nh healthy families

CLINICAL POLICY	
DEPARTMENT: Medical Management	**DOCUMENT NAME:** Cometriq, Cabometyx
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IMPORTANT REMINDER

This Clinical Policy has been developed by appropriately experienced and licensed health care professionals based on a thorough review and consideration of generally accepted standards of medical practice, peer-reviewed medical literature, government agency/program approval status, and other indicia of medical necessity.

The purpose of this Clinical Policy is to provide a guide to medical necessity. Benefit determinations should be based in all cases on the applicable contract provisions governing plan benefits ("Benefit Plan Contract") and applicable state and federal requirements, as well as applicable plan-level administrative policies and procedures. To the extent there are any conflicts between this Clinical Policy and the Benefit Plan Contract provisions, the Benefit Plan Contract provisions will control.

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

Subject

Medical necessity criteria for treatment with Cometriq, Cabometyx (cabozantinib)

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene® for Cometriq/Cabometyx.

FDA-approved indication

Cometriq/Cabometyx is indicated for the treatment of patients with progressive, metastatic medullary thyroid cancer (MTC). [1] Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia.

Policy/Criteria

It is the policy of Health Plans affiliated with Centene Corporation® that Cometriq/Cabometyx is **medically necessary** when meeting the following algorithm criteria:

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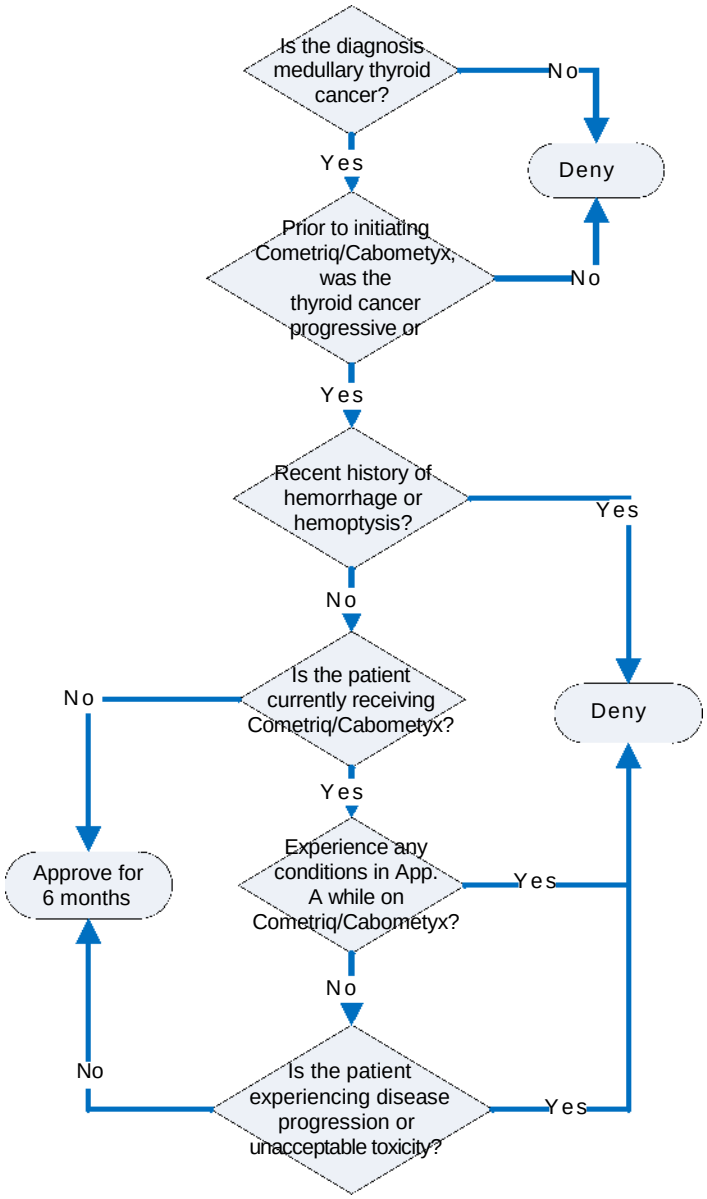
Cometriq/Cabometyx Algorithm



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Background

It is estimated that 62,980 new cases of thyroid cancer will be diagnosed and 1,890 will die in the United States in 2014.[2] About 75% of new diagnosis will occur in women; however, thyroid cancer is the fastest-increasing cancer in both men and women.[2] There are three main histological types of thyroid cancer: 1) differentiated (papillary, follicular, and Hürthle cell), 2) medullary and 3) anaplastic.[3] Most thyroid cancers are differentiated cancers while medullary and anaplastic thyroid cancer only make up 4% and 2%, respectively.[2]

Medullary thyroid carcinoma (MTC) develops in the C cells of the thyroid gland and typically secretes calcitonin and carcinoembryonic antigen (CEA).[2] There are two types of MTC: sporadic (about 80% of cases) and inherited.[2,3] Inherited MTC is further subdivided into three tumor syndromes: familial MTC, multiple endocrine neoplasia type 2A (MEN2A), and MEN2B.[3] Germline point mutations in the rearranged during transfection (*RET)* proto-oncogene are found in at least 95% of MTC with MEN 2A, 88% of familial MTC and 6% of sporadic MTC.[3] Therefore, National Comprehensive Cancer Network (NCCN) recommends genetic testing for *RET* proto-oncogene mutations for all newly diagnosed patients with clinically apparent sporadic MTC, and for those at risk for familial MTC.

MTC cells do not concentrate radioactive iodine and as a result, MTC cannot be managed with radioiodine imaging or radioiodine treatment.[3] Conventional cytotoxic chemotherapy is generally not effective for MTC.[3] The main initial treatment for MTC is surgery, usually total thyroidectomy with or without lymph node dissection.[3] External beam radiation therapy (EBRT) may provide some improvement in selected patients, but has not been adequately studied as adjuvant therapy in MTC.[3]

Postoperatively, levothyroxine treatment is given to MTC patients to maintain thyroid stimulating hormone levels in the normal range.[3] Measurement of calcitonin and CEA levels are the cornerstone of long-term follow-up and assessment for residual disease in patients with MTC.[3] Patients with detectable or increasing calcitonin or CEA levels require imaging studies to identify residual or metastatic tumors. Treatment options for locoregional recurrent or persistent disease without distant metastases include surgical resection and EBRT.[3] For distant metastases, typically involving the bone or liver, regional treatment (eg, palliative resection, radiofrequency ablation, embolization) may be considered. NCCN guidelines state that when disseminated symptomatic metastases are present, treatment options include the following: 1) clinical trial; 2) EBRT for focal symptoms; 3) vandetanib; 4) sorafenib or sunitinib if a clinical trial or vandetanib is not an option or if the patient progresses on vandetanib (note: sorafenib and sunitinib are not FDA-approved for thyroid cancer); 5) dacarbazine-based systemic chemotherapy; 6) bisphosphonate or denosumab for bone metastases; and 7) best supportive care.[3] However since these guidelines were published prior to the approval of Cometriq, they do not address this drug specifically.

Cometriq is a new oral kinase inhibitor.[1] Cometriq inhibits the activity of RET, vascular endothelial growth factor receptors (VEGFR-1,-2, and -3) and other kinases.[1] In a randomized, double-blind, controlled trial of 330 patients with metastatic MTC, Cometriq resulted in a statistically significant prolongation in progression-free survival (PFS).[1] The median PFS was 11.2 months for Cometriq and 4 months for placebo.[1] Partial responses, not observed in the placebo group, occurred in 27% of Cometriq-treated patients.[1] The median duration of objective responses was 14.7 months.[1] There was no statistically significant difference in overall survival between the treatment arms at the planned interim analysis.[1]

Safety

BLACKBOX WARNINGS: PERFORATIONS AND FISTULAS, and HEMORRHAGE[1]

Perforations and Fistulas:

Gastrointestinal (GI) perforations occurred in 3% and fistulas formation in 1% of Cometriq-treated patients. Discontinue Cometriq in patients with perforation or fistula.

Hemorrhage:

Serious, sometimes fatal, hemorrhage including hemoptysis and gastrointestinal hemorrhage occurred in 3% of Cometriq-treated patients. Monitor patients for signs and symptoms of bleeding. Do not administer Cometriq to patients with a recent history of hemorrhage or hemoptysis.

Thrombotic events: discontinue use of Cometriq in patients who develop an acute myocardial infarction or any other clinically significant arterial thrombotic complication

Wound complications: stop treatment with Cometriq at least 28 days prior to schedule surgery. Resume Cometriq therapy after surgery based on clinical judgment of adequate wound healing. Withhold Cometriq in patients with dehiscence or wound healing complications requiring medical intervention

Hypertension: increased incidence of treatment-emergent hypertension. Monitor blood pressure prior to initiation and regularly during Cometriq treatment. Withhold Cometriq for hypertension that is not adequately controlled with medical management; when controlled, resume Cometriq at a reduced dose.

Osteonecrosis of the jaw (ONJ): ONJ can manifest as jaw pain, osteomyelitis, osteitis, bone erosion, tooth or periodontal infection, toothache, gingival ulceration or erosion, persistent jaw pain or slow healing of hte mouth or jaw after dental surgery. Patients are recommended to have an oral examination prior to initiation of Cometriq and periodically during Cometriq therapy. For invasive

dental procedure, withhold Cometriq treatment for at least 28 days prior to scheduled surgery, if possible.

Palmar-plantar erythrodysesthesia syndrome (PPES): withhold Cometriq in patients who develop intolerable Grade 2 PPES or Grade 3-4 PPES until improvement to Grade 1; resume at a reduced dose.

Proteinuria: monitor urine protein regularly during Cometriq treatment. Discontinue Cometriq in patients who develop nephrotic syndrome.

Reversible posterior leukoencephalopathy syndrome (RPLS): monitor in any patient presenting with seizures, headache, visual disturbances, confusion or altered mental function. Discontinue Cometriq in patients who develop RPLS.

Appendix A: Permanently discontinue Cometriq for the any of the following conditions

Development of GI visceral perforation or fistula formation
Severe hemorrhage
Serious arterial thromboembolic event (i.e. myocardial infarction, cerebral infarction)
Nephrotic syndrome
Malignant hypertension, hypertensive crisis, or persistent uncontrolled hypertension (despite optimal medical management)
Osteonecrosis of the jaw
Reversible posterior leukoencephalopathy syndrome

References

1. Cometriq [package insert]. South San Francisco, CA: Exelixis; November 2012.
2. American Cancer Society. Cancer Facts and Figures 2012. http://www.cancer.org. Accessed May 14, 2014.
3. The NCCN Clinical Practice Guidelines in OncologyTM Thyroid Carcinoma (Version 3.2012). ©2012 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed May 14, 2014

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Revision Log	Date
Removed prospective monitoring questions and changed it to Appendix A and related question for denial of existing conditions Updated background and safety information	05/14
Added Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia.	07/15
Annual Review No changes	08/16
Updated policy to include Cabometyx	07/17