**dabrafenib** (dabra-fen-ib)

**Table**

**Classification**
Antineoplastics

**Pharmacologic**
Kinase inhibitors

**Pregnancy Category**
D

### Indications

Treatment of metastatic/unresectable melanoma in patients with the BRAF V600E mutation.

### Action

Inhibits kinase, an enzyme that promotes cell proliferation. Therapeutic Effects: Decreased spread/progression of melanoma.

### Pharmacokinetics

- **Absorption:** Well absorbed (95%) following oral administration.
- **Distribution:** Unknown.
- **Protein Binding:** 99.7%.
- **Metabolism and Excretion:** Mostly metabolized by CYP 2C8 and CYP3A4 enzyme systems. Two metabolites (hydroxy-dabrafenib and desmethyl-1–dabrafenib) have antineoplastic activity. Excreted as metabolites in feces (72%) and urine (23%).
- **Half-life:** Dabrafenib—8 hr; hydroxy-dabrafenib—10 hr; desmethyl-1–dabrafenib—21–22 hr.

### Contraindications/Precautions

**Contraindicated in:**
- OB: Pregnancy (may cause fetal harm);
- Lactation: Breastfeeding should be avoided;
- Concurrent use of CYP 3A4/CYP2C8 inhibitors or inducers (may significantly alter levels and effects).

**Use Cautiously in:**
- BRAF Wild-type melanoma (may increase proliferation);
- History of Glucose-6–Phosphate Dehydrogenase Deficiency (may cause hemolytic anemia);
- Moderate to severe hepatic impairment (blood levels may be ↑);
- Moderate to severe renal impairment.

### Adverse Reactions/Side Effects

- **CNS:** headache, fatigue.
- **EENT:** iritis, uveitis.
- **Resp:** cough, nasal congestion.
- **GI:** constipation, pancreatitis.
- **Derm:** alopecia, hyperkeratosis, palmar-plantar erythrodysesthesia, papilloma, cutaneous squamous cell carcinoma.
- **F and E:** hypophosphatemia, hyponatremia.
- **MS:** arthralgia, back pain, myalgia.
- **Misc:** fever including serious febrile reactions, rash, neutropenia.

### Interactions

- **Drug-Drug:** Concurrent use of strong inhibitors of CYP3A4 or CYP2C8, including ketoconazole, nefazodone, clarithromycin, gemfibrozil blood levels and the risk of toxicity and should be avoided. Careful monitoring for toxicity is required. Concurrent use of strong inducers of CYP3A4 or CYP2C8 including carbamazepine, phenobarbital, phenytoin, and rifampin blood levels and effectiveness. Careful monitoring for decreased results is required. Drugs that ↓ gastric pH including antacids, H₂-receptor antagonists and proton pump inhibitors may ↓ blood levels and effectiveness. May ↓ effectiveness of other drugs that are substrates of CYP3A4, CYP2D6, CYP2C9, CYP2C19 or CYP2B6 including midazolam.

### Route/Dosage

**PO (Adults):** 150 mg twice daily, continued until disease progression or unacceptable toxicity. Dose modifications recommended for various levels of related toxicities.

### Nursing Implications

- **Assessment:** Perform skin examinations prior to starting therapy and every 2 months during and for 6 months after completion of therapy.
- **Monitor temperature.** If fever is 101.3°F to 104°F withhold until fever resolves, then resume at same dose. If fever is >104°F or complicated by rigors, dehydration, or renal failure, then resume at a reduced dose. For first reduction, decrease dose to 100 mg twice daily.
For second dose reduction, decrease dose to 75 mg twice daily. For third dose reduction, decrease dose to 50 mg twice daily (if unable to tolerate 50 mg ite daily, discontinue dabrafenib).

- Monitor for signs and symptoms of uveitis (change in vision, photophobia, eye pain). May require named and mydriatic ophthalmic drops.
- Lab Test Considerations: May cause hyperglycemia requiring increase in dose of or initiation of insulin or oral hypoglycemic agents. Monitor serum glucose levels in patients with pre-existing diabetes or hyperglycemia.
- May cause hyperphosphatemia, alkaline phosphatase, and hypophosphatemia.
- Monitor for hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

**Potential Nursing Diagnoses**

- Impaired skin integrity (Indications)

**Implementation**

- Evidence of BRAF V600E mutation status must be confirmed prior to starting therapy with dabrafenib.
- PO: Administer twice daily about 12 hrs apart. Administer on an empty stomach at least 1 hr before or 2 hrs after a meal. Swallow capsules whole, do not open, crush, break, or chew.

**Patient/Family Teaching**

- Instruct patient to take dabrafenib as directed at least 1 hr before or 2 hrs after meals. Take missed doses as soon as remembered unless within 6 hrs of next dose, then skip missed dose and take regular scheduled dose.
- Instruct patient that dabrafenib increases risk of developing new cutaneous malignancies. Notify health care professional immediately if new lesions (wet, skin sore or reddish bump that bleeds or does not heal or changes in size or color of existing lesion) occur.
- Instruct patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and to consult with health care professional before taking other medications.
- Instruct patient to use a highly effective form of contraception during and for at least 4 months after treatment. Use a non-hormonal form of contraception; dabrafenib may decrease effectiveness of hormonal contraceptives. Advise patient to notify health care professional if pregnancy is suspected and to avoid breast feeding. Advise male patients to use condoms on oral, and family planning prior to beginning therapy; may cause spermatogenesis.

**Evaluation/Desired Outcomes**

- Decrease in progression of malignant melanoma.

**Why was this drug prescribed for your patient?**