Clinical Policy: Cabozantinib (Cometriq, Cabometyx)

Reference Number: PA.CP.PHAR.111
Effective Date: 06/13
Last Review Date: 01/19

Coding Implications
Revision Log

Description
Cabozantinib (Cabometyx®, Cometriq®) is a kinase inhibitor.

FDA Approved Indication(s)
Cometriq is indicated the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC).

Cabometyx is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Cometriq and Cabometyx are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Renal Cell Carcinoma (must meet all):
1. Diagnosis of relapsed or Stage IV (unresectable or metastatic) RCC;
2. Prescribed by or in consultation with an oncologist;
3. Request is for Cabometyx;
4. Age ≥ 18 years;
5. Request is for Cabometyx;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 80 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

B. Thyroid Cancer (must meet all):
1. Diagnosis of one of the following (a or b)
   a. Recurrent, unresectable, progressive, metastatic medullary thyroid carcinoma (MTC);
   b. Differentiated thyroid carcinoma (DTC; i.e., follicular, Hurthle cell, or papillary thyroid carcinoma) (off-label);
2. Prescribed by or in consultation with an oncologist;
3. Request is for Cometriq;
4. Age ≥ 18 years;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 180 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval Duration: 6 months

C. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**
1. Diagnosis of non-small cell lung cancer (NSCLC) with an RET gene rearrangement;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval Duration: 6 months

D. Hepatocellular Carcinoma (off-label) (must meet all)**:**
1. Diagnosis of hepatocellular carcinoma (HCC);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Failure of Nexavar® unless contraindicated or clinically significant adverse effects are experienced;
5. Request is for Cabometyx;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval Duration: 6 months

E. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. All Indications in Section I (must meet all Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or Continuity of Care Policy (PA.LTSS.PHAR.01) applies;

2. Documentation of positive response to therapy (e.g.: no disease progression, no unacceptable toxicity);3.If request is for a dose increase, request meets one of the following (a or b):

a. New dose does not exceed the maximum dosing listed in Section I;
b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval Duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or Continuity of Care Policy (PA.LTSS.PHAR.01) applies; **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:
Cabozantinib is an oral kinase inhibitor. In vitro biochemical and/or cellular assays have shown that cabozantinib inhibits the tyrosine kinase activity of RET, MET, VEGFR-1, -2 and -3, KIT, TRKB, FLT-3, AXL, and TIE-2. These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, and maintenance of the tumor microenvironment.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DTC: differentiated thyroid carcinoma
FDA: Food and Drug Administration
HCC: hepatocellular carcinoma
MTC: medullary thyroid cancer
NSCLC: non-small cell lung cancer
RCC: renal cell carcinoma

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Lenvima (lenvatinib)	DTC: 24 mg PO QD	24 mg/day
Nexavar (sorafenib)	DTC: 400 mg PO BID	400 mg/day
Nexavar (sorafenib)	HCC: 400 mg PO BID	800 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): None reported.
- Boxed warning(s): Cometriq - perforations and fistulas, and hemorrhage.

Appendix D: General Information
Cometriq capsules are not interchangeable with Cabometyx tablets.

IV. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Cabometyx	RCC	60 mg PO QD Strong CYP3A4 inhibitors: Reduce the daily cabozantinib dose by 20 mg Strong CYP3A4 inducers: Increase the daily cabozantinib dose by 20 mg	80 mg/day
Cometriq	MTC	140 mg PO QD Strong CYP3A4 inhibitors: Reduce the daily cabozantinib dose by 40 mg Strong CYP3A4 inducers: Increase the daily cabozantinib dose by 40 mg	180 mg/day

V. Product Availability

Drug Name	Availability
Cabometyx	Tablets: 20 mg, 40 mg, 60 mg
Cometriq	Capsules: 20 mg, 80 mg

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J8999	Prescription drug, oral, chemotherapeutic, NOS

Reviews, Revisions, and Approvals	Date	Approval Date
Removed safety requirement for hemorrhage and hemoptysis per CPAC safety guidance endorsed by medical affairs. For RCC, modified redirection to apply only for clear cell histology, requiring NCCN Category 1 recommended alternatives. Added off-label use for RCC with non-clear cell histology and NSCLC. References reviewed and updated.	02/18	
1Q 2019 annual review; recurrent or unresectable added to MTC per NCCN; off-label DTC and HCC uses added; references reviewed and updated.	01/19	

References

1. Cabometyx Prescribing Information. South San Francisco, CA: Exelixis, Inc.; December 2017. Available at: https://www.cabometyx.com/downloads/CABOMETYXUSPI.pdf. Accessed October 10, 2018.
2. Cometriq Prescribing Information. South San Francisco, CA: Exelixis, Inc.; January 2018. Available at http://www.cometriq.com/downloads/Cometriq_Full_Prescribing_Information.pdf. Accessed October 10, 2018.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed October 10, 2018.
4. National Comprehensive Cancer Network. Kidney Cancer, Version 2.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed October 10, 2018.
5. National Comprehensive Cancer Network. Thyroid Carcinoma, Version 1.2018. Available at https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed October 10, 2018.
6. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer, Version 6.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 10, 2018.

7. National Comprehensive Cancer Network. Hepatobiliary Cancers, Version 3.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 10, 2018.