Clinical Policy: Cabozantinib (Cabometyx, Cometriq)

Reference Number: ERX.SPA.62
Effective Date: 03.01.14
Last Review Date: 02.21
Line of Business: Commercial, Medicaid

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)
- Advanced RCC, as a first-line treatment in combination with nivolumab
- Hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

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

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

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. Request is for Cabometyx;
2. Diagnosis of relapsed or stage IV (unresectable or metastatic) RCC;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. For Cabometyx request, medical justification supports inability to use cabozantinib, if available (e.g., contraindications to excipients);
6. Request meets one of the following (a, b, c, or d):*
   a. Dose does not exceed 60 mg (1 tablet) per day (monotherapy);
   b. Dose does not exceed 40 mg (1 tablet) per day (combination with Opdivo);
   c. Dose does not exceed 80 mg (2 tablets) per day and documentation that member is concurrently taking a strong CYP3A4 inducer (*see Appendix D*);
   d. 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 – 6 months
Commercial – Length of Benefit

B. Hepatocellular Carcinoma (must meet all)**:**
1. Request is for Cabometyx;
2. Diagnosis of HCC;
3. Prescribed by or in consultation with an oncologist;

4. Age ≥ 18 years;
5. For Cabometyx request, medical justification supports inability to use cabozantinib, if available (e.g., contraindications to excipients);
6. Failure of Nexavar, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed 60 mg (1 tablet) per day;
   b. Dose does not exceed 80 mg (2 tablets) per day and documentation that member is concurrently taking a strong CYP3A4 inducer (*see Appendix D*);
   c. 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 – 6 months
Commercial – Length of Benefit

C. Thyroid Carcinoma (must meet all)**:**
1. Request is for Cometriq;
2. 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);
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. For Cometriq request, medical justification supports inability to use cabozantinib, if available (e.g., contraindications to excipients);
6. If DTC, failure of Lenvima® or Nexavar®*, unless contraindicated or clinically adverse effects are experienced;

   **Prior authorization may be required for Lenvima and Nexavar*
7. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed 140 mg (1 capsule) per day;
   b. Dose does not exceed 180 mg (3 capsules) per day and documentation that member is concurrently taking a strong CYP3A4 inducer (*see Appendix D*);
   c. 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 – 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. For Cabometyx or Cometriq request, medical justification supports inability to use cabozantinib, if available (e.g., contraindications to excipients);
5. 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 – 6 months
Commercial – Length of Benefit

E. Gastrointestinal Stromal Tumor (off-label) (must meet all)**:**
1. Request is for Cabometyx;

2. Diagnosis of gastrointestinal stromal tumor (GIST);
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Prescribed as single-agent subsequent therapy for unresectable, recurrent, or metastatic disease;
6. For Cabometyx request, medical justification supports inability to use cabozantinib, if available (e.g., contraindications to excipients);
7. 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 – 6 months
Commercial – Length of Benefit

F. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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. For Cabometyx or Cometriq request, medical justification supports inability to use cabozantinib, if available (e.g., contraindications to excipients);
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For Cabometyx, one of the following:
      i. Dose does not exceed 60 mg (1 tablet) per day (monotherapy);
      ii. Dose does not exceed 40 mg (1 tablet) per day (combination with Opdivo);
      iii. Dose does not exceed 80 mg (2 tablets) per day and documentation that member is concurrently taking a strong CYP3A4 inducer (*see Appendix D*);
   b. For Cometriq, one of the following:
      i. Dose does not exceed 140 mg (1 capsule) per day;
      ii. Dose does not exceed 180 mg (3 capsules) per day and documentation that member is concurrently taking a strong CYP3A4 inducer (*see Appendix D*);
   c. Dose does not exceed 180 mg (3 capsules) per day and documentation that member is concurrently taking a strong CYP3A4 inducer (see Appendix D);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 – 12 months
Commercial – Length of Benefit

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DTC: differentiated thyroid carcinoma
FDA: Food and Drug Administration
GIST: gastrointestinal stromal tumor
HCC: hepatocellular carcinoma
MTC: medullary thyroid cancer
NCCN: National Comprehensive Cancer Network
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
Nexavar (sorafenib)	DTC, HCC: 400 mg PO BID	800 mg/day
Lenvima (lenvatinib)	DTC: 24 mg PO QD	24 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

None reported

Appendix D: General Information

Cometriq capsules are not interchangeable with Cabometyx tablets.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Cabozantinib (Cabometyx)	HCC, RCC	Monotherapy: 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 Combination therapy: 40 mg PO QD with Opdivo (nivolumab) 240 mg IV every 2 weeks or 480 mg IV every 4 weeks	80 mg/day
Cabozantinib (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
Cabozantinib (Cabometyx)	Tablets: 20 mg, 40 mg, 60 mg
Cabozantinib (Cometriq)	Capsules: 20 mg, 80 mg

VII. References

1. Cabometyx Prescribing Information. South San Francisco, CA: Exelixis, Inc.; January 2021. Available at: https://www.cabometyx.com/downloads/CABOMETYXUSPI.pdf. Accessed February 3, 2021.
2. Cometriq Prescribing Information. South San Francisco, CA: Exelixis, Inc.; October 2020. Available at http://www.cometriq.com/downloads/Cometriq_Full_Prescribing_Information.pdf. Accessed November 15, 2020.

3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed November 15, 2020.
4. National Comprehensive Cancer Network. Kidney Cancer Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed February 3, 2021.
5. National Comprehensive Cancer Network. Thyroid Carcinoma Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed November 15, 2020.
6. National Comprehensive Cancer Network. Hepatobiliary Cancers Version 5.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed November 15, 2020.
7. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer, Version 8.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed October 28, 2019.
8. National Comprehensive Cancer Network. Gastrointestinal Stromal Tumors (GISTs) Version 1.2021 Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed November 15, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Added criteria for renal cell cancer and Cabometyx to policy. Added dosing information if used with taking a strong CYP3A4 inducer.	07.17	08.17
1Q18 annual review: 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.	11.08.17	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; updated Cabometyx FDA approved indications to include HCC and removed off-label designation; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	10.28.19	02.20
1Q 2021 annual review: oral oncology generic redirection language added; for Cometriq, boxed warning removed; GIST added per NCCN; RT4: added new FDA-approved indication for combination use with nivolumab as first-line treatment for advanced RCC references reviewed and updated.	11.15.20	02.21
Delineated maximum dose based on drug interactions per prescribing information.	03.23.21	

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.