Clinical Policy Title:	cabozantinib
Policy Number:	RxA.52
Drug(s) Applied:	Cabometyx®, Cometriq®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Cabozantinib (Cabometyx®, Cometriq®) is a kinase inhibitor.
Cabometyx® is indicated for the treatment of:

- Patients with advanced renal cell carcinoma (RCC).
- Patients with advanced renal cell carcinoma, as a first-line treatment in combination with nivolumab.
- Patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
cabozantinib (Cabometyx®)	RCC, HCC	60 mg PO once daily RCC: In combination with nivolumab: Cabometyx®, 40 mg PO once daily & nivolumab 240 mg every 2 weeks. 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 In combination with nivolumab: 40 mg Cabometyx® and 480 mg nivolumab every 4 weeks.
cabozantinib (Cometriq®)	MTC	140 mg PO once daily 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

Dosage Forms

- cabozantinib (Cabometyx®): Tablets: 20 mg, 40 mg, 60 mg
- cabozantinib (Cometriq®): Capsules: 20 mg, 80 mg

Clinical Policy

Provider must submit documentation (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. Request is for one of the following (a or b):
   a. Cabometyx® for advanced renal cell carcinoma;
   b. Cabometyx®, in combination with nivolumab for patients with advanced renal cell carcinoma, as a first-line treatment;
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. 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, b or c):
   a. Dose does not exceed 80 mg per day;
   b. Cabometyx®, in combination with nivolumab 40 mg for Cabometyx® and 480 mg nivolumab every 4 weeks;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

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
Commercial: 6 months
Medicaid: 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
Commercial: 6 months
Medicaid: 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
Commercial: 6 months
Medicaid: 6 months

E. Other NCCN Compendium Indication (off-label) (must meet all):

1. Diagnosis of one of the following (a or b):
   a. Relapsed/refractory or metastatic high-grade intramedullary + surface osteosarcoma or Ewing sarcoma;
   b. Unresectable, recurrent, or metastatic Gastrointestinal Stromal Tumors (GIST);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Request is for Cabometyx® as a single agent therapy;
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).

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications 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, b or c):
   a. New dose does not exceed 80 mg per day (Cabometyx®) or 180 mg per day (Cometriq®);
   b. Cabometyx® in combination with nivolumab, 40 mg for Cabometyx® and 480 mg nivolumab every 4 weeks;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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
GIST: Gastrointestinal Stromal Tumors

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Lenvima® (lenvatinib)	DTC: 24 mg PO once daily	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.
- Boxed Warning(s):
  - None.

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.; January 2021. Available at:

https://www.cabometyx.com/downloads/CABOMETYXUSPI.pdf. Accessed February 08, 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 February 08, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 08, 2021.
4. National Comprehensive Cancer Network. Kidney Cancer, Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed February 08, 2021.
5. National Comprehensive Cancer Network. Thyroid Carcinoma, Version 3.2020 . Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed February 08, 2021.
6. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer, Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 08, 2021.
7. National Comprehensive Cancer Network. Hepatobiliary Cancers, Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed February 08, 2021.
8. National Comprehensive Cancer Network. Bone Cancer, Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed February 11, 2021.
9. National Comprehensive Cancer Network. Gastrointestinal Stromal Tumors. Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed February 11, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	2/7/2020
Policy was reviewed: 1. Clinical policy title was updated. 2. Line of business policy applies to was updated to all lines of business. 3. Background was updated: added new indication “patients with advanced renal cell carcinoma, as a first-line treatment in combination with nivolumab” and HCC. 4. Dosing information was updated: dosing regimen of Cabometyx® in combination with nivolumab was added. 5. Initial criteria updated: added I.A.1. & I.A.6.b. 6. Initial approval criteria was updated to include “Other NCCN Compendium indication” criteria. 7. Commercial approval duration was updated to 6 months and 12 months from ‘length of benefit’ & removed HIM from Initial and continued therapy criteria respectively. 8. Continued therapy criteria II.A.1 was rephrased to “Member is currently receiving medication..”.	02/11/2021	03/09/2021

9. Continued therapy criteria was updated: added II.A.3.b. 10. Updated Appendix A: added GIST. 11. Updated Appendix C: removed Boxed warning. 12. References were reviewed and updated.		