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Tasigna

(Nilotinib) - Novartis

BOXED WARNING

Prolongs QT interval. Prior to administration and periodically, monitor for hypokalemia or hypomagnesemia and correct deficiencies. Obtain ECGs to monitor QTc at baseline, 7 days after initiation, and periodically thereafter, and following any dose adjustments. Sudden deaths reported. Do not administer to patients with hypokalemia, hypomagnesemia, or long QT syndrome. Avoid with drugs known to prolong the QT interval and strong CYP3A4 inhibitors. Avoid food 2 hrs before and 1 hr after taking the dose.

THERAPEUTIC CLASS

Kinase inhibitor

DEA CLASS

RX

INDICATIONS

Treatment of adults with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP). Treatment of CP and accelerated phase (AP) Ph+ CML in adults resistant or intolerant to prior therapy that included imatinib.

ADULT DOSAGE

Adults: Newly Diagnosed Ph+ CML-CP: 300mg bid. Resistant or Intolerant Ph+ CML-CP and CML-AP: 400mg bid. Take at approximately 12-hr intervals and on an empty stomach. Refer to PI for dose adjustments or modifications based on hematologic and nonhematologic toxicities, QT prolongation, hepatic impairment, and drug interactions.

HOW SUPPLIED

Cap: 150mg, 200mg

CONTRAINDICATIONS

Hypokalemia, hypomagnesemia, long QT syndrome.

WARNINGS/PRECAUTIONS

Myelosuppression (eg, neutropenia, thrombocytopenia, anemia) may occur; perform CBC every 2 weeks for the first 2 months, then monthly thereafter, or as clinically indicated. Cardiovascular (CV) events, including arterial vascular occlusive events, reported; evaluate CV status and monitor and actively manage CV risk factors during therapy. May increase serum lipase; increased risk in patients with history of pancreatitis. Interrupt dosing and consider appropriate diagnostics to exclude pancreatitis if lipase elevations are accompanied by abdominal symptoms. May result in hepatotoxicity as measured by elevations in bilirubin, AST/ALT, and alkaline phosphatase. Monitor serum lipase levels and LFTs monthly or as clinically indicated. May cause hypophosphatemia, hypokalemia, hyperkalemia, hypocalcemia, and hyponatremia; correct electrolyte abnormalities prior to initiation and monitor periodically. Exposure is increased in patients with impaired hepatic function. Tumor lysis syndrome cases reported; maintain adequate hydration and correct uric acid levels prior to initiation. Reduced exposure in patients with total gastrectomy; perform more frequent monitoring and consider dose increase or alternative therapy. Contains lactose; not recommended with galactose intolerance, severe lactase deficiency with a severe degree of intolerance to lactose-containing products, or glucose-galactose malabsorption. May cause fetal harm. Caution with relevant cardiac disorders.

ADVERSE REACTIONS

QT prolongation, rash, pruritus, headache, nasopharyngitis, fatigue, N/V, alopecia, myalgia, arthralgia, abdominal pain, constipation, upper respiratory tract infection, diarrhea, cough.

DRUG INTERACTIONS

See Boxed Warning. Avoid with strong CYP3A4 inducers (eg, dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, phenobarbital), grapefruit products and other foods that inhibit CYP3A4, St. John's wort, and antiarrhythmic drugs. May increase concentrations of drugs eliminated by CYP3A4 (eg, midazolam), CYP2C8, CYP2C9, CYP2D6, and UGT1A1 enzymes and may decrease concentrations of drugs eliminated by CYP2B6, CYP2C8, and CYP2C9 enzymes; caution with substrates for these enzymes with narrow therapeutic index. May increase concentrations of P-glycoprotein (P-gp) substrates. Increased concentrations with P-gp inhibitors. Decreased solubility and reduced bioavailability with drugs that inhibit gastric acid secretion to elevate the gastric pH; concomitant use with PPIs is not recommended. Administer an H_2 blocker approximately 10 hrs before and 2 hrs after the dose of nilotinib. Administer an antacid approximately 2 hrs before or 2 hrs after the dose of nilotinib.

PREGNANCY

Category D, not for use in nursing.

MECHANISM OF ACTION

Kinase inhibitor; binds to and stabilizes the inactive conformation of the kinase domain of ABL protein.

PHARMACOKINETICS

Absorption: T_{max}=3 hrs. **Distribution:** Plasma protein binding (98%). **Metabolism:** Via oxidation and hydroxylation. **Elimination:** Feces (93%, 69% unchanged); $T_{1/2}$=17 hrs.

ASSESSMENT

Assess for electrolyte abnormalities, history of pancreatitis, long QT syndrome, cardiac disorders, total gastrectomy, hepatic impairment, galactose intolerance, lactase deficiency, glucose-galactose malabsorption, pregnancy/nursing status, and possible drug interactions. Obtain baseline ECG, uric acid levels, and chemistry panels, including lipid profile and glucose.

MONITORING

Monitor for myelosuppression; perform CBC every 2 weeks for the first 2 months of therapy, then monthly thereafter or as clinically indicated. Periodically check chemistry panels, including electrolytes, lipid profile, and glucose. Monitor for signs/symptoms of QT prolongation; obtain ECG 7 days after initiation, periodically thereafter, and after any dose adjustments. Monitor for tumor lysis syndrome, hydration status, and CV status/risk factors. Monitor serum lipase levels and LFTs monthly or as clinically indicated.

PATIENT COUNSELING

Instruct to take ud. Advise to seek immediate medical attention with any symptoms suggestive of a CV event. Instruct not to consume grapefruit products at any time during treatment. Instruct to inform physician of other medicines being taken, including OTC drugs or herbal supplements (eg, St. John's wort). Advise women of childbearing potential to use highly effective contraceptives while on therapy. Instruct not to d/c or change dose without consulting physician.

ADMINISTRATION/STORAGE

Administration: Oral route. Take on an empty stomach; avoid food for at least 2 hrs before and 1 hr after taking the dose. Swallow caps whole, with water. May disperse contents of each cap in 1 tsp of applesauce if unable to swallow caps; take immediately (within 15 min) and do not store for future use. **Storage:** 25°C (77°F); excursions permitted between 15-30°C (59-86°F).