Clinical Policy Title: **Cabozantinib (Cabometyx, Cometriq)**

Policy Number: **RxA.52**

Drug(s) Applied: **Cabozantinib (Cabometyx®, Cometriq®)**

Last Review Date: **04/2020**

Line of Business: **Commercial**

Background

Cabozantinib (Cabometyx®, Cometriq®) is a kinase inhibitor. Cabometyx is indicated for the treatment of patients with advanced renal cell carcinoma (RCC). Cometriq is indicated the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC).

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

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

Clinical Policy

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

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. The member must have poor or intermediate risk defined as the following:
   a. Low-risk group: no prognostic factors
   b. Intermediate risk group: one or two prognostic factors

c. Poor-risk group: three or more prognostic factors

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).

Approval duration:
Medicaid – 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).

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

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:
Medicaid – 6 months
Commercial – Length of Benefit

II. Continued Therapy

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

1. Currently receiving medication that has been authorized by Rxadvance, 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).

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

III. Appendices

Appendix A: Abbreviation/Acroym 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.

Appendix E: Prognostic factors

- *Interval from diagnosis to treatment of less than 1 year*

- *Karnofsky performance status less than 80%*
- *Serum lactate dehydrogenase (LDH) greater than 1.5 times the upper limit of normal (ULN)*
- *Corrected serum calcium greater than the ULN*
- *Serum hemoglobin less than the lower limit of normal (LLN)*

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 April 22, 2020.
4. National Comprehensive Cancer Network. Kidney Cancer, Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed April 22,2020
5. National Comprehensive Cancer Network. Thyroid Carcinoma, Version2.2019
6. . Available at https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed April 22,2020.
7. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer, Version 3.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed April 22, 2020.
8. 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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	2/7/2020
Updated references	04/15/2020	05/21/2020
Updated Criteria II, A, i to: Currently receiving medication that has been authorized by Rxadvance, 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;	05/08/2020	05/21/2020