Evolent Clinical Guideline 3103 for Cometriq/Cabometyx™ (cabozantinib)

Guideline Number: Evolent_CG_3103	**Applicable Codes**	
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STATEMENT

Purpose

To define and describe the accepted indications for Cometriq/Cabometyx (cabozantinib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Hepatocellular Carcinoma (HCC)

- The member has HCC and Cabometyx (cabozantinib) is being used as a single agent for subsequent therapy for unresectable or metastatic disease in members with Child-Pugh Class A only.

Kidney Cancer

- Cabometyx (cabozantinib) may be used for relapsed/metastatic clear cell renal cell carcinoma for ANY of the following clinical setting:
    - As first line treatment as a single agent or in combination with nivolumab for intermediate/poor risk disease
    - As subsequent therapy as a single agent for any risk disease (for favorable/intermediate/poor risk).
- NOTE: The use of Cabometyx (cabozantinib) as monotherapy is not supported by Evolent Policy for IMDC favorable risk disease when used as first line treatment for clear cell renal cell carcinoma. This policy position is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes with

Cabometyx (cabozantinib) compared to alternative agents/regimens recommended by Evolent available at **Evolent Pathways**.

IMDC criteria table below:

CRITERIA= Assign 1 point for each	RISK CATEGORIES= RISK SCORE
Time to systemic treatment less than 1 year from diagnosis	Favorable Risk = 0
Performance Status < 80% Karnofsky Scale	Intermediate Risk = 1-2
Hemoglobin < LLN; <12 g/dL	Poor Risk= 3-6
Calcium > ULN; > 12 mg/dL	
Neutrophils > ULN	
Platelets > ULN	

Pancreatic Neuroendocrine Tumor (pNET) and Extra-pancreatic Neuroendocrine Tumor (epNET)

- Cabometyx (cabozantinib) may be used as monotherapy in adult and pediatric members 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated pancreatic neuroendocrine tumors (pNET) and well-differentiated extra-pancreatic neuroendocrine tumors (epNET).

Thyroid Cancer

- Cometriq/Cabometyx (cabozantinib) may be used as monotherapy for members with any of the following:
  - For Cometriq use only: Unresectable or metastatic medullary thyroid cancer OR
  - For Cabometyx use only: In adult and pediatric members 12 years of age and older with unresectable or metastatic papillary, follicular, or Hurthle cell thyroid cancer, and the member is refractory to a VEGFR-targeted therapy [e.g., Nexavar (sorafenib)] AND the member is not a candidate for or is refractory to radioactive iodine treatment.

CONTRAINDICATIONS/WARNINGS

- None

EXCLUSION CRITERIA

- Disease progression while taking Cometriq/Cabometyx (cabozantinib).
- Dosing exceeds single dose limit of Cometriq 140 mg and Cabometyx 60 mg.

- Treatment exceeds the maximum limit of Cometriq 84 (20 mg) or 28 (80 mg) capsules per month; Cabometyx 30 (20 mg), 30 (40 mg) or 30 (60 mg) tablets per month.
- Investigational use of Cometriq/Cabometyx (cabozantinib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
    - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
    - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
    - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
    - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
    - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J8999 - cabozantinib

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
May 2026	• Updated references
May 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1237 Cometriq/Cabometyx (cabozantinib) • Added new indication for pancreatic neuroendocrine tumors (pNET) and extra-pancreatic neuroendocrine tumors (epNET). • Updated maximum dosage form quantities in exclusion criteria • Updated references
August 2024	• Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization

management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Chan JA, et al. Phase 3 Trial of Cabozantinib to Treat Advanced Neuroendocrine Tumors. *N Engl J Med*. 2025 Feb 13;392(7):653-665. doi: 10.1056/NEJMoa2403991.
2. Choueiri TK, et al; CheckMate 9ER Investigators . Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2021 Mar 4;384(9):829-841. doi: 10.1056/NEJMoa2026982.
3. Koehler V, et al. Real-World Efficacy and Safety of Cabozantinib and Vandetanib in Advanced Medullary Thyroid Cancer. *Thyroid*. 2021 Mar;31(3):459-469. doi: 10.1089/thy.2020.0206.
4. Abou-Alfa GK, et al. Cabozantinib in Patients with Advanced and Progressing Hepatocellular Carcinoma. *N Engl J Med*. 2018 Jul 5;379(1):54-63. doi: 10.1056/NEJMoa1717002.
5. Choueiri T, et al: METEOR Investigators. Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2015 Nov 5;373(19):1814-23. doi: 10.1056/NEJMoa1510016.
6. Choueiri TK, et al. Cabozantinib Versus Sunitinib As Initial Targeted Therapy for Patients With Metastatic Renal Cell Carcinoma of Poor or Intermediate Risk: The Alliance A031203 CABOSUN Trial. *J Clin Oncol*. 2017 Feb 20;35(6):591-597. doi: 10.1200/JCO.2016.70.7398.
7. Cometriq/Cabometyx prescribing information. Exelixis, Inc. Alameda, CA 2025.
8. Clinical Pharmacology Elsevier Gold Standard 2026.
9. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2026.
10. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2026.
11. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2026.
12. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
13. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
14. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.