# Dosing and Administration Guide

CABOMETYX® (cabozantinib) tablets + OPDIVO® (nivolumab)

**ADVANCED RENAL CELL CARCINOMA (aRCC)**
CABOMETYX® (cabozantinib), in combination with nivolumab, is indicated for the first-line treatment of patients with advanced renal cell carcinoma (RCC).

CABOMETYX® (cabozantinib) tablets

**ADVANCED RENAL CELL CARCINOMA (aRCC)**
CABOMETYX is indicated for the treatment of patients with advanced RCC.

**HEPATOCELLULAR CARCINOMA (HCC)**
CABOMETYX is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

**DIFFERENTIATED THYROID CANCER (DTC)**
CABOMETYX is indicated for the treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer (DTC) that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible.

## IMPORTANT SAFETY INFORMATION

## WARNINGS AND PRECAUTIONS

**Hemorrhage:** Severe and fatal hemorrhages occurred with CABOMETYX. The incidence of Grade 3 to 5 hemorrhagic events was 5% in CABOMETYX patients in RCC, HCC, and DTC studies. Discontinue CABOMETYX for Grade 3 or 4 hemorrhage and prior to surgery as recommended. Do not administer CABOMETYX to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

**Please see additional Important Safety Information and full Prescribing Information.**

# CABOMETYX®: Once-daily oral starting dose as combination therapy or monotherapy[1]

## COMBINATION THERAPY

CABOMETYX® (cabozantinib) tablets + OPDIVO® (nivolumab)

**CABOMETYX 40-mg recommended starting dose—optimized for combination treatment with OPDIVO® in 1L aRCC**

**CABOMETYX**


**40 mg once daily**

+

**OPDIVO**

**240 mg every 2 weeks (30-minute IV infusion)** or **480 mg every 4 weeks (30-minute IV infusion)**

Treatment with CABOMETYX should be continued until disease progression or unacceptable toxicity.

Treatment with OPDIVO should be continued until disease progression or unacceptable toxicity for up to 2 years.

## MONOTHERAPY

CABOMETYX® (cabozantinib) tablets

**CABOMETYX 60-mg recommended starting dose for single-agent treatment in aRCC, HCC*, or DTC†,‡**

**CABOMETYX**


**60 mg once daily**

*For patients who have been previously treated with sorafenib.
†For 2L patients with DTC who have progressed following prior VEGFR-targeted therapy and who are RAI-R or ineligible.
‡For adult and pediatric patients with DTC ≥12 years of age with BSA ≥1.2 $m^2$. For pediatric patients with DTC ≥12 years of age with BSA <1.2 $m^2$, start at 40 mg once daily.

Treatment with CABOMETYX should be continued until disease progression or unacceptable toxicity.

Tablets shown are not actual size.

## Recommended dose of CABOMETYX for patients with hepatic impairment[1]

- **Child-Pugh B:** Reduce the starting dose of CABOMETYX 60 mg daily to 40 mg daily in patients with moderate hepatic impairment. For pediatric patients with DTC and BSA less than 1.2 $m^2$, reduce the starting dose from 40 mg daily to 20 mg daily
- **Child-Pugh C:** Avoid CABOMETYX in patients with severe hepatic impairment, since it has not been studied in this population

1L=first-line; 2L=second-line; BSA=body surface area; IV=intravenous; RAI-R=radioactive iodine-refractory; VEGFR=vascular endothelial growth factor receptor.

**Please see Important Safety Information and full Prescribing Information.**

CABOMETYX® (cabozantinib) tablets

# Recommended administration of CABOMETYX®[1]

**DO NOT ADMINISTER CABOMETYX WITH FOOD**

**Administer CABOMETYX at least 1 hour before or at least 2 hours after eating**

**Swallow CABOMETYX tablet whole**

**DO NOT CRUSH**

- Withhold CABOMETYX for at least 3 weeks prior to elective surgery, including dental surgery. Do not administer CABOMETYX for at least 2 weeks after major surgery and until adequate wound healing is observed
- Do not substitute CABOMETYX tablets with cabozantinib capsules
- Modify the CABOMETYX dose for patients taking drugs known to strongly induce or inhibit CYP3A4 and for patients with moderate hepatic impairment
- Avoid ingesting food (eg, grapefruit or grapefruit juice) or nutritional supplements (eg, St. John's wort) that are known to strongly induce or inhibit CYP3A4 during CABOMETYX treatment
- A high-fat meal increased $C_{max}$ and AUC values by 41% and 57%, respectively, relative to fasting conditions in healthy subjects administered a single oral dose of a cabozantinib capsule formulation
- When administering CABOMETYX in combination with OPDIVO® for the treatment of aRCC, refer to the OPDIVO Prescribing Information

For more information on drug interactions, see **Drug Interactions**.

**Advise patients of the following, if a dose is missed and the next scheduled dose is:**


**in less than 12 hours**

- Do not make up the missed dose
- Take the next dose at the usual time


**in 12 hours or more**

- Talk to their doctor or nurse

## Pharmacokinetics

- The predicted terminal half-life of CABOMETYX is approximately 99 hours[1]

AUC=area under the curve; $C_{max}$=maximum concentration; CYP3A4=cytochrome P450 3A4.

**Please see Important Safety Information and full Prescribing Information.**

CABOMETYX® (cabozantinib) tablets

# You may need to adjust the CABOMETYX® dose based on individual patient safety and tolerability[1]

FOR INTOLERABLE GRADE 2 ARs, GRADE 3-4 ARs, AND ONJ

**Withhold**
CABOMETYX

**Wait**
until resolution/improvement (ie, return to baseline or resolution to Grade 1 AR)

**Reduce**
the dose based on chart below

| | Recommended starting dose | First reduction | Second reduction |
|---|---|---|---|
| CABOMETYX® (cabozantinib) tablets + OPDIVO® (nivolumab) | 40 mg once daily | 20 mg once daily | 20 mg once every other day* |
| CABOMETYX® (cabozantinib) tablets | 60 mg once daily† | 40 mg once daily | 20 mg once daily* |
| CABOMETYX® (cabozantinib) tablets | For pediatric patients with DTC ≥12 years of age and BSA <1.2 m²: 40 mg once daily | 20 mg once daily | 20 mg once every other day* |

Tablets shown are not actual size.

*If previously receiving the lowest dose, resume at same dose. If not tolerated, discontinue CABOMETYX.
†For DTC, in adult and pediatric patients with BSA ≥1.2 m².

Permanently discontinue CABOMETYX for Grade 3 or 4 hemorrhage, development of a GI perforation or Grade 4 fistula, acute myocardial infarction or Grade 2 or higher cerebral infarction, Grade 3 or 4 arterial thromboembolic events or Grade 4 venous thromboembolic events, Grade 4 hypertension/hypertensive crisis or Grade 3 hypertension/hypertensive crisis that cannot be controlled, nephrotic syndrome, or reversible posterior leukoencephalopathy syndrome.

For patients being treated with CABOMETYX in combination with OPDIVO®:

- If ALT or AST >3 × ULN but ≤10 × ULN with concurrent total bilirubin <2 × ULN, both CABOMETYX and OPDIVO should be withheld until hepatic ARs recover to Grades 0 or 1. Corticosteroid therapy may be considered. Rechallenge with a single medicine or rechallenge with both medicines after recovery may be considered. If rechallenging with OPDIVO, refer to OPDIVO Prescribing Information
- If ALT or AST >10 × ULN or >3 × ULN with concurrent total bilirubin ≥2 × ULN, both CABOMETYX and OPDIVO should be permanently discontinued

## Dose Exchange Program

Provides **a free 15-tablet supply in the lower dose** to help patients who require a dose reduction.‡,§

‡Additional restrictions and eligibility rules apply.
§Patients are required to return unused product.

To learn more, **contact your sales representative,**

call EASE at **1-844-900-EASE(3273)**,

or visit **www.EASE.US**

ALT=alanine aminotransferase; AR=adverse reaction; AST=aspartate aminotransferase; GI=gastrointestinal; ONJ=osteonecrosis of the jaw; ULN=upper limit of normal.

**Please see Important Safety Information and full Prescribing Information.**

CABOMETYX® (cabozantinib) tablets

# Drug interactions[1]

## When strong CYP3A4 inhibitors cannot be avoided

**REDUCE DOSE BY 20 mg**

**Reduce the daily dose of CABOMETYX® if concomitant use with strong CYP3A4 inhibitors cannot be avoided.**

- For example, from 60 mg to 40 mg daily or from 40 mg to 20 mg daily or from 20 mg daily to 20 mg every other day in pediatric patients with DTC and BSA less than 1.2 $m^2$ and in patients with 1L aRCC when taken in combination with OPDIVO
- Resume the dose that was used prior to initiating the strong CYP3A4 inhibitor 2 to 3 days after discontinuation of the strong inhibitor

**Examples of strong CYP3A4 inhibitors[2,*]**

Boceprevir, clarithromycin, cobicistat, danoprevir/ritonavir, elvitegravir/ritonavir, grapefruit juice, idelalisib, indinavir/ritonavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, paritaprevir/ritonavir/(ombitasvir and/or dasabuvir), posaconazole, ritonavir, saquinavir/ritonavir, telaprevir, tipranavir/ritonavir, telithromycin, troleandomycin, and voriconazole

## When strong CYP3A4 inducers cannot be avoided

**INCREASE DOSE BY 20 mg**

**Increase the daily dose of CABOMETYX if concomitant use with strong CYP3A4 inducers cannot be avoided.**

- For example, from 60 mg to 80 mg daily, 40 mg to 60 mg daily, or 20 mg to 40 mg daily, as tolerated
  — Do not exceed a daily dose of 80 mg
- Resume the dose that was used prior to initiating the strong CYP3A4 inducer 2 to 3 days after discontinuation of the strong inducer

**Examples of strong CYP3A4 inducers[2,*]**

Apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, and St. John's wort

*Examples listed may not be comprehensive.

For more information about CYP3A4 inhibitors and inducers, click **here**.

**Please see Important Safety Information and full Prescribing Information.**

CABOMETYX® (cabozantinib) tablets

# Specific populations[1]

## Renal impairment

- No dosage adjustment is recommended in patients with mild or moderate renal impairment
- There is no experience with CABOMETYX® in patients with severe renal impairment

## Hepatic impairment

- Reduce the CABOMETYX dose in patients with moderate hepatic impairment (Child-Pugh B)
- Avoid CABOMETYX in patients with severe hepatic impairment (Child-Pugh C), since it has not been studied in this population

## Pediatrics

- The safety and effectiveness of CABOMETYX in pediatric patients less than 12 years of age have not been established

## Geriatrics

- No dose modification required

## Surgery

- Withhold CABOMETYX for at least 3 weeks prior to elective surgery, including dental surgery
- Do not administer CABOMETYX for at least 2 weeks after major surgery and until adequate wound healing is observed

## Lactation

- Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with CABOMETYX and for 4 months after the final dose

## Females and males of reproductive potential

- Verify the pregnancy status of females of reproductive potential prior to initiating CABOMETYX and advise them to use effective contraception during treatment and for 4 months after the final dose
- Based on findings in animals, CABOMETYX may impair fertility in females and males of reproductive potential

## Pregnancy

- Based on findings from animal studies and its mechanism of action, CABOMETYX can cause fetal harm when administered to a pregnant woman
- Advise pregnant women of the potential risk to a fetus

**Please see Important Safety Information and full Prescribing Information.**

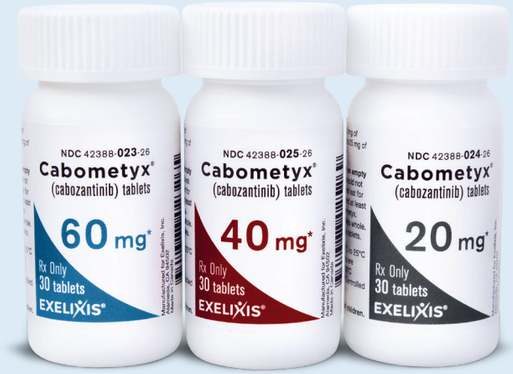
CABOMETYX® (cabozantinib) tablets

# CABOMETYX®[1]: Product Supply, Storage, and Handling

## CABOMETYX tablets are supplied as follows:

| Strength | NDC |
|---|---|
| 60 mg, 30 tablets | 42388-**023**-26 |
| 40 mg, 30 tablets | 42388-**025**-26 |
| 20 mg, 30 tablets | 42388-**024**-26 |

Tablets shown are not actual size.




## Storage and Handling Considerations

- Store CABOMETYX at room temperature: 20°C to 25°C (68°F to 77°F); excursions are permitted from 15°C to 30°C (59°F to 86°F)
- Keep CABOMETYX and all medications out of the reach of children
- CABOMETYX tablets are not scored

**Please see Important Safety Information and full Prescribing Information.**

CABOMETYX® (cabozantinib) tablets

EASE EXELIXIS ACCESS SERVICES®

# Access. Assistance. Along the journey.

Exelixis Access Services® (EASE) provides a variety of support to help your patients start treatment quickly. EASE can help meet the unique needs of your patients and practice at each step along the access journey.

## YOUR EASE CASE MANAGER

**EASE offers regionally dedicated Case Managers as a single point of contact.**

- Offers **prompt support** with payer coverage, financial assistance, and treatment coordination
- Can **provide the status** of your patients' access journey
- Provides **proactive follow-up**

## HELP PATIENTS START AND STAY ON CABOMETYX® (cabozantinib)

### 15-Day Free Trial Program

Provides a free trial to help new CABOMETYX patients start treatment quickly, regardless of insurance type.*,†

### Quick Start Program

Provides a limited supply of free drug to eligible patients who experience **a payer decision delay of 5 days or more**.*,†

### Co-pay Program

Eligible commercially insured patients pay **$0 per month, for a maximum benefit of $25,000 per year**.†

### Dose Exchange Program

Provides **a free 15-tablet supply in the lower dose** to help patients who require a dose reduction.†,‡

### Patient Assistance Program

Eligible patients who cannot afford their drug costs may receive CABOMETYX **free of charge**.†

## SUPPORT FOR COVERAGE DETERMINATION

At your request, EASE can provide support with:

- **Benefits investigations**
- **Prior authorization assistance**
- **Appeals support and follow-up**

covermymeds®

**Enroll your patients in EASE through CoverMyMeds. EASE will confirm your patient's eligibility for requested services.**

Contact your EASE Case Manager for questions or help.

## CONTACT EASE FOR MORE INFORMATION AND TO ENROLL

**CALL: 1-844-900-EASE** (1-844-900-3273)
Monday to Friday, 8:00 AM to 8:00 PM (ET)

**FAX: 1-844-901-EASE** (1-844-901-3273)

**VISIT: www.EASE.US**

Patient Education ›

*Limited to on-label indications. †Additional restrictions and eligibility rules apply. ‡Patients are required to return any unused product.

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**Please see Important Safety Information and full Prescribing Information.**

CABOMETYX® (cabozantinib) tablets

# BE CONNECTED
## with CABOMETYX® (cabozantinib)

- The BE CONNECTED program is designed to offer educational support to patients and caregivers. Your patients may sign up to learn more about what they may expect while on treatment with CABOMETYX
  - — Recognizing side effects and working with your health care team
  - — Lifestyle tips offering wellness support
  - — Where to find useful resources
  - — Information about organizations that may offer support

### Encourage patients and caregivers to sign up today

There are 2 ways your patients can sign up:

**1. ONLINE**

Go to
signup.CABOMETYX.com

OR

**2. MAIL**

Complete and return the **sign-up card included in the Patient Care Kit**

To request a Patient Care Kit, contact your local CABOMETYX sales representative

EASE

**Please see Important Safety Information and full Prescribing Information.**

CABOMETYX® (cabozantinib) tablets

# Indications and Important Safety Information

## INDICATIONS

CABOMETYX® (cabozantinib) is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

CABOMETYX, in combination with nivolumab, is indicated for the first-line treatment of patients with advanced RCC.

CABOMETYX is indicated for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

CABOMETYX is indicated for the treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer (DTC) that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible.

## IMPORTANT SAFETY INFORMATION

## WARNINGS AND PRECAUTIONS

**Hemorrhage:** Severe and fatal hemorrhages occurred with CABOMETYX. The incidence of Grade 3 to 5 hemorrhagic events was 5% in CABOMETYX patients in RCC, HCC, and DTC studies. Discontinue CABOMETYX for Grade 3 or 4 hemorrhage and prior to surgery as recommended. Do not administer CABOMETYX to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

**Perforations and Fistulas:** Fistulas, including fatal cases, occurred in 1% of CABOMETYX patients. Gastrointestinal (GI) perforations, including fatal cases, occurred in 1% of CABOMETYX patients. Monitor patients for signs and symptoms of fistulas and perforations, including abscess and sepsis. Discontinue CABOMETYX in patients who experience a Grade 4 fistula or a GI perforation.

**Thrombotic Events:** CABOMETYX increased the risk of thrombotic events. Venous thromboembolism occurred in 7% (including 4% pulmonary embolism) and arterial thromboembolism in 2% of CABOMETYX patients. Fatal thrombotic events occurred in CABOMETYX patients. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or serious arterial or venous thromboembolic events that require medical intervention.

**Hypertension and Hypertensive Crisis:** CABOMETYX can cause hypertension, including hypertensive crisis. Hypertension was reported in 37% (16% Grade 3 and <1% Grade 4) of CABOMETYX patients. Do not initiate CABOMETYX in patients with uncontrolled hypertension. Monitor blood pressure regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled with medical management; when controlled, resume at a reduced dose. Permanently discontinue CABOMETYX for severe hypertension that cannot be controlled with anti-hypertensive therapy or for hypertensive crisis.

**Diarrhea:** Diarrhea occurred in 62% of CABOMETYX patients. Grade 3 diarrhea occurred in 10% of CABOMETYX patients. Monitor and manage patients using antidiarrheals as indicated. Withhold CABOMETYX until improvement to ≤ Grade 1, resume at a reduced dose.

**Palmar-Plantar Erythrodysesthesia (PPE):** PPE occurred in 45% of CABOMETYX patients. Grade 3 PPE occurred in 13% of CABOMETYX patients. Withhold CABOMETYX until improvement to Grade 1 and resume at a reduced dose for intolerable Grade 2 PPE or Grade 3 PPE.

**Hepatotoxicity:** CABOMETYX in combination with nivolumab can cause hepatic toxicity with higher frequencies of Grades 3 and 4 ALT and AST elevations compared to CABOMETYX alone.

Monitor liver enzymes before initiation of and periodically throughout treatment. Consider more frequent monitoring of liver enzymes than when the drugs are administered as single agents. For elevated liver enzymes, interrupt CABOMETYX and nivolumab and consider administering corticosteroids.

With the combination of CABOMETYX and nivolumab, Grades 3 and 4 increased ALT or AST were seen in 11% of patients. ALT or AST >3 times ULN (Grade ≥2) was reported in 83 patients, of whom 23 (28%) received systemic corticosteroids; ALT or AST resolved to Grades 0-1 in 74 (89%). Among the 44 patients with Grade ≥2 increased ALT or AST who were rechallenged with either CABOMETYX (n=9) or nivolumab (n=11) as a single agent or with both (n=24), recurrence of Grade ≥2 increased ALT or AST was observed in 2 patients receiving CABOMETYX, 2 patients receiving nivolumab, and 7 patients receiving both CABOMETYX and nivolumab. Withhold and resume at a reduced dose based on severity.

**Adrenal Insufficiency:** CABOMETYX in combination with nivolumab can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold CABOMETYX and/or nivolumab and resume CABOMETYX at a reduced dose depending on severity.

Adrenal insufficiency occurred in 4.7% (15/320) of patients with RCC who received CABOMETYX with nivolumab, including Grade 3 (2.2%), and Grade 2 (1.9%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of CABOMETYX and nivolumab in 0.9% and withholding of CABOMETYX and nivolumab in 2.8% of patients with RCC.

Approximately 80% (12/15) of patients with adrenal insufficiency received hormone replacement therapy, including systemic corticosteroids. Adrenal insufficiency resolved in 27% (n=4) of the 15 patients. Of the 9 patients in whom CABOMETYX with nivolumab was withheld for adrenal insufficiency, 6 reinstated treatment after symptom improvement; of these, all (n=6) received hormone replacement therapy and 2 had recurrence of adrenal insufficiency.

**Proteinuria:** Proteinuria was observed in 8% of CABOMETYX patients. Monitor urine protein regularly during CABOMETYX treatment. For Grade 2 or 3 proteinuria, withhold CABOMETYX until improvement to ≤ Grade 1 proteinuria, resume CABOMETYX at a reduced dose. Discontinue CABOMETYX in patients who develop nephrotic syndrome.

ISI (cont'd) ›

Please see full Prescribing Information.

CABOMETYX® (cabozantinib) tablets

# Indications and Important Safety Information (cont'd)

## IMPORTANT SAFETY INFORMATION (cont'd)

## WARNINGS AND PRECAUTIONS

**Osteonecrosis of the Jaw (ONJ):** ONJ occurred in <1% of CABOMETYX patients. 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 the mouth or jaw after dental surgery. Perform an oral examination prior to CABOMETYX initiation and periodically during treatment. Advise patients regarding good oral hygiene practices. Withhold CABOMETYX for at least 3 weeks prior to scheduled dental surgery or invasive dental procedures, if possible. Withhold CABOMETYX for development of ONJ until complete resolution, resume at a reduced dose.

**Impaired Wound Healing:** Wound complications occurred with CABOMETYX. Withhold CABOMETYX for at least 3 weeks prior to elective surgery. Do not administer CABOMETYX for at least 2 weeks after major surgery and until adequate wound healing. The safety of resumption of CABOMETYX after resolution of wound healing complications has not been established.

**Reversible Posterior Leukoencephalopathy Syndrome (RPLS):** RPLS, a syndrome of subcortical vasogenic edema diagnosed by characteristic findings on MRI, can occur with CABOMETYX. Evaluate for RPLS in patients presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.

**Thyroid Dysfunction:** Thyroid dysfunction, primarily hypothyroidism, has been observed with CABOMETYX. Based on the safety population, thyroid dysfunction occurred in 19% of patients treated with CABOMETYX, including Grade 3 in 0.4% of patients.

Patients should be assessed for signs of thyroid dysfunction prior to the initiation of CABOMETYX and monitored for signs and symptoms of thyroid dysfunction during CABOMETYX treatment. Thyroid function testing and management of dysfunction should be performed as clinically indicated.

**Hypocalcemia:** CABOMETYX can cause hypocalcemia. Based on the safety population, hypocalcemia occurred in 13% of patients treated with CABOMETYX, including Grade 3 in 2% and Grade 4 in 1% of patients. Laboratory abnormality data were not collected in CABOSUN.

In COSMIC-311, hypocalcemia occurred in 36% of patients treated with CABOMETYX, including Grade 3 in 6% and Grade 4 in 3% of patients.

Monitor blood calcium levels and replace calcium as necessary during treatment. Withhold and resume at reduced dose upon recovery or permanently discontinue CABOMETYX depending on severity.

**Embryo-Fetal Toxicity:** CABOMETYX can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to initiating CABOMETYX and advise them to use effective contraception during treatment and for 4 months after the last dose.

## ADVERSE REACTIONS

The most common (≥20%) adverse reactions are:

CABOMETYX as a single agent: diarrhea, fatigue, PPE, decreased appetite, hypertension, nausea, vomiting, weight decreased, constipation.

CABOMETYX in combination with nivolumab: diarrhea, fatigue, hepatotoxicity, PPE, stomatitis, rash, hypertension, hypothyroidism, musculoskeletal pain, decreased appetite, nausea, dysgeusia, abdominal pain, cough, and upper respiratory tract infection.

## DRUG INTERACTIONS

**Strong CYP3A4 Inhibitors:** If coadministration with strong CYP3A4 inhibitors cannot be avoided, reduce the CABOMETYX dosage. Avoid grapefruit or grapefruit juice.

**Strong CYP3A4 Inducers:** If coadministration with strong CYP3A4 inducers cannot be avoided, increase the CABOMETYX dosage. Avoid St. John's wort.

## USE IN SPECIFIC POPULATIONS

**Lactation:** Advise women not to breastfeed during CABOMETYX treatment and for 4 months after the final dose.

**Hepatic Impairment:** In patients with moderate hepatic impairment, reduce the CABOMETYX dosage. Avoid CABOMETYX in patients with severe hepatic impairment.

**Please see accompanying full Prescribing Information by clicking here.**

**You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.**

ISI | NCCN/References

CABOMETYX® (cabozantinib) tablets

# RECOMMENDATIONS by the National Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

## Cabozantinib (CABOMETYX) + nivolumab (OPDIVO):

- National Comprehensive Cancer Network® (NCCN®) Category 1, Preferred designation across all risk groups in 1L clear cell aRCC[3,*,†]

## Cabozantinib (CABOMETYX):

- NCCN Category 1, Preferred recommendation in 2L clear cell aRCC[3,*,†]
- NCCN Category 2A, Preferred recommendation in 1L intermediate-/poor-risk clear cell aRCC[3,†,‡]
- NCCN Category 2A, Preferred recommendation in 1L non-clear cell aRCC[3,†,‡]

## Cabozantinib (CABOMETYX):

- NCCN Category 1 recommendation in 2L HCC for Child-Pugh A patients,[§] following disease progression on first-line systemic treatment[4,*]
- Data reflect use on or after sorafenib in patients who previously tolerated sorafenib at a dose of at least 400 mg/day[4,¶]

## Cabozantinib (CABOMETYX):

- NCCN Category 1 recommendation for patients with RAI-R papillary thyroid carcinoma that has progressed following VEGFR-targeted therapy[5,*,#]

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
*Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
†Preferred designation based on superior efficacy, safety, and evidence; and when appropriate, affordability.
‡Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
§With unresectable, liver-confined (inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease), or metastatic disease.
¶Our indication does not require prior sorafenib tolerance, and our study did not require prior sorafenib tolerance.
#If progression after lenvatinib and/or sorafenib.
IMDC=International Metastatic RCC Database Consortium.

## SELECT IMPORTANT SAFETY INFORMATION

The full Prescribing Information for CABOMETYX includes Warnings and Precautions for: hemorrhage, perforations and fistulas, thrombotic events, hypertension and hypertensive crisis, diarrhea, palmar-plantar erythrodysesthesia, hepatotoxicity, adrenal insufficiency, proteinuria, osteonecrosis of the jaw, impaired wound healing, reversible posterior leukoencephalopathy syndrome, thyroid dysfunction, hypocalcemia, and embryo-fetal toxicity.

**References: 1.** Cabometyx. Prescribing information. Exelixis, Inc, 2021. **2.** US Food and Drug Administration website. Drug development and drug interactions: table of substrates, inhibitors and inducers. Updated March 10, 2020. Accessed September 23, 2021. https://www.fda.gov/drugs/drug-interactions-labeling/drug-development-and-drug-interactions-table-substrates-inhibitors-and-inducers. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Kidney Cancer V.3.2022. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed November 8, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. **4.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatobiliary Cancers V.5.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed November 8, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. **5.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Thyroid Carcinoma V.3.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed November 8, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org.

**Please see Important Safety Information and full Prescribing Information.**







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Learn more at CABOMETYXhcp.com