Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO010

Description

Cabozantinib (Cabometyx, Cometriq) is an orally administered tyrosine kinase inhibitor of RET, MET, VEGFR1/2/3, KIT, TRKB, FLT3, and TIE2.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity limits

cabozantinib (Cabometyx)	Indication	Quantity Limit	DDID
20 mg tablet	Renal cell carcinoma (RCC), advanced Liver carcinoma, in patients previously treatment with sorafenib	30 tablets/30 days	192650
40 mg tablet		30 tablets/30 days	192651
60 mg tablet		30 tablets/30 days	192652
cabozantinib (Cometriq)	**Indication**	**Quantity Limit**	**DDID**
60 mg per day blister cards	Medullary thyroid carcinoma, progressive, metastatic	84 capsules/28 days	177131
100 mg per day blister cards		56 capsules/28 days	177130
140 mg per day blister cards		112 capsules/28 days	177129

Initial Evaluation

I. Cabozantinib (Cabometyx or Cometriq) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Treatment is prescribed by, or in consultation with, an oncologist; **AND**
   C. Medication is used as monotherapy; **AND**
   D. A diagnosis of one of the following:
      1. **Medullary thyroid carcinoma**; **AND**
         i. Disease is progressive and metastatic (stage IV); **AND**
         ii. Member has RET M918T mutational status; **AND**
         iii. Cabozantinib (COMETRIQ) is prescribed; of note, cabozantinib (Cabometyx) shall not to be used for thyroid cancer; **OR**
      2. **Renal cell carcinoma**; **AND**
         i. Disease is advanced or greater (stage III or IV); **AND**

ii. Cabozantinib (CABOMETYX) is prescribed; of note, cabozantinib (Cometriq) shall not be used for renal cell carcinoma

3. Hepatocellular (Liver) carcinoma

i. Disease is progressive and advanced stage or greater (stage III or IV); **AND**
ii. Member has been previously treated with sorafenib (Nexavar); **AND**
iii. Member has not received more than two previous systemic treatment for advanced or metastatic disease; **AND**
iv. Cabozantinib (CABOMETYX) is prescribed; of note, cabozantinib (COMETRIQ) shall not to be used for hepatocellular carcinoma

II. Cabozantinib (Cabometyx or Cometriq) is considered investigational when used for all other conditions, including but not limited to:

A. Adrenocortical carcinoma
B. Salivary gland cancer
C. Neurofibromas
D. Cholangiocarcinoma
E. Prostate cancer
F. Colorectal cancer
G. Phenochromocytomas and paraganglioma
H. Merkel cell carcinoma and skin cancer
I. Multiple myeloma, acute myeloid leukemia
J. Head and neck cancer
K. Breast cancer

Renewal Evaluation

I. Medication is used as monotherapy; **AND**
II. Medication is prescribed by or in consultation with an oncologist; **AND**
III. There is clinical documentation of response to treatment, such as stabilization of disease or decrease in tumor size or tumor spread; **AND**

A. **Medullary thyroid carcinoma**; **AND**
- Cabozantinib (COMETRIQ) is prescribed; **OR**

B. **Renal cell carcinoma; AND**
1. Cabozantinib (CABOMETYX) is prescribed; **OR**

C. **Hepatocellular (Liver) carcinoma; AND**
1. Cabozantinib (CABOMETYX) is prescribed

Supporting Evidence

I. Cabozantinib (COMETRIQ) is FDA-approved for the treatment of medullary thyroid carcinoma in the advance or greater setting. This medication was studied in patients with progressive disease in the phase III EXAM trial against placebo. The follow up analysis, published in 2017, indicated that cabozantinib did not show a statistically significant difference in overall survival compared to placebo for the overall group of 330 patients; however, in an exploratory assessment of overall survival, cabozantinib showed a statistically significant difference in overall survival for the RET M918T mutation population (44.3 months vs 18.9 months [HR 0.60; CI 0.38-.094;

p=0.03]). Cabozantinib (COMETRIQ) shall be used for this indication due to its specific formulary, dosing, and packaging differences compared to cabozantinib (Cabometyx)

II. Cabozantinib (Cabometyx) was evaluated in advance renal cell carcinoma against everolimus in an open-label trial. Cabozantinib (Cabometyx) showed a statistically significant improvement in progression-free survival, overall survival, and objective response rate compared to everolimus. Up to 80mg per day may be used in the setting of CYP3A4 interactions; however, 60mg per day is the usual dose.

III. Cabozantinib (Cabometyx) was evaluated in patients with advanced and progressing hepatocellular carcinoma against placebo. All patients had been previously treated with sorafenib in this phase III trial, and had received a maximum of two previous systemic therapies for advanced hepatocellular carcinoma. Overall survival was statistically significantly longer with cabozantinib (Cabmetyx) compared to placebo. (10.2 months vs. 8 months [HR 0.76; CI 0.63-0.92; p=0.005]). Up to 80mg per day may be used in the setting of CYP3A4 interactions; however, 60mg per day is the usual dose.

Investigational or Not Medically Necessary Uses

All indications listed below have not been sufficiently studied for safety and efficacy, or have insufficient or inconclusive evidence for use of cabozantinib (Cabometyx and/or Cometriq).

I. Non-small cell lung cancer
II. Adrenocortical carcinoma
III. Salivary gland cancer
IV. Neurofibromas
V. Cholangiocarcinoma
VI. Prostate cancer
VII. Colorectal cancer
VIII. Phenochromocytomas and paraganglioma
IX. Merkel cell carcinoma and skin cancer
X. Multiple myeloma, acute myeloid leukemia
XI. Head and neck cancer
XII. Breast cancer

References

1. Cometriq [Package Insert]. South San Francisco, CA. Exelixis, Inc. November 2012.
2. Cabometyx [Package Insert]. Alameda, CA. Exelixis, Inc. January 2019.
3. Schoffski P., Elisei R., Muller S., et al. An international, double-blind, randomized, placebo-controlled phase III trial (EXAM) of cabozantinib in medullary thyroid carcinoma patients with document RECIST progression at baseline. Journal of Clinical Oncology. 30.(15). May 2012.
4. Abou-alfa GK, Meyer T, Cheng AL, et al. Cabozantinib in Patients with Advanced and Progressing Hepatocellular Carcinoma. N Engl J Med. 2018;379(1):54-63.
5. Choueiri TK, Escudier B, Powles T, et al. Cabozantinib versus everolimus in advanced renal cell carcinoma (METEOR): final results from a randomised, open-label, phase 3 trial. Lancet Oncol. 2016;17(7):917-927.
6. National Comprehensive Cancer Network. Kidney Cancer Guidelines Version 3.2019. Available at https://www.nccn.org/professionals/physician_gls/default.aspx. [Accessed February 15, 2019].
7. National Comprehensive Cancer Network. Thyroid Carcinoma Guidelines Version 3.2018. Available at https://www.nccn.org/professionals/physician_gls/default.aspx. [Accessed February 15, 2019].

8. National Comprehensive Cancer Network. Hepatobiliary Cancer Guidelines Version 1.2019. Available at https://www.nccn.org/professionals/physician_gls/default.aspx. [Accessed February 15, 2019].

Policy Implementation/Update:

Date Created	December 2012
Date Effective	December 2012
Last Updated	February 2019
Last Reviewed	01/2018, 02/2019

Action and Summary of Changes	**Date**
Transitioned criteria to policy format, added hepatocellular carcinoma indication, added age criteria and monotherapy criteria to all indications.	02/2019
Removed step therapy in RCC; Updated renewal language to assess response to therapy	01/2018