Clinical Policy: Cabozantinib (Cabometyx, Cometriq)

Reference Number: CP.PHAR.111
Effective Date: 06.01.13
Last Review Date: 02.20
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

Cabometyx is indicated for the treatment of patients with:

- Advanced renal cell carcinoma (RCC)
- Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

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

Policy/Criteria

Provider must submit documentation (including such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Cabometyx and Cometriq 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. Age ≥ 18 years;
4. Request is for Cabometyx;
5. 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

B. Thyroid Cancer (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Recurrent, unresectable, progressive, or 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. Age ≥ 18 years;
4. If DTC, failure of Lenvima® or Nexavar®* unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required.*
5. Request is for Cometriq;
6. 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*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

C. Hepatocellular Carcinoma (must meet all)**:**
1. Diagnosis of 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. 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*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

D. 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*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

E. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Cabometyx or Cometriq for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 80 mg per day (Cabometyx) or 180 mg per day (Cometriq);
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. 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.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Cabometyx	HCC, 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

VI. Product Availability

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

VII. References

1. Cabometyx Prescribing Information. South San Francisco, CA: Exelixis, Inc.; January 2019. Available at: https://www.cabometyx.com/downloads/CABOMETYXUSPI.pdf. Accessed October 28, 2019.
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 28, 2019.

3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed October 28, 2019.
4. National Comprehensive Cancer Network. Kidney Cancer, Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed October 28, 2019.
5. National Comprehensive Cancer Network. Thyroid Carcinoma, Version 2.2019. Available at https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed October 28, 2019.
6. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer, Version 7.2019 Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 28, 2019.
7. National Comprehensive Cancer Network. Hepatobiliary Cancers, Version 3.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 28, 2019.

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	P&T Approval Date
Policy converted to new template. Criteria: added age and max dose requirements per PI; added moderate to severe hepatic impairment to contraindications per PI; changed initial approval duration to 3 months; added disease progression to reasons to discontinue per NCCN thyroid carcinoma guidelines which present alternative TKIs in such cases.	03.16	04.16
Updated policy title to include Cabometyx. MTC initial: removed requirements related to age and hepatic function; modified max dose requirement to include usual max dose. Re-auth: added max dose; removed safety criteria. Created criteria for RCC. Added additional Cometriq/Cabometyx uses as outlined per NCCN compendium under section IC: Other diagnoses/indications.	03.17	04.17
1Q18 annual review: Combined Medicaid and commercial policies. 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.	11.08.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added off-label use for RCC with non-clear cell histology and NSCLC References reviewed and updated.		
Cabometyx's FDA indication for advanced RCC is expanded from second- to first- or second line therapy. Redirection to other therapies and delineation by histology removed. Added specialist. "Progressive" removed from MTC descriptors; recent history of hemorrhage removed. Restriction limiting NSCLC treatment to only Cabometyx rather than including both Cabometyx and Cometriq is removed per NCCN. References reviewed and updated. New policy for HIM	01.23.18	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.	11.13.18	02.19
1Q 2020 annual review: no significant changes; removed HIM NF disclaimer statements; updated Cabometyx FDA approved indications to include HCC and removed off-label designation; references reviewed and updated.	10.28.19	02.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.