Cazar™ FCT

Cabozantinib-S-Malate INN

Jenphar Bangladesh | جنفار بنغلاديش

Composition:
Cazar™ FCT 60: Each film coated tablet contains Cabozantinib-S-Malate INN equivalent to Cabozantinib 60 mg.

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

Indications:
Cabozatinib is indicated for the treatment of patients with
• Advanced renal cell carcinoma (RCC).
• Advanced renal cell carcinoma, as a first-line treatment in combination with nivolumab.
• Patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.
• 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.

Dose & administration:
• Stop treatment with Cabozantinib tablet at least 3 weeks prior to scheduled surgery, including dental surgery.
• Do not substitute Cabozantinib tablets with Cabozantinib Capsules.
• Administer at least 1 hour before or at least 2 hours after eating.

Recommended Dose:
• 60 mg orally, once daily.
• 40 mg orally, once daily, in pediatric patients with BSA less than 1.2 m^2
• 40 mg orally, once daily, administered in combination with nivolumab 240 mg every 2 weeks or 480 mg every 4 weeks.

Recommended Dosage Reductions for Cabozantinib Tablet for Adverse Reactions:

Recommended Dosage	First Dosage Reduction To	Second Dosage Reduction To
60 mg daily in adult & pediatric patients with BSA greater than or equal to 1.2 m^2	40 mg daily	20 mg daily
40 mg daily in pediatric patients with BSA less than 1.2 m^2	20 mg daily	20 mg every other day
40 mg daily in combination with nivolumab	20 mg daily	20 mg every other day

Contra-indication:
Hypersensitivity to the active substance or to any of the excipients.

Warnings & precautions:
Hemorrhage: Do not administer Cabozantinib if recent history of hemorrhage.

Perforations and Fistulas: Monitor for symptoms. Discontinue Cabozantinib for Grade 4 fistula or perforation.

Thrombotic Events: Discontinue Cabozantinib for myocardial infarction or serious arterial or venous thromboembolic events.

Hypertension and hypertensive crisis: Monitor blood pressure regularly. Discontinue Cabozantinib for hypertensive crisis or severe hypertension that cannot be controlled with anti-hypertensive therapy.

Diarrhea: May be severe. Interrupt Cabozantinib immediately until diarrhea resolves or decreases to Grade 1. Recommend standard antidiarrheal treatments.

Palmar-Plantar Erythrodysesthesia (PPE): Interrupt Cabozantinib until PPE resolves or decreases to Grade1.

Hepatotoxicity: When used in combination with nivolumab, higher frequencies of Grade 3 and 4 ALT and AST elevation may occur than with Cabozantinib alone. Monitor liver enzymes and permanently discontinuing the combination for severe or life threatening hepatotoxicity.

Adrenal Insufficiency: When used in combination with nivolumab, primary or secondary adrenal insufficiency may occur. Withhold Cabozantinib and nivolumab depending on severity.

Proteinuria: Monitor urine protein. Discontinue for nephrotic syndrome.

Osteonecrosis of the Jaw (ONJ): Withhold Cabozantinib for at least 3 weeks prior to invasive dental procedure and for development of ONJ.

Impaired Wound Healing: Withhold Cabozantinib for at least 3 weeks before elective surgery.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): Discontinue Cabozantinib.

Thyroid Dysfunction: Monitor thyroid function before and during treatment with Cabozantinib.

Hypocalcemia: Withhold Cabozantinib and resume at reduced dose upon recovery or permanently discontinue Cabozantinib depending on severity.

Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.

Adverse reactions:
The most common (20%) adverse reactions are:
• As a single agent: diarrhea, fatigue, PPE, decreased appetite, hypertension, nausea, vomiting, weight decreased, constipation.
• 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.

Use in Special Population:
Pregnancy: Pregnancy Category "D". Based on its mechanism of action, Cabozantinib can cause fatal harm when administered to a pregnant woman.
Lactation: There is no information regarding the presence of Cabozantinib or its metabolites in human milk or their effects on the breastfed infant or milk production. Because of the potential for serious adverse reactions in a breastfed infant from Cabozantinib, advise a lactating woman not to breastfeed during treatment with Cabozantinib and for 4 months after the final dose.

Females and Males of Reproductive Potential: Advise females of reproductive potential to use effective contraception during treatment with Cabozantinib and for 4 months after the final dose. Cabozantinib may impair fertility in females and males of reproductive potential.

Pediatric Use: The safety and effectiveness of Cabozantinib for the treatment of differentiated thyroid cancer (DTC) have been established in pediatric patients aged 12 years and older.

Geriatric Use: No overall differences in safety or effectiveness were observed between these patients and younger patients.

Hepatic Impairment: Increased exposure to Cabozantinib has been observed in patients with moderate (Child-Pugh B) hepatic impairment. Reduce the Cabozantinib dose in patients with moderate hepatic impairment. Avoid Cabozantinib in patients with severe hepatic impairment (Child-Pugh C), since it has not been studied in this population.

Renal Impairment: No dose adjustment is recommended for patients with mild or moderate renal impairment. There is no experience with Cabozantinib in patients with severe renal impairment.

Drug interactions:
Strong CYP3A4 Inhibitors: Co-administration of a Cabozantinib tablet formulation with a strong CYP3A4 inhibitor increased the exposure of Cabozantinib. Avoid co-administration of Cabozantinib with strong CYP3A4 inhibitors. Reduce the dosage of Cabozantinib if co-administration with strong CYP3A4 inhibitors cannot be avoided. Avoid grapefruit or grapefruit juice which may also increase exposure of Cabozantinib.

Strong CYP3A Inducers: Co-administration of a Cabozantinib tablet formulation with a strong CYP3A4 inducer decreased the exposure of Cabozantinib, which may reduce efficacy. Avoid co-administration of Cabozantinib with strong CYP3A4 inducers. Increase the dosage of Cabozantinib if co-administration with strong CYP3A4 inducers cannot be avoided.

Overdose:
One case of overdosage was reported following administration of another formulation of Cabozantinib; a patient inadvertently took twice the intended dose for 9 days. The patient suffered Grade 3 memory impairment, Grade 3 mental status changes, Grade 3 cognitive disturbance, Grade 2 weight loss and Grade 1 increase in BUN. The extent of recovery was not documented.

Storage:
Store in a cool and dry place below 30° C, protect from light. Keep out of the reach of children.

Packing:
Cazar™ FCT 60: Each box contains 7 tablets and one packet silica gel in a sealed HDPE container.

Manufactured by:
Jenphar Bangladesh Ltd.
Sreepur, Gazipur, Bangladesh.

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