Cabometyx

Description

Cabometyx (cabozantinib)

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 indication: Cabometyx is a kinase inhibitor indicated for the treatment of: (1)

1. Patients with advanced renal cell carcinoma (RCC).
2. Patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

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 Palmer plantar erthrodysesthesia, until improvement to Grade 1 occurs (1).

Cabometyx should be stopped at least 28 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).

The safety and efficacy of Cabometyx in pediatric patients have not been established (1).

Related policies
Cometriq

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Cabometyx may be considered medically necessary in patients that are 18 years of age and older with advanced renal cell carcinoma, hepatocellular carcinoma, or non-small cell lung cancer (NSCLC) and if the conditions indicated below are met.

Cabometyx is considered investigational in patients that are less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Advanced renal cell carcinoma (RCC)
2. Hepatocellular carcinoma (HCC) previously treated with Nexavar (sorafenib)
3. Non-small cell lung cancer

AND ALL of the following:
  a. NO recent history of severe hemorrhage
b. Physician agrees to discontinue if the patient has uncontrolled GI perforations or fistulas
c. Physician agrees to withhold the medication if intolerable Palmer plantar erthrodysesthesia Grade 2 or 3 occurs, until improvement to Grade 1
d. **NO** uncontrolled severe hypertension
e. Physician agrees to discontinue if the patient develops reversible posterior leukoencephalopathy syndrome or nephrotic syndrome
f. Physician agrees to discontinue if the patient develops an acute myocardial infarction or any other venous or arterial thromboembolic complication

**Prior – Approval Renewal Requirements**

**Age**

18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Advanced renal cell carcinoma (RCC)
2. Hepatocellular carcinoma (HCC)
3. Non-small cell lung cancer

**AND NONE** of the following:

a. Severe hemorrhage
b. Unmanaged gastrointestinal perforations or fistulas
c. Palmer plantar erthrodysesthesia Grade 2 or 3
d. Uncontrolled severe hypertension
e. Reversible posterior leukoencephalopathy syndrome
f. Acute myocardial infarction or any other venous or arterial thromboembolic complication
g. Nephrotic syndrome

**Policy Guidelines**

**Pre - PA Allowance**

None
Prior - Approval Limits

<table>
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<tr>
<th>Strength</th>
<th>Quantity per 90 days</th>
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<tr>
<td>20 mg</td>
<td>90 tablets per 90 days OR</td>
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<tr>
<td>40 mg</td>
<td>90 tablets per 90 days OR</td>
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<tr>
<td>60 mg</td>
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Duration 12 months

Prior – Approval Renewal Limits

Same as above

Rationale

Summary

Cabometyx is a kinase inhibitor indicated for the treatment of advanced renal cell carcinoma, hepatocellular carcinoma, 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, diarrhea, or palmar-plantar erythrodysethesia syndrome (PPES). The safety and efficacy of Cabometyx in pediatric patients have not been established (1).

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

References


Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>May 2016</td>
<td>Addition to PA</td>
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<td>Date</td>
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<tr>
<td>June 2016</td>
<td>Annual review</td>
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<tr>
<td>October 2016</td>
<td>Change of physician agrees to discontinue if Palmer plantar erythrodysesthesia Grade 2 or 3 occurs</td>
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<tr>
<td>December 2016</td>
<td>Annual review</td>
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<tr>
<td>February 2017</td>
<td>Addition of quantity limits</td>
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<td>March 2017</td>
<td>Annual review</td>
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<tr>
<td>September 2017</td>
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<tr>
<td>November 2017</td>
<td>Addition of severe to hemorrhage requirement and the removal of hemorrhage</td>
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<td>Additions</td>
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<tr>
<td>January 2018</td>
<td>Addition of Non-small cell lung cancer</td>
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<td>March 2018</td>
<td>Annual review</td>
</tr>
<tr>
<td>January 2019</td>
<td>Addition of new indication: hepatocellular carcinoma</td>
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<tr>
<td>March 2019</td>
<td>Annual review and reference update. Revised requirements to no uncontrolled severe hypertension, prescriber will discontinue if patient develops nephrotic syndrome, and no venous or arterial thromboembolic complication per SME.</td>
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</table>

**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 15, 2019 and is effective on April 1, 2019.