

Cabozantinib (Cometriq®; Cabometyx®) (Oral)

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I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

Cometriq capsules:

- 140 mg daily dose carton: 112 capsules per 28 days
(4 cards each containing: #21 x 20 mg capsules and #7 x 80 mg capsules)
- 100 mg daily dose carton: 56 capsules per 28 days
(4 cards each containing: #7 x 20 mg capsules and #7 x 80 mg capsules)
- 60 mg daily dose carton: 84 capsules per 28 days
(4 cards each containing: #21 x 20 mg capsules)

Cabometyx tablets:

- Cabometyx 20 mg tablet: 1 tablet per day
- Cabometyx 40 mg tablet: 1 tablet per day
- Cabometyx 60 mg tablet: 1 tablet per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- Cometriq: 140 mg daily
- Cabometyx: 60 mg daily

III. Initial Approval Criteria¹

Coverage is provided in the following conditions:

- Patient age is 18 years or older; **AND**

Universal Criteria

- Patient does not have a recent history of severe hemorrhage; **AND**
- Patient does not have a recent history of gastrointestinal perforations and/or fistula; **AND**
- Patient does not have severe hepatic impairment (Child-Pugh Class C); **AND**

- Patient must not have had major surgery within the preceding 2 weeks or have a surgical wound that has not fully healed; **AND**
- Used as a single agent; **AND**

Thyroid Carcinoma (Cometriq) $\Phi^{1,3,5}$

- Patient has medullary disease †; **AND**
 - Patient has progressive, metastatic disease; **OR**
 - Patient has unresectable symptomatic or structurally progressive locoregional disease; **OR**
- Patient has Follicular, Hürthle Cell, or Papillary carcinoma ‡; **AND**
 - Patient has unresectable recurrent, persistent, or metastatic disease; **AND**
 - Patient has progressive and/or symptomatic iodine-refractory disease; **AND**
 - Clinical trials or other therapies are not available or appropriate

Renal Cell Carcinoma (Cabometyx) †^{2,3,6,7}

- Patient has advanced, relapsed, or metastatic disease; **AND**
 - Used as first-line therapy for clear cell histology; **AND**
 - Patient has intermediate/poor risk disease with at least one of the following:
 - Less than one year from time of diagnosis to systemic therapy
 - Performance status < 80% (Karnofsky)
 - Hemoglobin < lower limit of normal (Normal: 12 g/dL)
 - Calcium > upper limit of normal (Normal: 8.5-10.2 mg/dL)
 - Neutrophil > upper limit of normal (Normal: 2.0-7.0 x 10⁹/L)
 - Platelets > upper limit of normal (Normal: 150,000-400,000)
 - Used as subsequent therapy for clear cell histology; **OR**
 - Patient has non-clear cell histology

Hepatocellular Carcinoma (Cabometyx) † $\Phi^{2,3,8}$

- Used as subsequent therapy in patients with Child-Pugh Class A hepatic impairment (i.e., excludes class B and C impairments); **AND**
 - Patient had disease progression on or after sorafenib therapy †; **OR**
 - Patient has metastatic disease or extensive liver tumor burden; **OR**
 - Patient has unresectable disease and is not a transplant candidate; **OR**
 - Patient has local disease, or local disease with minimal extrahepatic disease, and considered inoperable due to performance status or comorbidities

Non-Small Cell Lung Cancer (Cometriq & Cabometyx) †^{3,4}

- Patient has confirmed RET gene rearrangements

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria¹

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: development of visceral perforation or fistula formation, severe hemorrhage, serious thrombotic events (e.g., myocardial infarction or arterial/venous thromboembolism), severe hypertension/hypertensive crisis, osteonecrosis of the jaw, severe diarrhea, palmar-plantar erythrodysesthesia syndrome (PPES), reversible posterior leukoencephalopathy syndrome, nephrotic syndrome, proteinuria, impaired wound healing, etc.

V. Dosage/Administration^{1,4}

Indication	Dose
Thyroid Carcinoma, Non-Small Cell Lung Cancer (NSCLC) (Cometriq)	140 mg orally once daily (capsule formulation) until disease progression or unacceptable toxicity
Renal Cell Carcinoma (RCC), Hepatocellular Carcinoma (HCC), Non-Small Cell Lung Cancer (NSCLC) (Cabometyx)	60 mg orally once daily (tablet formulation) until disease progression or unacceptable

***Please refer to the Cometriq and Cabometyx prescribing information for dose modifications for concomitant use with CYP3A4 inhibitors and/or inducers and for use in patients with hepatic impairment.

VI. Billing Code/Availability Information

HCPCS Code:

J8999 – Prescription drug, oral, chemotherapeutic, not otherwise specified
C9399 – Unclassified drugs or biologicals (*Hospital Outpatient Use ONLY*)

NDC:

- Cometriq 140 mg daily-dose carton: 42388-0011-xx
- Cometriq 100 mg daily-dose carton: 42388-0012-xx
- Cometriq 60 mg daily-dose carton: 42388-0013-xx
- Cabometyx 20 mg tablet: 42388-0024-xx
- Cabometyx 40 mg tablet: 42388-0025-xx
- Cabometyx 60 mg tablet: 42388-0023-xx

VII. References

1. Cometriq® [package insert]. South San Francisco, CA; Exelixis, Inc; January 2020. Accessed March 2020.
2. Cabometyx® [package insert]. South San Francisco, CA; Exelixis, Inc.; January 2020; Accessed March 2020.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for cabozantinib. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2020.
4. Drillon A, Wang L, Hasanovic A, et al. Response to cabozantinib in patients with RET fusion-positive lung adenocarcinomas. *Cancer Discov* 2013; 3:630-635.
5. Schlumberger M, Elisei R, Müller S, et al. Overall survival analysis of EXAM, a phase III trial of cabozantinib in patients with radiographically progressive medullary thyroid carcinoma. *Ann Oncol*. 2017;28(11):2813–2819. doi:10.1093/annonc/mdx479.
6. Choueiri TK, Escudier B, Powles T, et al. Cabozantinib versus Everolimus in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2015;373(19):1814–1823. doi:10.1056/NEJMoa1510016.
7. Choueiri TK, Hessel C, Halabi S, et al. Cabozantinib versus sunitinib as initial therapy for metastatic renal cell carcinoma of intermediate or poor risk (Alliance A031203 CABOSUN randomised trial): Progression-free survival by independent review and overall survival update [published correction appears in *Eur J Cancer*. 2018 Nov;103:287]. *Eur J Cancer*. 2018;94:115–125. doi:10.1016/j.ejca.2018.02.012.
8. Abou-Alfa GK, Meyer T, Cheng AL, 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.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C22.0	Liver cell carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung

C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus or lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus or lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
C73	Malignant neoplasm of thyroid gland
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.528	Personal history of other malignant neoplasm of kidney

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Article (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC