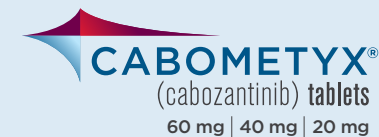


# Dosing and Administration Guide



## 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).



## 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)


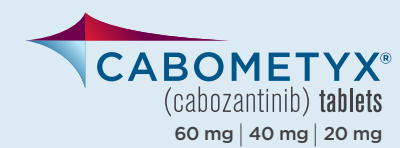



CABOMETYX is indicated for the treatment of adult and pediatric patients 12 years of age and older with locally advanced or metastatic differentiated thyroid cancer (DTC) that has progressed following prior VEGFR-targeted therapy and who are radioactive iodine-refractory or ineligible.

## 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.

Please see additional [Important Safety Information](#) and [full Prescribing Information](#).

# CABOMETYX®: Once-daily oral starting dose as combination therapy or monotherapy<sup>1</sup>

COMBINATION THERAPY	MONOTHERAPY
	
<b>CABOMETYX 40-mg recommended starting dose—optimized for combination treatment with OPDIVO® in 1L aRCC</b>	<b>CABOMETYX 60-mg recommended starting dose for single-agent treatment in aRCC, HCC*, or DTC<sup>†,‡</sup></b>
<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">  <p><b>CABOMETYX</b> <b>40 mg</b> once daily</p> </div> <div style="font-size: 2em; font-weight: bold;">+</div> <div style="text-align: center;">  <p><b>OPDIVO</b> <b>240 mg</b> or <b>480 mg</b> every 2 weeks (30-minute IV infusion) or every 4 weeks (30-minute IV infusion)</p> </div> </div>	<div style="text-align: center;">  <p><b>CABOMETYX</b> <b>60 mg</b> once daily</p> </div> <p style="font-size: 0.8em; margin-top: 10px;">*For patients who have been previously treated with sorafenib.  <sup>†</sup>For 2L patients with locally advanced or metastatic DTC who have progressed following prior VEGFR-targeted therapy and who are RAI-R or ineligible.  <sup>‡</sup>For adult and pediatric patients with DTC ≥12 years of age with BSA ≥1.2 m<sup>2</sup>. For pediatric patients with DTC ≥12 years of age with BSA &lt;1.2 m<sup>2</sup>, start at 40 mg once daily.</p>
<p>Treatment with CABOMETYX should be continued until disease progression or unacceptable toxicity.</p> <p>Treatment with OPDIVO should be continued until disease progression or unacceptable toxicity for up to 2 years.</p>	<p>Treatment with CABOMETYX should be continued until disease progression or unacceptable toxicity.</p>

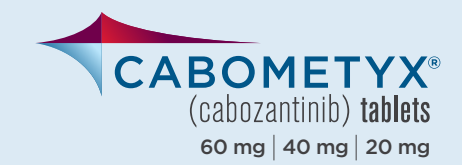
Tablets shown are not actual size.

### Dosing of CABOMETYX for patients with hepatic impairment<sup>1</sup>

- ▶ **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<sup>2</sup>, 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

<sup>1</sup>L=first-line; <sup>2</sup>L=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](#).



## Recommended administration of CABOMETYX<sup>®1</sup>



**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<sup>®</sup> 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<sup>1</sup>

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

Please see [Important Safety Information](#) and [full Prescribing Information](#).

# You can modify CABOMETRYX® dosing for safety and tolerability<sup>1</sup>













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



**Withhold**  
CABOMETRYX

**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
 (cabozantinib) tablets + (nivolumab)	 40 mg once daily	 20 mg once daily	 20 mg once every other day*
 (cabozantinib) tablets 60 mg   40 mg   20 mg	 60 mg once daily <sup>†</sup>	 40 mg once daily	 20 mg once daily*
 (cabozantinib) tablets 60 mg   40 mg   20 mg	<b>For pediatric patients with DTC ≥12 years of age and BSA &lt;1.2 m<sup>2</sup>:</b>  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 CABOMETRYX.

<sup>†</sup>For DTC, in adult and pediatric patients with BSA ≥1.2 m<sup>2</sup>.

Permanently discontinue CABOMETRYX 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 CABOMETRYX in combination with OPDIVO®:

- ▶ If ALT or AST >3 × ULN but ≤10 × ULN with concurrent total bilirubin <2 × ULN, both CABOMETRYX 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 CABOMETRYX and OPDIVO should be permanently discontinued


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](#).

## Drug interactions<sup>1</sup>

### When strong CYP3A4 inhibitors cannot be avoided

**REDUCE  
DOSE BY  
20 mg**



Reduce the daily dose of CABOMETYX<sup>®</sup> 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<sup>2</sup> 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<sup>2,\*</sup>

Ceritinib, clarithromycin, cobicistat, elvitegravir/ritonavir, idelalisib, indinavir/ritonavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, paritaprevir/ritonavir (ombitasvir and/or dasabuvir), posaconazole, ritonavir, saquinavir/ritonavir, telithromycin, tipranavir/ritonavir, 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<sup>2,\*</sup>

Apalutamide, carbamazepine, enzalutamide, ivosidenib, lumacaftor/ivacaftor, 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](#).

## Specific populations<sup>1</sup>



### Renal impairment

- ▶ No dosage adjustment is recommended in patients with mild or moderate renal impairment
- ▶ There is no experience with CABOMETYX<sup>®</sup> 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
- ▶ Monitor open growth plates in adolescent patients with DTC. Consider interrupting or discontinuing CABOMETYX if abnormalities occur



### 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

# CABOMETYX<sup>®1</sup>: Product Supply, Storage, and Handling

CABOMETYX tablets are supplied as follows:

Strength	
	60 mg, 30 tablets
	40 mg, 30 tablets
	20 mg, 30 tablets

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



### Dose Exchange Program

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



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



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



or visit [www.EASE.US](http://www.EASE.US)

\*Additional restrictions and eligibility rules apply.

\*\*Patients are required to return unused product.

Please see [Important Safety Information](#) and [full Prescribing Information](#).



## 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)



#### 30-Day Free Trial Program

Provides a free trial to help new CABOMETYX patients start treatment quickly, regardless of insurance type, with a 30-day additional supply available for patients with a payer decision delay of 5 days or more.\*,†



#### Co-Pay Program

Eligible, commercially insured patients **may pay as little as \$0 per month.** Annual and transaction limits apply.‡



#### 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**

\*Limited to on-label indications. †Additional restrictions and eligibility rules apply. ‡The Co-Pay Program is not available to patients receiving prescription reimbursement under any federal, state, or government-funded insurance programs or where prohibited by law. Additional [Terms and Conditions](#) apply. §Patients are required to return any unused product.

This description of the Exelixis Access Services® program is for informational purposes only. Exelixis® makes no representation or guarantee concerning reimbursement or coverage for any service or item. Information provided through the Exelixis Access Services program does not constitute medical or legal advice and is not intended to be a substitute for a consultation with a licensed healthcare provider, legal counsel, or applicable third-party payer(s). Exelixis reserves the right to modify the program at any time without notice.

CoverMyMeds is a registered trademark of CoverMyMeds, LLC.

Please see [Important Safety Information](#) and [full Prescribing Information](#).

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

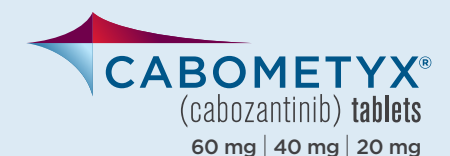
Contact your EASE Case Manager for questions or help.

**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](http://www.EASE.US)**





# BE CONNECTED




with CABOMETRYX® (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 CABOMETRYX

- ▶ **Recognizing side effects and working with the healthcare team**
- ▶ **Where to find useful resources**
- ▶ **Lifestyle tips offering wellness support**
- ▶ **Information about organizations that may offer support**

## ENCOURAGE PATIENTS AND CAREGIVERS TO SIGN UP TODAY

There are 2 ways your patients can sign up:

<p><b>1. ONLINE</b></p>  <p>Go to <a href="https://cabometryx.com/be-connected">cabometryx.com/be-connected</a></p> 	<p>OR</p>	<p><b>2. MAIL</b></p>  <p><b>Complete and return the sign-up card included in the Patient Care Kit</b></p> <p>To request a Patient Care Kit, contact your local CABOMETRYX sales representative*</p>
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\*Limit one Patient Care Kit per patient. US residents only. Additional restrictions and eligibility rules apply. Exelixis may at its sole option modify these terms and conditions without notice.

Please see [Important Safety Information](#) and [full Prescribing Information](#).

## Important Safety Information

### WARNINGS AND PRECAUTIONS

**Hemorrhage:** Severe and fatal hemorrhages occurred with CABOMETYX. Discontinue CABOMETYX for Grade 3-4 hemorrhage and before surgery. Do not administer to patients who have a recent history of hemorrhage, including hemoptysis, hematemesis, or melena.

**Perforations and Fistulas:** Fistulas, including fatal cases, and gastrointestinal (GI) perforations, including fatal cases, occurred in CABOMETYX patients. Monitor for signs and symptoms and discontinue in patients with Grade 4 fistulas or GI perforation.

**Thrombotic Events:** CABOMETYX increased the risk of thrombotic events. Fatal thrombotic events have occurred. Discontinue CABOMETYX in patients who develop an acute myocardial infarction or serious arterial or venous thromboembolic events.

**Hypertension and Hypertensive Crisis:** CABOMETYX can cause hypertension including hypertensive crisis. Monitor blood pressure regularly during CABOMETYX treatment. Withhold CABOMETYX for hypertension that is not adequately controlled; 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 may be severe. Monitor and manage patients using antidiarrheals as indicated. Withhold CABOMETYX until improvement to  $\leq$  Grade 1, resume at a reduced dose.

**Palmar-Plantar Erythrodysesthesia (PPE):** Withhold CABOMETYX until PPE resolves or decreases 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 withholding CABOMETYX and/or nivolumab, initiating corticosteroid therapy, and/or permanently discontinuing the combination for severe or life-threatening hepatotoxicity.

**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.

**Proteinuria:** Monitor urine protein regularly during CABOMETYX treatment. For Grade 2 or 3 proteinuria, withhold CABOMETYX until improvement to  $\leq$  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**<sup>®</sup>  
(cabozantinib) tablets  
60 mg | 40 mg | 20 mg

## Important Safety Information (cont'd)

### WARNINGS AND PRECAUTIONS

**Osteonecrosis of the Jaw (ONJ):** 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. Withhold CABOMETYX for development of ONJ until complete resolution, resume at a reduced dose.

**Impaired Wound Healing:** Withhold CABOMETYX for at least 3 weeks prior to elective surgery. Do not administer 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 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. Assess for signs of thyroid dysfunction prior to the initiation of CABOMETYX and monitor for signs and symptoms during treatment.

**Hypocalcemia:** 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 of the potential risk to fetus. Verify pregnancy status and advise use of effective contraception during treatment and for 4 months after last dose.

### ADVERSE REACTIONS

The most common ( $\geq 20\%$ ) adverse reactions are:

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

**Pediatric Use:** Monitor open growth plates in adolescent patients (12 years and older with DTC). Consider interrupting or discontinuing CABOMETYX if abnormalities occur.

**Please see accompanying full [Prescribing Information](#) for additional important safety information**

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

## Recommended Options by the National Comprehensive Cancer Network® (NCCN®)



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

- ▶ NCCN Category 1, preferred option across all risk groups in 1L clear cell aRCC<sup>a,\*</sup>
- ▶ NCCN Category 2A, preferred option in non-clear cell aRCC<sup>a,t,†</sup>

### Cabozantinib (CABOMETYX)

- ▶ NCCN Category 2A, preferred recommendation for in 1L intermediate-/poor-risk clear cell aRCC<sup>a,t,†</sup>
- ▶ NCCN Category 2A, other recommended subsequent therapy option regardless of prior IO therapy status for clear cell aRCC<sup>a,t,§</sup>



### Cabozantinib (CABOMETYX)

- ▶ NCCN Category 1 subsequent-line systemic treatment option for advanced progressive HCC<sup>b,\*</sup>



### Cabozantinib (CABOMETYX)

- ▶ NCCN Category 1 option for locally recurrent, advanced, and/or metastatic RAI-R papillary thyroid cancer that has progressed following VEGFR-targeted therapy<sup>c,\*</sup>

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.

\*NCCN Category 1: Based upon high-level evidence (≥1 randomized phase 3 trials or high-quality, robust meta-analyses), there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.

†Preferred designation based on superior efficacy, safety, and evidence and, when appropriate, affordability.

‡NCCN Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus (≥85% support of the Panel) that the intervention is appropriate.

§Other recommended interventions may be somewhat less efficacious, more toxic, or based on less mature data or significantly less affordable for similar outcomes.

¶If progression after lenvatinib and/or sorafenib.

NCCN=National Comprehensive Cancer Network® (NCCN®).

**References: a.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Kidney Cancer V.2.2025. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved.

Accessed September 11, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. **b.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hepatocellular Carcinoma V.2.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed September 11, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org.

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## ADVERSE REACTIONS

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

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

Please see [Important Safety Information](#) and [full Prescribing Information](#).

# Informing patients throughout their treatment journey about potential dose modifications helps set their expectations



▶ **Educate** patients on signs and symptoms of common adverse reactions (ARs)



▶ **Encourage** patients to report signs and symptoms early, so the healthcare team can quickly address them



▶ **Highlight** the importance of early reporting in effective management of ARs and appropriate dosing modifications for efficacy and tolerability



▶ **Advise** patients that their dose may need to be adjusted to help manage certain ARs



▶ **Assure** patients that dose reductions may help them stay on treatment, as appropriate; they should not consider them setbacks

**It is important for patients to understand that treatment of advanced cancer involves finding a balance between efficacy and managing ARs<sup>3</sup>**



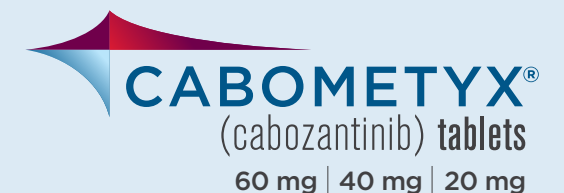
Go to [cabometryhcp.com/resources](https://cabometryhcp.com/resources) to access and download the **Treatment Management Guide**, which includes information on median time to first occurrence, management tips, dose adjustments, and grading for certain ARs



**References:** **1.** Cabometryx. Prescribing information. Exelixis, Inc. **2.** US Food and Drug Administration website. Drug development and drug interactions: table of substrates, inhibitors and inducers. Updated December 4, 2023. Accessed February 26, 2024. <https://www.fda.gov/drugs/drug-interactions-labeling/healthcare-professionals-fdas-examples-drugs-interact-cyp-enzymes-and-transporter-systems>. **3.** Cancer Treatment Centers of America website. Treatment for advanced cancer: what are my options? Updated March 5, 2021. Accessed June 15, 2023. <https://www.cancercenter.com/community/blog/2021/03/treatment-for-advanced-cancer>.

Please see [Important Safety Information](#) and [full Prescribing Information](#).

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Learn more at [CABOMETRYXhcp.com](https://CABOMETRYXhcp.com)