Clinical Policy Title:	cabozantinib
Policy Number:	RxA.052
Drug(s) Applied:	Cabometyx®, Cometriq®
Original Policy Date:	02/07/2020
Last Review Date:	08/28/2024
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Renal Cell Carcinoma (must meet all)**:**

1. Diagnosis of relapsed or Stage IV (unresectable or metastatic) RCC;
2. Request is for Cabometyx®.

Approval Duration

All Lines of Business (except Medicare): 6 months

B. Thyroid Cancer (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Recurrent, unresectable, progressive, or metastatic medullary thyroid carcinoma (MTC)
   b. Locally advanced or metastatic differentiated thyroid carcinoma (DTC; i.e., follicular, Hurthle cell, or papillary thyroid carcinoma);
2. If DTC, the disease has progressed on both of the following (a and b):
   a. Member has previously tried a vascular endothelial growth factor (VEGFR)-targeted therapy (e.g. Lenvima® or Nexavar®)* unless contraindicated or clinically significant side effects are experienced;
   b. Disease or patient is refractory to radioactive iodine treatment or ineligible;

   *Prior authorization may be required.
3. Request is for one of the following (a or b):
   a. If MTC, request is for Cometriq®;
   b. If DTC, request is for either Cabometyx®.

Approval Duration

All Lines of Business (except Medicare): 6 months

C. Hepatocellular Carcinoma (must meet all)**:**

1. Diagnosis of hepatocellular carcinoma (HCC);
2. Request meets one of the following (a, b, c, d or e):
   a. Trial and failure of Nexavar® unless contraindicated or clinically significant adverse effects are experienced;
   b. Patient has metastatic disease;
   c. Patient has extensive liver tumor burden;
   d. Patient is inoperable by performance status or comorbidity (local disease or local disease with minimal extrahepatic disease only);
   e. Disease is unresectable;

3. Confirmation of Child-Pugh class A status;
4. Request is for Cabometyx®.

Approval Duration
All Lines of Business (except Medicare): 6 months

D. Non-Small Cell Lung Cancer (off-label) (must meet all)**:**
1. Diagnosis of non-small cell lung cancer (NSCLC) with an RET gene rearrangement;
2. Prescribed as single-agent therapy for recurrent, advanced or metastatic disease.

Approval Duration
All Lines of Business (except Medicare): 6 months

E. Other NCCN Compendium Indication (off-label) (must meet all):
1. Diagnosis of one of the following (a, b or c):
   a. Relapsed/refractory or metastatic high-grade intramedullary + surface osteosarcoma or Ewing sarcoma;
   b. Unresectable, recurrent, or metastatic Gastrointestinal Stromal Tumors (GIST);
   c. Uterine Neoplasms - Endometrial Carcinoma;
2. Request is for Cabometyx® as a single agent therapy.

Approval duration
All Lines of Business (except Medicare): 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**
1. Auto-approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.

Approval Duration
All Lines of Business (except Medicare): 12 months

References

1. National Comprehensive Cancer Network. Kidney Cancer, Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed August 28, 2024.
2. National Comprehensive Cancer Network. Thyroid Carcinoma, Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf . Accessed August 28, 2024
3. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer, Version 8.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed August 28, 2024.
4. National Comprehensive Cancer Network. Hepatobiliary Cancers, Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf . Accessed August 28, 2024.
5. National Comprehensive Cancer Network. Bone Cancer, Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf. Accessed August 28, 2024.
6. National Comprehensive Cancer Network. Gastrointestinal Stromal Tumors. Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf. Accessed August 28, 2024.
7. National Comprehensive Cancer Network. Uterine neoplasm. Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed August 28, 2024.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	2/7/2020

Policy was reviewed: 1. Clinical policy title was updated. 2. Line of business policy applies to was updated to all lines of business. 3. Initial criteria updated: added I.A.1. & I.A.6.b. 4. Initial approval criteria was updated to include "Other NCCN Compendium indication" criteria. 5. Commercial approval duration was updated to 6 months and 12 months from 'length of benefit' & removed HIM from Initial and continued therapy criteria respectively. 6. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication..". 7. Continued therapy criteria was updated: added II.A.3.b. 8. References were reviewed and updated.	02/11/2021	03/09/2021
Policy was reviewed: 1. Initial Approval Criteria, I.A.5.a, 1.A.5.b, I.A.5.c was removed. I.A.5.a included low-risk group, I.A.5.b included intermediate risk group and I.A.5.c included poor risk group. 2. Initial Approval Criteria, I.B.1.b: Updated indication from Differentiated thyroid carcinoma (DTC; i.e., follicular, Hurthle cell, or papillary thyroid carcinoma) to Locally advanced or metastatic differentiated thyroid carcinoma (DTC; i.e., follicular, Hurthle cell, or papillary thyroid carcinoma); 3. Initial Approval Criteria, I.B.3: Updated to include new criteria pertaining to indication DTC, If DTC; disease has progressed following both (a and b): a. Prior VEGFR-targeted therapy; b. Who are radioactive iodine-refractory or ineligible 4. Initial approval criteria I.B.4: Updated age criteria from Age ≥ 18 years to Meets one of the following: a. Age ≥ 18 years for Cometriq®; b. Age ≥ 12 years for Cabometyx®. 5. Initial Approval Criteria, I.B.5: Updated drug request criteria from Request is for Cometriq to Request is for one of the following (a or b): a. Cometriq® for MTC; b. Cabomrtyx® for DTC 6. Initial Approval Criteria, I.B.6: Updated dose	12/7/2021	01/17/2022

criteria from Request meets one of the following (a or b): a. Cometriq®: Dose does not exceed 180 mg per day; b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence to Request meets one of the following (a or b or c): a. Cometriq®: Dose does not exceed 180 mg per day; b. Cabometyx®: Dose does not exceed 80 mg per day; c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence) 7. Initial Approval Criteria, 1.C.6: Updated dosing criteria from Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence) to Request meets one of the following (a or b): a. Dose does not exceed 80 mg per day; b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). 8. Initial Approval Criteria, I.E.1: Updated indication from Diagnosis of one of the following (a or b): a. Relapsed/refractory or metastatic high-grade intramedullary + surface osteosarcoma or Ewing sarcoma; b. Unresectable, recurrent, or metastatic Gastrointestinal Stromal Tumors (GIST); to Diagnosis of one of the following (a, b or c): a. Relapsed/refractory or metastatic high-grade intramedullary + surface osteosarcoma or Ewing sarcoma; b. Unresectable, recurrent, or metastatic Gastrointestinal Stromal Tumors (GIST); c. Uterine Neoplasms - Endometrial Carcinoma. 9. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.1: "Request is for one of the following (a or b):	9/29/2022	01/17/2023

a. Cabometyx® for advanced renal cell carcinoma; b. Cabometyx®, in combination with nivolumab for patients with advanced renal cell carcinoma, as a first-line treatment" was replaced with Request is for Cabometyx®. 2. Initial Approval Criteria, I.A.5.a, I.A.5.b: Updated dosing criteria from a. Dose does not exceed 80 mg per day; b. Cabometyx®, in combination with nivolumab 40 mg for Cabometyx® and 480 mg nivolumab every 4 weeks to a. Dose does not exceed 80 mg per day (monotherapy); b. Dose does not exceed 40 mg per day (combination with Opdivo). 3. Initial Approval Criteria, I.A.5.c: Updated to include new dosing criteria Dose does not exceed 80 mg per day and documentation that member is concurrently taking a strong CYP3A4 inducer. 4. Initial Approval Criteria, I.B.3.b: Updated trial and failure criteria from Who are radioactive iodine-refractory or ineligible to Disease or patient is refractory to radioactive iodine treatment or ineligible. 5. Initial Approval Criteria, I.C.2: Updated prescriber criteria from Prescribed by or in consultation with an oncologist to Prescribed by or in consultation with an oncologist, hepatologist or gastroenterologist. 6. Initial Approval Criteria, I.C.4: updated from "Failure of Nexavar® unless contraindicated or clinically significant adverse effects are experienced" to Request meets one of the following (a, b, c, d or e): a. Trial and failure of Nexavar® unless contraindicated or clinically significant adverse effects are experienced; b. Patient has metastatic disease; c. Patient has extensive liver tumor burden; d. Patient is inoperable by performance status or comorbidity (local disease or local disease with minimal extrahepatic disease only);		

e. Disease is unresectable. 7. Initial Approval Criteria, I.C.5: Updated to include new diagnostic criteria Confirmation of Child-Pugh class A status. 8. Initial Approval Criteria, I.C.7.a: Updated dosing criteria from Dose does not exceed 80 mg per day to Dose does not exceed 60 mg per day. 9. Initial Approval Criteria, I.C.7.b: Updated to include new dosing criteria Dose does not exceed 80 mg per day and documentation that member is concurrently taking a strong CYP3A4 inducer. 10. Initial Approval Criteria, I.D.4: Updated to include new prescribing criteria Prescribed as single-agent therapy for recurrent, advanced or metastatic disease. 11. References were reviewed and updated.		
Policy was reviewed.	10/19/2023	10/19/2023
Policy was reviewed: 1. Removed age restrictions. 2. Removed prescriber restrictions. 3. Removed dose restrictions. 4. Updated Continued therapy approval with auto-approval based on lookback functionality within the past 120 days. 5. Removed reauthorization requirement for positive response to therapy. 6. Updated approval duration verbiage. 7. References were reviewed and updated.	08/28/2024	09/13/2024