Cabometyx

(cabozantinib)

New Product Slideshow

MPR

Introduction

- **Brand name:** Cabometyx
- **Generic name:** Cabozantinib
- **Pharmacological class:** Kinase inhibitor
- **Strength and Formulation:** 20mg, 40mg, 60mg; tablets
- **Manufacturer:** Exelixis
- **How supplied:** Bottle—30
- **Legal Classification:** Rx

CABOMETYX


NDC 42388-024-26
Cabometyx™
(cabozantinib) tablets
20 mg*
Rx Only
30 tablets
EXELIXIS®
NDC 42388-025-26
Cabometyx™
(cabozantinib) tablets
40 mg*
Rx Only
30 tablets
EXELIXIS®
NDC 42388-028-26
Cabometyx™
(cabozantinib) tablets
60 mg*
Rx Only
30 tablets
EXELIXIS®

Indications

- Treatment of **advanced renal cell carcinoma (RCC)** in patients who have received prior anti-angiogenic therapy

Dosage & Administration

- Swallow whole. 60mg daily
- Do not eat at least 2 hours before or 1 hour after dose
- Continue until disease progression or unacceptable toxicity
- Stop treatment at least 28 days prior to scheduled surgery (including dental)
- Withhold for Grade 4 adverse reactions, Grade 3 or intolerable Grade 2 adverse reactions that are unmanageable

Dosage & Administration

- Upon improvement to Grade 1 or to baseline, reduce dose as follows:
  - Previously on 60mg daily, resume at 40mg daily
  - Previously on 40mg daily, resume at 20mg daily
  - Previously on 20mg daily, resume at 20mg if tolerated, otherwise discontinue

Dosage & Administration

- Concomitant **strong CYP3A4 inhibitor:** reduce daily dose by 20mg; resume dose used prior to starting inhibitor 2–3 days after discontinuation of inhibitor
- Concomitant **strong CYP3A4 inducer:** increase daily dose by 20mg; resume dose used prior to starting inducer 2–3 days after discontinuation of inducer
- Max daily dose: 80mg
- Mild or moderate hepatic impairment: initially 40mg once daily

Considerations for Special Populations

- **Pregnancy:** Can cause fetal harm
- **Nursing mothers:** Not recommended (during and for 4 months after therapy completion)
- **Pediatric:** Not studied
- **Geriatric:** No differences in safety or efficacy
- **Hepatic impairment:** Severe impairment: not recommended

Warnings/Precautions

- **Do not substitute** with cabozantinib capsules
- **Permanently discontinue** if: unmanageable GI perforation/ fistula, severe hemorrhage, serious arterial thromboembolic events (eg, MI, cerebral infarction), hypertensive crisis or severe hypertension despite optimal medical management, nephrotic syndrome, reversible posterior leukoencephalopathy syndrome

Warnings/Precautions

- Recent history or risk of severe hemorrhage: do not administer
- **Monitor** for GI perforations/ fistulas
- **Monitor** BP regularly; withhold for hypertension inadequately controlled with medical management; resume at reduced dose when resolved

Warnings/Precautions

- **Withhold therapy** if intolerable Grade 2 diarrhea, unmanageable Grade 3/4 diarrhea, or Grade 2/3 palmar-plantar erythrodysesthesia syndrome (PPES) develops until improvement to Grade 1; resume at reduced dose
- Females of reproductive potential should use **effective contraception** during and for 4 months after therapy completion

Interactions

- **Avoid** concomitant strong CYP3A4 inhibitors: boceprevir, clarithromycin, conivaptan, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, posaconazole, ritonavir, saquinavir, telithromycin, voriconazole, grapefruit or grapefruit juice
- **Avoid** concomitant strong CYP3A4 inducers: rifampin, phenytoin, carbamazepine, phenobarbital, rifabutin, rifapentine, St. John's Wort
- If unavoidable, see **Adult dose**

Adverse Reactions

- Diarrhea
- Fatigue
- Nausea
- Decreased appetite
- PPES
- Hypertension
- Vomiting
- Weight decreased
- Constipation
- Lab abnormalities

Mechanism of Action

- *In vitro* biochemical and/or cellular assays have shown that cabozantinib inhibits the tyrosine kinase activity of MET, VEGFR-1, -2 and -3, AXL, RET, ROS1, TYRO3, MER, KIT, TRKB, FLT-3, and TIE-2
- These receptor tyrosine kinases are involved in both normal cellular function and pathologic processes (eg, oncogenesis, metastasis, tumor angiogenesis, drug resistance, and maintenance of the tumor microenvironment)

Pharmacokinetics

- **Distribution:** Highly protein bound in human plasma (≥99.7%)
- **Metabolism:** CYP3A4 substrate *in vitro*
- **Elimination:** Fecal (major)

Clinical Trials

- A randomized (1:1), open-label, multicenter trial (Study 1) of Cabometyx vs. everolimus was conducted in patients with advanced RCC who had received ≥1 prior antiangiogenic therapy
- Patients had to have a Karnofsky Performance Score ≥70%
- Patients were randomized to Cabometyx 60mg daily (n=330) or everolimus 10mg daily (n=328)

Clinical Trials

- The main efficacy outcome measure was progression-free survival (PFS) assessed by a blinded independent committee among the first 375 patients randomized
- Tumor assessments were conducted every 8 weeks for the first 12 months, then every 12 weeks thereafter
- Statistically significant improvements in PFS, overall survival (OS), and objective response rate (ORR) were seen with Cabometyx vs. everolimus

Clinical Trials

- Patients in the Cabometyx arm had a **longer median PFS** than the everolimus arm: 7.4 months vs. 3.8 months (HR 0.58, 95% CI: 0.45, 0.74; *P*<0.0001)
- Patients in the Cabometyx arm had a **longer median OS** than the everolimus arm: 21.4 months vs. 16.5 months (HR 0.66, 95% CI: 0.53, 0.83; *P*=0.0003)
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

http://www.empr.com/cabometyx/drug/34557/