Clinical Policy: Cabozantinib (Cometriq, Cabometyx)

Reference Number: CP.PHAR.111
Effective Date: 06.01.13
Last Review Date: 02.18
Line of Business: Commercial, Medicaid

Coding Implications Revision Log

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

Description

Cabozantinib (Cometriq™, Cabometyx™) 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) who have received prior anti-angiogenic therapy.

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) 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 RCC;
2. Prescribed by or in consultation with an oncologist;
3. Request is for Cabometyx;
4. Age ≥ 18 years;
5. One of the following (a or b):
   a. For RCC with predominant clear cell histology: Member has received prior anti-angiogenic therapy (e.g., Votrient; Sutent);
   b. RCC with non-clear cell histology (off-label);
6. Dose does not exceed 80 mg/day.

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

B. Medullary Thyroid Cancer (must meet all):

1. Diagnosis of progressive, metastatic MTC;
2. Prescribed by or in consultation with an oncologist;

3. Request is for Cometriq;
4. Age ≥ 18 years;
5. Dose does not exceed 180 mg/day.

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

C. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**
1. Diagnosis of non-small cell lung cancer (NSCLC) with RET gene rearrangements;
2. Prescribed by or in consultation with an oncologist;
3. Request is for Cabometyx;
4. Age ≥ 18 years;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 60 mg/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:
Medicaid – 6 months
Commercial – Length of Benefit

D. 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 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 and has received this medication for at least 30 days;
2. Member is responding positively 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:
Medicaid – 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 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 and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Sutent (sunitinib)	Advanced RCC: 50 mg PO QD for 4 weeks followed by 2 weeks off.	Advanced RCC:87.5 mg/day
Votrient (pazopanib)	Advanced RCC: 800 mg PO QD	Advanced RCC: 800 mg/day Treatment continues until no longer clinically beneficial or until unacceptable toxicity occurs.
Avastin (bevacizumab) in combination with Intron A (interferon alfa-2b)	Advanced RCC: 10 mg/kg IV infused over 60-90 minutes every 2 weeks in combination with interferon alfa 3 million IU SC/IM 5 times per week up to 36 million IU SC/IM 3 times per week	Advanced RCC: 15 mg/kg every 3 weeks or 10 mg/kg every 2 weeks in combination with interferon alfa 20 million IU/m2/day IV; 35 million IU/m2/dose SC/IM
Torisel (temsirolimus)	Advanced RCC: 25 mg IV once weekly until disease progression or unacceptable toxicity	Advanced RCC: 25 mg IV once weekly
Inlyta (axitinib)	Advanced RCC: 5 mg PO BID	Advanced RCC: 10 mg PO BID

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
		Treatment continues until no longer clinically beneficial or unacceptable toxicity occurs.
Proleukin (aldesleukin)	Advanced RCC: 600,000 units/kg every 8 hours for a maximum of 14 doses; repeat after 9 days for a total of 28 doses per course	Advanced RCC: 600,000 units/kg every 8 hours

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: General Information

- For RCC, NCCN guidelines have the following recommendations for cabozantinib as single-agent therapy for relapsed or surgically unresectable stage IV disease:
  - As first-line therapy for poor and intermediate risk groups with predominant clear cell histology (Category 2A). NCCN Kidney Cancer guidelines list the following with a Category 1 recommendation for first-line therapy for predominant clear cell histology: Votrient (preferred), Sutent (preferred), Avastin in combination with interferon alfa, and Torisel (for poor-prognosis patients).
  - As preferred subsequent therapy for predominant clear cell histology (Category 1)
  - As systemic therapy for non-clear cell histology (Category 2A)
- For NSCLC, cabozantinib has a 2A recommendation for use in RET gene rearrangements. Patients enrolled in the study cited by the NCCN NSCLC guidelines received 60 mg of cabozantinib in the tablet form orally once daily

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Cabometyx	Advanced RCC, NSCLC	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	180 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		daily cabozantinib dose by 40 mg Strong CYP3A4 inducers: Increase the daily cabozantinib dose by 40 mg	

VI. Product Availability

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

VII. References

1. Cometriq Prescribing Information. South San Francisco, CA: Exelixis, Inc.; October 2017. Available at http://www.cometriq.com/downloads/Cometriq_Full_Prescribing_Information.pdf. Accessed November 8, 2017.
2. Cabometyx Prescribing Information. South San Francisco, CA: Exelixis, Inc.; April 2016. Available at: https://www.cabometyx.com/downloads/CABOMETYXUSPI.pdf. Accessed November 8, 2017.
3. Cabozantinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed November 8, 2017.
4. Drilon A, Rekhtman N, Arcila M, et al. Cabozantinib in patients with advanced RET-rearranged non-small-cell lung cancer: an open-label, single-centre, phase 2, single-arm trial. Lancet Oncology. 2016 Dec;17(12):1653-1660.
5. National Comprehensive Cancer Network. Kidney Cancer Version 1.2018 – September 7, 2017. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed November 8, 2017.
6. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 9.2017 – September 28, 2017. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed November 8, 2017.
7. National Comprehensive Cancer Network. Thyroid carcinoma Version 2.2017. Available at https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed November 8, 2017.

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
Removed prospective monitoring questions and changed it to Appendix A and related question for denial of existing conditions. Updated background and safety information.	05.14	05.14
Updated clinical background and safety section.	03.15	04.15
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. - Added off-label use for RCC with non-clear cell histology and NSCLC - References reviewed and updated.	11.08.17	02.18

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.