-line therapy.
- **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).[4,7]

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 the following criteria:

FDA-Approved Indication

1. **Renal Cell Carcinoma (RCC).** Approve for 3 years in patients with relapsed or stage IV disease.

2. **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).

Other Uses with Supportive Evidence

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

4. **Gastrointestinal Stromal Tumors (GIST).** 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 Gavreto (ripretinib tablets).

5. **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.

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 (hazard ratio [HR] 0.90; 95% CI: 0.76, 1.06; P = 0.213). 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

1. Cabometyx™ [prescribing information]. San Francisco, CA: Exelixis Inc; February 2021.
2. The NCCN Kidney Cancer Clinical Practice Guidelines in Oncology (version 2.2021 – February 3, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 8, 2021.
3. The NCCN Hepatobiliary Cancers Clinical Practice Guidelines in Oncology (version 5.2020 – August 4, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 17, 2021.
4. The NCCN Drugs & Biologics Compendium. © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on February 14, 2021. Search term: cabozantinib.
5. The NCCN Non-Small Cell Lung Cancer Clinical Practice Guidelines in Oncology (version 3.2021 – February 16, 2021). © 2021 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 17, 2021.
6. The NCCN Gastrointestinal Stromal Tumors (GISTs) Clinical Practice Guidelines in Oncology (version 1.2021 – October 30, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 17, 2021.
7. The NCCN Bone Cancer Clinical Practice Guidelines in Oncology (version 1.2021 – November 20, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed February 17, 2021.
8. 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.
9. 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).