Drug Policy:

Cometriq/Cabometyx™ (cabozantinib)

POLICY NUMBER UM ONC_1237	SUBJECT Cometriq/Cabometyx™ (cabozantinib)		DEPT/PROGRAM UM Dept	PAGE 1 of 4
DATES COMMITTEE REVIEWED 01/09/13, 01/08/14, 06/10/15, 06/07/16, 05/10/17, 05/07/18, 05/08/19, 12/11/19, 04/08/20, 02/10/21, 04/14/21, 10/13/21, 11/15/21, 05/11/22, 10/12/22, 03/08/23, 04/12/23, 08/09/23, 08/14/24	APPROVAL DATE August 14, 2024	EFFECTIVE DATE August 30, 2024	COMMITTEE APPROVAL DATES 01/09/13, 01/08/14, 06/10/15, 06/07/16, 05/10/17, 05/07/18, 05/08/19, 12/11/19, 04/08/20, 02/10/21, 04/14/21, 10/13/21, 11/15/21, 05/11/22, 10/12/22, 03/08/23, 04/12/23, 08/09/23, 08/14/24	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. 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.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

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

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

B. Hepatocellular Carcinoma (HCC)

1. 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.

C. Kidney Cancer

1. Cabometyx (cabozantinib) may be used for relapsed/metastatic Clear Cell RCC for ANY of the following clinical setting:
    a. As first line treatment as a single agent or in combination with nivolumab for intermediate/poor risk disease
    b. As subsequent therapy as a single agent for any risk disease (for favorable/intermediate/poor risk).
2. 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 RCC. 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 (http://pathways.newcenturyhealth.com).

    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	

D. Thyroid Cancer

1. Cometriq/Cabometyx (cabozantinib) may be used as monotherapy for members with any of the following:
    a. For Cometriq use only: Unresectable or metastatic medullary thyroid cancer OR
    b. 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.

III. EXCLUSION CRITERIA

A. Disease progression while taking Cometriq/Cabometyx (cabozantinib).

B. Dosing exceeds single dose limit of Cometriq 140 mg and Cabometyx 60 mg.

C. Treatment exceeds the maximum limit of Cometriq 90 (20 mg) capsules or 30 (80 mg) capsules per month; Cabometyx 90 (20 mg), 30 (40 mg) or 30 (60 mg) tablets per month.

D. 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:
    1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.

3. 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.
4. 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).
5. 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.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. 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.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Choueiri TK, et al. CheckMate9ER Clinical Trial. Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma. N Engl J Med 2021;384:829-41. DOI:10.1056/NEJMoa2026982.

B. 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.

C. Abou-Alfa G, et al. CELESTIAL Clinical Trial. Cabozantinib in Patients with Advanced and Progressing Hepatocellular Carcinoma. N Engl J Med 2018; 379:54-63 DOI: 10.1056/NEJMoa1717002.

D. Choueiri T, et al, METEOR Clinical Trial Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma. N Engl J Med; 373:1814-1823. DOI: 10.1056/NEJMoa1510016.

E. 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.

F. Cometriq/Cabometyx prescribing information. Exelixis, Inc. Alameda, CA 2024.

G. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs Bethesda, MD 2024.

H. Clinical Pharmacology Elsevier Gold Standard 2024.

I. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2024.

J. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.

K. 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.

L. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.