BlueCross BlueShield Federal Employee Program

CABOMETYX
(cabozantinib)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Cabometyx (cabozantinib) inhibits the tyrosine kinase activity of MET, VEGFR-1, -2, and -3, AXL, RET, ROS1, TYRO3, MER, KIT, TRKB, FLT-3, and TIE-2. These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, drug resistance, and maintenance of the tumor microenvironment (1).

Regulatory Status

FDA-approved indications: Cabometyx is a kinase inhibitor indicated for the treatment of: (1)

1. Patients with advanced renal cell carcinoma (RCC)
2. Patients with advanced renal cell carcinoma, as a first-line treatment in combination with nivolumab
3. Patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib
4. Adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer (DTC) that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible
5. Adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated pancreatic neuroendocrine tumors (pNET)
6. Adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated extra-pancreatic neuroendocrine tumors (epNET)

Off-Label Use: (2-3)

1. Non-small cell lung cancer

Cabometyx should be used with caution in patients at increased risk for thrombotic events, hemorrhagic events, gastrointestinal perforation, and fistulas. Discontinue Cabometyx in patients who develop an acute myocardial infarction or any other arterial thromboembolic complication. Cabometyx should be stopped in patients with a hypertensive crisis or severe hypertension that cannot be controlled with anti-hypertensive therapy. Withhold Cabometyx in patients who develop

intolerable Grade 2 or Grade 3 palmar-plantar erythrodysesthesia (hand-foot syndrome), until improvement to Grade 1 occurs (1).

Cabometyx should be stopped at least 21 days prior to scheduled surgery, including dental surgery. Permanently discontinue Cabometyx if reversible posterior leukoencephalopathy syndrome (RPLS) occurs. Cabometyx is not recommended for use in patients with severe hepatic impairment (1).

Cabometyx can cause fetal harm when administered to a pregnant woman. Female patients of reproductive potential should be advised to use effective contraception during treatment with Cabometyx and for 4 months after the last dose (1).

The safety and effectiveness of Cabometyx in pediatric patients less than 18 years of age with RCC, HCC, and NSCLC have not been established. The safety and effectiveness of Cabometyx in pediatric patients less than 12 years of age with DTC and NETs have not been established (1).

Summary

Cabometyx (cabozantinib) is a kinase inhibitor indicated for the treatment of advanced renal cell carcinoma, hepatocellular carcinoma, differentiated thyroid cancer, pancreatic neuroendocrine tumors, extra-pancreatic neuroendocrine tumors, and has an off-label use for non-small cell lung cancer. Cabometyx should not be used in patients with reversible posterior leukoencephalopathy syndrome (RPLS). Cabometyx should be used with caution in patients at increased risk for thrombotic events, hemorrhagic events, gastrointestinal perforation, and fistulas. Cabometyx should be stopped in patients with hypertensive crisis, severe diarrhea, or palmar-plantar erythrodysesthesia (PPE) (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Cabometyx while maintaining optimal therapeutic outcomes.

References

1. Cabometyx [package insert]. Alameda, CA: Exelixis, Inc.; March 2025.
2. NCCN Drugs & Biologics Compendium®. Cabozantinib 2025. National Comprehensive Cancer Network, Inc. Accessed on March 26, 2025.

3. NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 3.2025). National Comprehensive Cancer Network, Inc. January 2025. Accessed on January 14, 2025.