Cabozantinib (Cometriq®; Cabometyx®)
(Oral)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

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

Cometriq capsules:

- Cometriq 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)
- Cometriq 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)
- Cometriq 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:
  - RCC in combination with nivolumab – 40 mg daily
  - All other indications – 60 mg daily

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age (unless otherwise specified); **AND**

Universal Criteria [1]

- Patient does not have a recent history of severe hemorrhage; **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**
- Patient will avoid concomitant therapy with all of the following, or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented:
  - Coadministration with strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, St. John's Wort, rifampin, etc.); **AND**
  - Coadministration with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, grapefruit/grapefruit juice, etc.); **AND**

Thyroid Carcinoma

Cometriq Φ [1,3,5]

- Used as a single agent; **AND**
  - Patient has medullary disease †; **AND**
    - Patient has progressive, unresectable, recurrent, persistent, or metastatic disease; **OR**
  - Patient has Follicular, Hürthle Cell, or Papillary carcinoma ‡; **AND**
    - Used for progressive and/or symptomatic disease after progression on lenvatinib and/or sorafenib; **AND**
    - Patient is not amenable to radioactive iodine (RAI) therapy; **AND**
    - Patient has unresectable recurrent, persistent, or metastatic disease

Cabometyx † Φ [2,3,12]

- Patient is at least 12 years of age; **AND**
- Patient has locally advanced or metastatic differentiated thyroid cancer (DTC); **AND**
- Disease has progressed following prior vascular endothelial growth factor receptor (VEGFR)-targeted therapy (e.g., sorafenib, lenvatinib, etc.); **AND**
- Patient is radioactive iodine-refractory or ineligible; **AND**
- Used as a single agent

Renal Cell Carcinoma (Cabometyx) † [2,3,6,7,9]

- Used as a single agent; **AND**
  - Patient has advanced, relapsed, or metastatic disease; **AND**
    - Used as first-line therapy for clear cell histology in patients with 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 10^9/L)
- Platelets > upper limit of normal (Normal: 150,000-400,000); **OR**

▪ Used as subsequent therapy for clear cell histology; **OR**

o Patient has relapsed or metastatic disease with non-clear cell histology; **OR**

- Used in combination with nivolumab; **AND**
  - Patient has clear cell histology; **AND**
    - Used as first-line therapy for advanced, relapsed, or metastatic disease; **OR**
    - Used as subsequent therapy for relapsed or metastatic disease

Hepatocellular Carcinoma (Cabometyx) † Φ [2,3,8]

- Used as a single agent; **AND**
- 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 liver-confined disease that is inoperable due to performance status or comorbidities ‡; **OR**
  - Patient has liver-confirmed disease with minimal or uncertain extrahepatic disease

Non-Small Cell Lung Cancer (Cometriq & Cabometyx) ‡ [3,4]

- Used as a single agent; **AND**
- Used for recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**
- Patient has RET rearrangement positive tumors

Bone Cancer (Cabometyx) ‡ [3,10]

- Used as a single agent; **AND**
- Used as second-line therapy for Osteosarcoma or Ewing's Sarcoma; **AND**
- Used for relapsed, refractory, or metastatic disease

Gastrointestinal Stromal Tumors - GIST (Cabometyx) ‡ [3,11]

- Used as a single agent; **AND**
  - Used as subsequent therapy for unresectable, recurrent/progressive, or metastatic disease after progression on imatinib, sunitinib or dasatinib, regorafenib, and ripretinib; **OR**

- Used as reinduction therapy for palliation of symptoms as part of best supportive care if prior Cabometyx treatment was tolerated and effective

Endometrial Carcinoma (Cabometyx) ‡ [3,13]

- Used as a single agent; **AND**
- Used as second-line therapy for recurrent or metastatic disease

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

IV. Renewal Criteria [1]

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 (PPE), reversible posterior leukoencephalopathy syndrome (RPLS), nephrotic syndrome, proteinuria, impaired wound healing, severe hepatotoxicity, severe adrenal insufficiency, severe thyroid dysfunction, severe hypocalcemia, etc.

V. Dosage/Administration [1,2,4,10,11,13,14]

Indication	Dose
Thyroid Carcinoma, Non-Small Cell Lung Cancer (NSCLC) **(Cometriq)**	Administer 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), Bone Cancer, GIST, Endometrial Carcinoma **(Cabometyx)**	Single-Agent Therapy – Administer 60 mg orally once daily (tablet formulation) until disease progression or unacceptable toxicity Combination with nivolumab (RCC only) – Administer 40 mg orally once daily (tablet formulation) until disease progression or unacceptable toxicity. Note: Refer to the nivolumab prescribing information for dosing.
Thyroid Carcinoma **(Cabometyx)**	BSA ≥1.2 m^2: – Administer 60 mg orally once daily (tablet formulation) until disease progression or unacceptable toxicity BSA <1.2 m^2:

	– Administer 40 mg orally once daily (tablet formulation) until disease progression or unacceptable toxicity
***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

NDC(s):

- Cometriq 140 mg capsule daily-dose carton: 42388-0011-xx
- Cometriq 100 mg capsule daily-dose carton: 42388-0012-xx
- Cometriq 60 mg capsule 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]. Alameda, CA; Exelixis, Inc; October 2020. Accessed April 2022.
2. Cabometyx® [package insert]. Alameda, CA; Exelixis, Inc.; September 2021; Accessed April 2022.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for cabozantinib. National Comprehensive Cancer Network, 2022. 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 April 2022.
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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
C40.00	Malignant neoplasm of scapula and long bones of unspecified upper limb
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb
C40.10	Malignant neoplasm of short bones of unspecified upper limb
C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.20	Malignant neoplasm of long bones of unspecified lower limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.30	Malignant neoplasm of short bones of unspecified lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.80	Malignant neoplasm of overlapping sites of bone and articular cartilage of unspecified limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.90	Malignant neoplasm of unspecified bones and articular cartilage of unspecified limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
C49.A0	Gastrointestinal stromal tumor unspecified site
C49.A1	Gastrointestinal stromal tumor of esophagus

C49.A2	Gastrointestinal stromal tumor of stomach
C49.A3	Gastrointestinal stromal tumor of small intestine
C49.A4	Gastrointestinal stromal tumor of large intestine
C49.A5	Gastrointestinal stromal tumor of rectum
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
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
Z85.831	Personal history of malignant neoplasm of soft tissue

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: https://www.cms.gov/medicare-coverage-database/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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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)
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