BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 9/15/2016
LAST REVIEW DATE: 8/20/2020
LAST CRITERIA REVISION DATE: 8/20/2020
ARCHIVE DATE:

CABOMETYX® (cabozantinib) oral
COMETRIQ™ (cabozantinib) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

CABOMETYX® (cabozantinib) oral
COMETRIQ™ (cabozantinib) oral

Cabometyx (cabozantinib)

- **Criteria for initial therapy:** Cabometyx (cabozantinib) oral tablet is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist, Nephrologist, Pulmonologist, or Gastroenterologist depending upon indication or use

2. Individual is 18 years of age or older

3. A confirmed diagnosis of **ONE** of the following:
    a. Renal cell carcinoma (RCC) as single agent therapy for relapse or surgically unresectable Stage IV disease as **ONE** of the following:
        i. Preferred first line therapy for poor/intermediate risk groups with predominant clear histology
        ii. Preferred subsequent therapy for predominant clear histology
        iii. Systemic therapy for non-clear cell histology

    b. Hepatocellular carcinoma (HCC) as:
        i. Subsequent treatment for progressive disease, as single agent therapy
        ii. In a patient with Child-Pugh Class A
        iii. Who have unresectable disease
        iv. Are not transplant candidates

    c. Non-small cell lung cancer with RET gene rearrangements that have histology types of adenocarcinoma (with mixed subtypes), large cell carcinoma, or squamous cell carcinoma as single-agent therapy for recurrent, advanced or metastatic disease as:
        i. First-line therapy
        ii. Subsequent therapy following progression on first-line systemic therapy with a non-RET rearrangement positive-targeted regimen

    d. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
    a. Oral examination performed by a medical provider or dentist to determine risk for osteonecrosis of the jaw, individuals with risk factors for ONJ (see Definition section) should receive appropriate preventive dentistry prior to initiation
    b. A negative pregnancy test in a woman of child bearing potential;

5. There is no recent history of severe hemorrhage or hemoptysis

6. There is no GI fistula or perforation

7. The individual does not have severe hepatic impairment (Child-Pugh Class C)

8. Individual does not have severe renal impairment (eGFR < 29 mL/min/1.73 m^2 by MDRS or requiring dialysis)

9. Individual does not have uncontrolled hypertension

10. Substituting Cometriq (cabozantinib) capsules for Cabometyx (cabozantinib) tablets will not be done

11. Simultaneous use of Cabometyx (cabozantinib) tablets with Cometriq (cabozantinib) capsules will not be done

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Cabometyx (cabozantinib) oral tablet is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist, Nephrologist, Pulmonologist, or Gastroenterologist depending upon indication or use

2. Individual's condition responded while on therapy
    a. Response is defined as:
        i. No evidence of disease progression
        ii. Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use, such as:
    a. Severe hemorrhage
    b. GI perforation or fistula
    c. Arterial thrombotic events: MI, cerebral infarction, or other serious arterial thromboembolic events
    d. Reversible posterior leukoencephalopathy syndrome (RPLS)
    e. Malignant hypertension, hypertensive crisis or severe hypertension that cannot be controlled with anti-hypertensive therapy
    f. Osteonecrosis of jaw
    g. Proteinuria or nephrotic syndrome

5. There are no significant interacting drugs

6. Substituting Cometriq (cabozantinib) capsules for Cabometyx (cabozantinib) tablets will not be done

7. Simultaneous use of Cabometyx (cabozantinib) tablets with Cometriq (cabozantinib) capsules will not be done

CABOMETYX® (cabozantinib) oral
COMETRIQ™ (cabozantinib) oral

Renewal duration: 6 months

Cometriq (cabozantinib)

- **Criteria for initial therapy:** Cometriq (cabozantinib) oral capsule is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist, Pulmonologist, or Oncologist

2. Individual is 18 years of age or older

3. A confirmed diagnosis of **ONE** of the following:

    a. Medullary thyroid cancer (MTC) that is either:
        i. Unresectable locoregional disease that is symptomatic or progressing
        ii. Asymptomatic recurrent or persistent distant metastases if unresectable and progressing
        iii. Recurrent or persistent distant metastases if symptomatic disease or progression

    b. Papillary, follicular, or Hurthle Cell thyroid carcinoma if other systemic therapies are not available or appropriate for progressive and/or symptomatic iodine refractory that is either:
        i. Unresectable locoregional recurrent or persistent disease
        ii. Distant metastatic disease

    c. Non-small cell lung cancer with RET gene rearrangements that have histology types of adenocarcinoma (with mixed subtypes), large cell carcinoma, or squamous cell carcinoma as single-agent therapy for recurrent, advanced or metastatic disease as:
        i. First-line therapy
        ii. Subsequent therapy following progression on first-line systemic therapy with a non-RET rearrangement positive-targeted regimen

    d. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
    a. Oral examination performed by a medical provider or dentist to determine risk for osteonecrosis of the jaw, individuals with risk factors for ONJ (see Definition section) should receive appropriate preventive dentistry prior to initiation

5. There is no recent history of severe hemorrhage or hemoptysis

6. There is no GI fistula or perforation

7. The individual does not have severe hepatic impairment (Child-Pugh Class C)

8. Substituting Cabometyx (cabozantinib) tablets for Cometriq (cabozantinib) capsules will not be done

9. Simultaneous use of Cabometyx (cabozantinib) tablets with Cometriq (cabozantinib) capsules will not be done

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Cometriq (cabozantinib) oral capsule is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist, Pulmonologist, or Oncologist

2. Individual's condition responded while on therapy
    a. Response is defined as:
        i. No evidence of disease progression
        ii. Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use, such as:
    a. Severe hemorrhage
    b. GI perforation or fistula
    c. Arterial thrombotic events: MI, cerebral infarction, or other serious arterial thromboembolic events
    d. Reversible Posterior leukoencephalopathy syndrome (RPLS)
    e. Malignant hypertension, hypertensive crisis or severe hypertension that cannot be controlled with anti-hypertensive therapy
    f. Osteonecrosis of jaw
    g. Proteinuria or nephrotic syndrome

5. There are no significant interacting drugs

6. Substituting Cabometyx (cabozantinib) tablets for Cometriq (cabozantinib) capsules will not be done

7. Simultaneous use of Cabometyx (cabozantinib) tablets with Cometriq (cabozantinib) capsules will not be done

Renewal duration: 12 months

CABOMETYX® (cabozantinib) oral
COMETRIQ™ (cabozantinib) oral

Description:

Cabometyx (cabozantinib) tablet is a kinase inhibitor indicated for the treatment of patients with advanced renal cell carcinoma (RCC) and hepatocellular carcinoma (HCC) who have previously been treated with sorafenib. Cabozantinib is also available as a capsule, under the brand name of Cometriq®, which is indicated for treatment of patients with progressive, metastatic medullary thyroid cancer. These dosage forms are not interchangeable due to differences in the pharmacokinetics of each formulation.

Renal Cell Carcinoma (RCC) is a common type of kidney cancer with three major sub-types: i) clear cell renal carcinoma (the most common RCC), ii) papillary renal cell carcinoma (second most common), and iii) chromophobe renal cell carcinoma (third most common). There are other rare types of renal cell carcinoma that make up less than 1% of the RCC.

RCC has a high mortality rate but if it is detected early, it is potentially curable by surgery. In localized disease, partial nephrectomy for small tumors and radical nephrectomy for large tumors continue to be the gold-standard treatments. Cytoreductive nephrectomy is often indicated before the start of systemic treatment in patients with metastatic disease as part of integrated management strategy.

Other oral agents used for RCC that affect VEGF development of blood vessels in cancer cells include Afinitor (everolimus), Inlyta (axatinib), Lenvima (lenvatinib), Nexavar (sorafenib), Sutent (sunatinib), and Votrient (pazopanib). Avastin (bevacizumab), given by an intravenous injection in combination with interferon alpha, also affects VEGF blood vessel development in cancer cells.

Thyroid cancer is the most common of the endocrine malignancies. The annual incidence of thyroid cancer varies considerably by geographic area, age and sex. The only recognized environmental risk factor for thyroid carcinoma is exposure to ionizing radiation.

Thyroid cancer can develop from follicular or non-follicular thyroid cells. Medullary thyroid cancer (MTC) arises from non-follicular thyroid cells called calcitonin-producing cells. Thyroid cancers from follicular cells include papillary thyroid cancer (PTC), follicular thyroid cancer (FTC), Hurthle cell cancer (HCC, also known as oxyphil thyroid cancer, a subtype of FTC), and anaplastic thyroid cancer (ATC). PTC and FTC are often referred to as differentiated thyroid cancer (DTC). There are several subtypes of DTC that includes tall cell, columnar and insular thyroid cancers. ATC is an undifferentiated thyroid cancer.

Targeted therapy is a treatment that targets the cancer's specific genes, proteins, or the tissue environment that contributes to cancer growth and survival. This type of treatment attempts to blocks the growth and spread of cancer cells while limiting damage to healthy cells. Anti-angiogenesis therapy is a type of treatment aimed at the process by which cancer cells make new blood vessels. Many of the anti-angiogenesis agents used attack the protein known as vascular endothelial growth factor (VEGF) that controls the formation of new blood vessels.

Cabozantinib inhibits the tyrosine kinase activity of MET, VEGFR-1, -2 and -3, AXL, RET, ROS1, TYRO3, MER, KIT, TRKB, FLT-3, and TIE-2. These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes such as oncogenesis, metastasis, tumor angiogenesis, drug resistance, and maintenance of the tumor microenvironment.

CABOMETYX® (cabozantinib) oral
COMETRIQ™ (cabozantinib) oral

Definitions:

Osteonecrosis of the jaw (ONJ):

According to the American College of Rheumatology, ONJ can be diagnosed on oral examination by the presence of exposed bone that has lasted more than eight weeks.

ONJ risk factors include:

- invasive dental procedures (e.g. tooth extraction, dental implants, oral surgery)
- diagnosis of cancer
- concomitant therapies (e.g. chemotherapy, corticosteroids, angiogenesis inhibitors)
- poor oral hygiene
- co-morbid disorders (e.g. periodontal and/or other pre-existing dental disease, anemia, coagulopathy, infection, ill-fitting dentures)

Resources:

Cabometyx. Package Insert. Revised by manufacturer 02/2020. Accessed 06-09-2020.

Cometriq. Package Insert. Revised by manufacturer 1/2018. Accessed 08-17-2018.

UpToDate: Anti-angiogenic and molecularly targeted therapy for advanced of metastatic clear-cell renal carcinoma. Current through July 2017

UpToDate: Medullary thyroid cancer: Chemotherapy and immunotherapy. Current through July 2017

NCCN Clinical Practice Guidelines in Oncology: Kidney cancer. Version 4.2018, April 23, 2018

NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 6.2018, Aug 17, 2018

NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma. Version 1.2018, May 22, 2018

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.