Dosing and Administration Guide

CABOMETYX® (cabozantinib) tablets + OPDIVO® (nivolumab) INJECTION FOR INTRAVENOUS USE 10 mg/mL

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

CABOMETYX® (cabozantinib) tablets
60 mg | 40 mg | 20 mg

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

NEUROENDOCRINE TUMORS
CABOMETYX is indicated for the treatment of adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated pancreatic neuroendocrine tumors (pNET).

CABOMETYX is indicated for the treatment of adult and pediatric patients 12 years of age and older with previously treated, unresectable, locally advanced or metastatic, well-differentiated extrapancreatic neuroendocrine tumors (epNET).

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

DIFFERENTIATED THYROID CANCER
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.

VEGFR, vascular endothelial growth factor receptor.

SELECT IMPORTANT SAFETY INFORMATION

The full Prescribing Information for CABOMETYX includes Warnings and Precautions for: hemorrhage, perforations and fistulas, thromboembolic events, hypertension and hypertensive crisis, cardiac failure, 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 Important Safety Information and full Prescribing Information.

CABOMETYX: Once-daily starting dose as combination therapy or monotherapy[1,2]

COMBINATION THERAPY

2 WAYS TO DELIVER CABOMETYX + NIVOLUMAB IN 1L aRCC

CABOMETYX 40 mg, once-daily starting dose—optimized for **combination treatment with OPDIVO in 1L aRCC**

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

An oral and intravenous option grounded in clinical evidence

CABOMETYX
40 mg
once daily

+

30 minutes

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

OR

CABOMETYX® (cabozantinib) tablets + OPDIVO Qvantig™ nivolumab + hyaluronidase-nhvy SUBCUTANEOUS INJECTION | 120 mg + 2,000 units / mL

An oral and 3- to 5-minute subcutaneous option that may streamline administration for patients[a]

CABOMETYX
40 mg
once daily

+

3-5 minutes

OPDIVO QVANTIG
600 mg nivolumab and 10,000 units hyaluronidase[a] every 2 weeks (3- to 5-minute injections)
or
1200 mg nivolumab and 20,000 units hyaluronidase[a] every 4 weeks (3- to 5-minute injections)

Treatment with CABOMETYX should be continued until disease progression or unacceptable toxicity.
Treatment with OPDIVO or OPDIVO QVANTIG should be continued until disease progression or unacceptable toxicity for up to 2 years.
[a]Individual results may vary.

MONOTHERAPY

CABOMETYX® (cabozantinib) tablets
60 mg | 40 mg | 20 mg

CABOMETYX
60 mg once daily

CABOMETYX 60-mg once-daily starting dose for single-agent treatment in aRCC, HCC[b], NET[c] or DTC[d]
(for adult and pediatric patients with NET and DTC ≥12 years of age with bodyweight ≥40 kg)

40 mg once daily

CABOMETYX 40-mg once-daily starting dose for single-agent treatment in NET[c] and DTC[d]
(for pediatric patients ≥12 years of age with bodyweight <40 kg)

[b]For patients with HCC who have been previously treated with sorafenib.
[c]For patients with previously treated, unresectable, locally advanced or metastatic, well-differentiated pNET or epNET.
[d]For patients with locally advanced or metastatic DTC that has progressed following prior VEGFR-targeted therapy and who are RAI-R or ineligible.

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

Dosing of CABOMETYX for patients with hepatic impairment

- **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 ≥12 years of age with bodyweight <40 kg, 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

CABOMETYX® (cabozantinib) tablets + OPDIVO® (nivolumab) OR OPDIVO Qvantig™ nivolumab + hyaluronidase-nhvy SUBCUTANEOUS INJECTION | 120 mg + 2,000 units / mL

Tablets shown are not actual size.

1L, first-line; aRCC, advanced renal cell carcinoma; IV, intravenous; NET, neuroendocrine tumor; RAI-R, radioactive iodine-refractory.

Please see Important Safety Information and full Prescribing Information.

Recommended administration of CABOMETYX[1]



ADMINISTER ON AN EMPTY STOMACH

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



SWALLOW CABOMETYX TABLET WHOLE

Do not crush, chew, or split CABOMETYX tablets

- Withhold CABOMETYX for at least 3 weeks prior to scheduled surgery, including dental surgery to reduce the risk of hemorrhage. Do not administer CABOMETYX for at least 2 weeks after major surgery and until adequate wound healing
- Do not substitute CABOMETYX tablets with cabozantinib capsules
- Modify the dosage for patients with moderate hepatic impairment and for patients taking drugs known to moderately or strongly induce CYP3A4 or strongly inhibit CYP3A4
- Avoid ingesting food (eg, grapefruit or grapefruit juice) or nutritional supplements (eg, St. John's wort) that are known to moderately or strongly induce CYP3A4 or strongly 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 or OPDIVO QVANTIG for the treatment of aRCC, refer to the OPDIVO or OPDIVO QVANTIG 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

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
60 mg | 40 mg | 20 mg

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

If ARs occur, consider supportive care and/or adjust the dose
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[a]	First reduction	Second reduction
CABOMETYX® (cabozantinib) tablets + OPDIVO® (nivolumab) OR OPDIVO Qvantig® nivolumab + hyaluronidase-nhvy SUBCUTANEOUS INJECTION 120 mg + 2,000 units / mL	40 mg once daily	20 mg once daily	20 mg once every other day[b]
CABOMETYX® (cabozantinib) tablets 60 mg | 40 mg | 20 mg	60 mg once daily[c]	40 mg once daily	20 mg once daily[b]
CABOMETYX® (cabozantinib) tablets 60 mg | 40 mg | 20 mg	For pediatric patients with NET and DTC ≥12 years of age and bodyweight <40 kg: 40 mg once daily	20 mg once daily	20 mg once every other day[b]

Tablets shown are not actual size.

[a]Until disease progression or unacceptable toxicity, administer as recommended.
[b]If previously receiving the lowest dose, resume at same dose. If not tolerated, discontinue CABOMETYX.
[c]For NET and DTC, in adult and pediatric patients ≥12 years of age and bodyweight ≥40 kg.

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 or OPDIVO QVANTIG:

- If ALT or AST >3 × ULN but ≤10 × ULN without concurrent total bilirubin ≥2 × ULN, both CABOMETYX and OPDIVO or OPDIVO QVANTIG 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 or OPDIVO QVANTIG, refer to OPDIVO or OPDIVO QVANTIG Prescribing Information
- If ALT or AST >10 × ULN or >3 × ULN with concurrent total bilirubin ≥2 × ULN, both CABOMETYX and OPDIVO or OPDIVO QVANTIG 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.[d,e]

[d]Additional restrictions and eligibility rules apply; [e]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**

CABOMETYX® (cabozantinib) tablets + OPDIVO® (nivolumab) OR OPDIVO Qvantig® nivolumab + hyaluronidase-nhvy SUBCUTANEOUS INJECTION 120 mg + 2,000 units / mL

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[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 ≥12 years of age with bodyweight <40 kg and in patients with 1L aRCC when taken in combination with OPDIVO or OPDIVO QVANTIG
- 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[3,a]

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 MODERATE OR STRONG CYP3A4 INDUCERS CANNOT BE AVOIDED

INCREASE DOSE BY **20 mg**

Increase the daily dose of CABOMETYX if concomitant use with moderate or 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 or moderate CYP3A4 inducer 2 to 3 days after discontinuation of the inducer

EXAMPLES OF STRONG CYP3A4 INDUCERS[3,a]

Apalutamide, carbamazepine, enzalutamide, ivosidenib, lumacaftor/ivacaftor, mitotane, phenytoin, rifampin, and St. John's wort

EXAMPLES OF MODERATE CYP3A4 INDUCERS[3,a]

Bosentan, phenobarbital, etravirine, and dabrafenib

[a]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
60 mg | 40 mg | 20 mg

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 <12 years of age have not been established
- Monitor open growth plates in adolescent patients. 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® (cabozantinib) tablets
60 mg | 40 mg | 20 mg

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

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

CABOMETYX®
(cabozantinib) tablets
60 mg | 40 mg | 20 mg

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**

Complete enrollment by visiting:
www.EASE.US

EASE will confirm your patient's eligibility for requested services.

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. For patients with a payer decision delay of 5 days or more, up to three additional 15-day supplies are available.[a,b]

Co-Pay Program

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

Dose Exchange Program

Provides **a free 15-tablet supply in the lower dose** to help patients who require a dose reduction.[b,d]

Patient Assistance Program

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

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

SUPPORT FOR COVERAGE DETERMINATION

At your request, EASE can provide support with:

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

[a]Limited to on-label indications.
[b]Additional restrictions and eligibility rules apply.
[c]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.
[d]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.

CABOMETYX® (cabozantinib) tablets
60 mg | 40 mg | 20 mg

Please see Important Safety Information and full Prescribing Information.

ENCOURAGE PATIENTS AND CAREGIVERS TO SIGN UP TODAY

BE CONNECTED with CABOMETYX® (cabozantinib)

A free support program with tools and resources to help educate patients and caregivers during treatment with CABOMETYX

Your patients may sign up to learn more about what they may expect while on treatment with CABOMETYX

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

> "The CABOMETYX BE CONNECTED program is especially useful to a number of our patients. The support they provide, the education... [It] really does benefit patients in a multitude of ways."
>
> — From a doctor who encourages his patients to sign up for BE CONNECTED

SIGNING UP IS EASY

ONLINE

Go to:
cabometyx.com/be-connected

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[a]

[a]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.

CABOMETYX® (cabozantinib) tablets
60 mg | 40 mg | 20 mg

Please see Important Safety Information and full Prescribing Information.

Important Safety Information

WARNINGS AND PRECAUTIONS

Hemorrhage: CABOMETYX can cause severe and fatal hemorrhages. The incidence of Grade 3-5 hemorrhagic events was 5% in CABOMETYX patients in RCC, HCC, and DTC studies. 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, each occurred in 1% of CABOMETYX patients. Monitor for signs and symptoms, and discontinue CABOMETYX in patients with Grade 4 fistulas or GI perforation.

Thromboembolic Events: CABOMETYX can cause arterial or venous thromboembolic events. Venous thromboembolism occurred in 7% (including 4% pulmonary embolism) and arterial thromboembolism in 2% of CABOMETYX patients. 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. Hypertension was reported in 37% (16% Grade 3 and <1% Grade 4) of CABOMETYX patients. In CABINET (n=195), hypertension occurred in 65% (26% Grade 3) 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; when controlled, resume at a reduced dose. Permanently discontinue CABOMETYX for severe hypertension that cannot be controlled with antihypertensive therapy or for hypertensive crisis.

Cardiac Failure: CABOMETYX can cause severe and fatal cardiac failure. Cardiac failure occurred in 0.5% of patients treated with CABOMETYX as a single agent, including fatal cardiac failure in 0.1% of patients. Consider baseline and periodic evaluations of left ventricular ejection fraction. Monitor for signs and symptoms of cardiovascular events. Withhold and resume at a reduced dose upon recovery or permanently discontinue depending on the severity.

Diarrhea: CABOMETYX can cause diarrhea and it occurred in 62% (10% Grade 3) of treated 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): CABOMETYX can cause PPE and it occurred in 45% of treated patients (13% Grade 3). 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 in RCC can cause hepatic toxicity with higher frequencies of Grades 3 and 4 ALT and AST elevations compared to CABOMETYX alone. With the combination of CABOMETYX and nivolumab, Grades 3 and 4 increased ALT or AST were seen in 11% of patients. Monitor liver enzymes before initiation of treatment and periodically. Consider more frequent monitoring as compared to when the drugs are administered as single agents. 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. 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. Withhold CABOMETYX and/or nivolumab and resume CABOMETYX at a reduced dose depending on severity.

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.

Osteonecrosis of the Jaw (ONJ): CABOMETYX can cause ONJ and it occurred in <1% of treated patients. 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.

ISI (cont'd) ▶

CABOMETYX® (cabozantinib) tablets
60 mg | 40 mg | 20 mg

Please see full Prescribing Information.

Important Safety Information (cont'd)

WARNINGS AND PRECAUTIONS

Impaired Wound Healing: CABOMETYX can cause 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): CABOMETYX can cause RPLS. Perform evaluation for RPLS and diagnose by characteristic finding on MRI any patient presenting with seizures, headache, visual disturbances, confusion, or altered mental function. Discontinue CABOMETYX in patients who develop RPLS.

Thyroid Dysfunction: CABOMETYX can cause thyroid dysfunction, primarily hypothyroidism, and it occurred in 19% of treated patients (0.4% Grade 3). Assess for signs of thyroid dysfunction prior to the initiation of CABOMETYX and monitor for signs and symptoms during treatment.

Hypocalcemia: CABOMETYX can cause hypocalcemia, with the highest incidence in DTC patients. Based on the safety population, hypocalcemia occurred in 13% of CABOMETYX patients (2% Grade 3 and 1% Grade 4).

Monitor blood calcium levels and replace calcium as necessary during treatment. Withhold and resume CABOMETYX at a 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 a fetus and advise females of reproductive potential to use effective contraception during treatment with CABOMETYX 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, 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 or Moderate CYP3A4 Inducers: If coadministration with strong or moderate 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: Physeal widening has been observed in children with open growth plates when treated with CABOMETYX. Physeal and longitudinal growth monitoring is recommended in children (12 years and older) with open growth plates. Consider interrupting or discontinuing CABOMETYX if abnormalities occur. The safety and effectiveness of CABOMETYX in pediatric patients less than 12 years of age have not been established.

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 or call 1-800-FDA-1088.

◀ ISI BACK

CABOMETYX®
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Please see full Prescribing Information.

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

- **Educate** patients on signs and symptoms of common 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 the right dose that balances efficacy, safety, and tolerability[4,5]

Go to cabometyxhcp.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. CABOMETYX®. Prescribing information. Exelixis, Inc. **2.** OPDIVO QVANTIG™ (nivolumab and hyaluronidase nvhy) injection, for subcutaneous use Prescribing Information. Bristol Myers Squibb Company. **3.** US Food and Drug Administration website. Drug development and drug interactions: table of substrates, inhibitors and inducers. Content current as of June 27, 2025. Accessed October 2, 2025. https://www.fda.gov/drugs/drug-interactions-labeling/healthcare-professionals-fdas-examples-drugs-interact-cyp-enzymes-and-transporter-systems. **4.** City of Hope website. Treatment for advanced cancer: what are my options? Updated March 5, 2021. Accessed October 2, 2025. https://www.cancercenter.com/community/blog/2021/03/treatment-for-advanced-cancer. **5.** U.S. Food and Drug Administration. Project Optimus. Updated December 6, 2024. Accessed October 2, 2025. https://www.fda.gov/about-fda/oncology-center-excellence/project-optimus.

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CABOMETYX® (cabozantinib) tablets
60 mg | 40 mg | 20 mg

Learn more at CABOMETYXhcp.com

Please see Important Safety Information and full Prescribing Information.