

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Cometriq™ (cabozantinib capsules – Exelixis Inc.)

TAC APPROVAL DATE: 04/17/2019

OVERVIEW

Cometriq is a kinase inhibitor indicated for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC).¹ *In vitro* biochemical and cellular assays have shown Cometriq to inhibit the tyrosine kinase activity of rearranged during transfection (RET), MET, vascular endothelial cell growth factor receptor (VEGFR)-1, -2, and -3, KIT, tyrosine-related kinase B (TrkB), Fms-like tyrosine kinase 3 (FLT-3), AXL, and TIE-2.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for thyroid carcinoma (version 1.2019 – March 28, 2019) lists surgery as the main treatment option for MTC.²⁻³ Postoperative levothyroxine is recommended in all patients to normalize thyroid stimulating hormone (TSH) levels. For recurrent or persistent disease after surgery, the choice of therapy is as follows: for *locoregional* disease, Caprelsa® (vandetanib tablets) [category 1] or Cometriq (category 1) are recommended for unresectable locoregional disease that is symptomatic or structurally progressive. For recurrent or persistent *asymptomatic* disease with distant metastases, Caprelsa (category 1), or Cometriq (category 1) can be considered if the disease is structurally progressive and not resectable. For recurrent or persistent *symptomatic disease or progression* with distant metastases, the guidelines recommend the following treatment options: 1) Caprelsa [category 1]; 2) Cometriq [category 1]; 3) clinical trial; 4) consider other small molecule kinase inhibitors (Nexavar® [sorafenib tablets], Sutent® [sunitinib capsules], or Votrient® [pazopanib tablets]) if clinical trials, Caprelsa or Cometriq are not available or appropriate, or if the patient progresses on Caprelsa or Cometriq; or 5) dacarbazine-based systemic chemotherapy. Kinase inhibitor therapy may not be appropriate for patients with stable or slowly progressive indolent disease. The guidelines recommend that Cometriq be considered if clinical trials or other systemic therapies are not available or appropriate for the treatment of progressive and/or symptomatic iodine refractory thyroid cancer that is unresectable recurrent or persistent locoregional disease or that is distant metastatic disease.²⁻³ This recommendation is for follicular, Hürthle cell, and papillary_cancer subtypes (all category 2A).

The NCCN Compendium recommends the use of cabozantinib for RET gene rearrangements in non-small cell lung cancer (category 2A).³

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Cometriq. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Cometriq is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Medullary Thyroid Cancer (MTC).** Approve for 3 years.

Other Uses with Supportive Evidence

2. **Non-Small Cell Lung Cancer with RET Gene Rearrangements.** Approve for 3 years.
3. **Differentiated (i.e., papillary, follicular, and Hürthle) Thyroid Carcinoma.** Approve for 3 years if the disease is refractory to radioactive iodine therapy.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Cometriq has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

Metastatic Castration-Resistant Prostate Cancer (mCRPC). Results from the COMET-1 Phase III pivotal study with cabozantinib 60 mg tablets in men with mCRPC are published.⁸ Patients included in the study had disease progressed after treatment with docetaxel as well as Zytiga[®] (abiraterone acetate tablets) and/or Xtandi[®] (enzalutamide capsules). The study failed to meet its primary endpoint of demonstrating statistically significant increase in overall survival (OS) compared with prednisone. The median OS with cabozantinib was 11.0 months vs. 9.8 months with prednisone (hazard ratio [HR] 0.90; 95% CI: 0.76, 1.06; P = 0.213). Based on these results, the second Phase III study, COMET-2 has been discontinued.⁹

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Cometriq[™] [prescribing information]. San Francisco, CA: Exelixis Inc; January 2018.
2. The NCCN Thyroid Carcinoma Clinical Practice Guidelines in Oncology (Version 1.2019 – March 28, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed April 15, 2019.
3. The NCCN Drugs and Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed April 15, 2019. Search term: cabozantinib.
4. Smith M, De Bono J, Sternberg C, et al. Phase III study of cabozantinib in previously treated metastatic castration-resistant prostate cancer: COMET-1. *J Clin Oncol*. 2016;34:3005-3013.
5. Exelixis. Study of cabozantinib (XL184) versus mitoxantrone plus prednisone in men with previously treated symptomatic castration-resistant prostate cancer (COMET-2). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2017 March 13]. Available from: <http://www.clinicaltrials.gov/ct2/show/NCT01522443?term=NCT01522443&rank=1>. NLM identifier: NCT01522443.
6. Cabanillas ME, de Souza JA, Geyer S, et al. Cabozantinib as salvage therapy for patients with tyrosine kinase inhibitor-refractory differentiated thyroid cancer: results of a multicenter Phase II International Thyroid Oncology Group Trial. *J Clin Oncol*. 2017;35:3315-3321.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Selected revision	Approval duration increased to 3 years from 1 year.	08/06/2014
Annual revision	No criteria changes	03/04/2015
Selected revision	Added approval criteria for renal cell carcinoma and non-small cell lung cancer with RET gene rearrangements based on NCCN guidelines.	12/09/2015
Annual revision	Simplified medullary thyroid and renal cell carcinoma criteria, in line with other tyrosine kinase inhibitor approval for these conditions.	03/16/2016
Selected revision	Removed Renal Cell Carcinoma indication from “Other Uses with Supportive Evidence” since this will be addressed in Cabometyx (cabozantinib tablets) prior authorization policy under FDA-approved use.	05/04/2016
Annual revision	No criteria changes	03/15/2017
Annual revision	Added new approval condition for use in Differentiated thyroid cancer under Other Uses with Supportive Evidence, based on guidelines/compendium.	04/11/2018
Annual revision	No criteria changes	04/17/2019

TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; * For a summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.