vemurafenib (vem-u-raf-e-nib)

Classification
Therapeutic: antineoplastics
Pharmacologic: kinase inhibitors

Pregnancy Category D

Indications
Treatment of unresectable or metastatic melanoma with BRAF V600E mutation.

Action
Blocks mutated forms of the enzyme kinase. Inhibits proliferation that occurs in conjunction with activated BRAF proteins.

Therapeutic Effects:
Decreased spread of melanoma.

Pharmacokinetics
Absorption: Some absorption follows oral administration, bioavailability is not known.
Distribution: Unknown.
Protein Binding: 99%.
Metabolism and Excretion: Mostly metabolized by the liver (mostly by the CYP3A4 enzyme system), 1% eliminated in urine.
Half-life: 57 hr (range 30–120 hr).

TIME/ACTION PROFILE (blood levels)
ROUTE ONSET PEAK DURATION
PO unk 3 hr 12 hr

Contraindications/Precautions
Contraindicated in:
OB: Should not be used during pregnancy, may cause fetal harm;
Lactation: Breast feeding should be avoided;
Use Cautiously in:
Pre-existing severe hepatic or renal impairment;
Geri: Increased risk of cutaneous squamous cell carcinoma, nausea, decreased appetite, peripheral edema, keratoacanthoma and atrial fibrillation; Concurrent use of strong inhibitors of the CYP3A4 enzyme system or drugs that are substrates of CYP3A4, CYP1A2 or CYP2D6 enzyme systems; monitoring of effects and necessary dose adjustments may be necessary;
OB: Patients with child-bearing potential:

Adverse Reactions/Side Effects
CNS: Fatigue, weakness, headache.
EENT: Iritis, retinal vein occlusion, uveitis.
Resp: Cough.
CV: QTC prolongation, peripheral edema.
GI: Hepatotoxicity, pruritus, rash (q1d in females), photosensitivity (q1d in females), skin papilloma, keratoacanthoma (q1d in males).
GU:
MS: Arthralgia (q1d in females), myalgia, back pain.
Misc: Hypersensitivity reactions including anaphylaxis, fever.

Interactions
Drug-Drug: Concurrent use with agents with narrow therapeutic indices that are metabolized by the CYP3A4 enzyme systems is not recommended. Concurrent use with agents with narrow therapeutic indices that are metabolized by the CYP1A2 enzyme systems is contraindicated. Concurrent use of substrates of the CYP3A4 enzyme system is not recommended. May increase levels and effects of substrates of the CYP3A4 enzyme system. May decrease levels and effectiveness of erlotinib, gefitinib, imatinib, nelfinavir, ondansetron, rituximab, vemurafenib. May increase risk of bleeding with warfarin. May increase risk of hepatotoxicity with ipilimumab.

Route/Dosage
PO (Adults): 960 mg twice daily. Treatment should continue until unacceptable toxicity or disease progression occurs.

NURSING IMPLICATIONS
Assessment
● Perform dermatologic evaluation prior to initiation and every 2 mo during therapy. Excision of suspicious lesions, smaller dermato logic evaluation, and treatment with standard care. Continue monitoring for 6 mo following discontinuation of therapy.
● Monitor ECG 15 days after initiation of therapy, monthly during first 3 mo, every 3 mo thereafter, and more often if clinically indicated.
● Monitor for hypersensitivity reactions (rash, pruritus, hypotension).

Nursing Considerations
● Generic Implication: CYP3A4 inhibitors and inducers indicate most frequent. Identical discontinued.
Monitor for signs and symptoms of uveitis periodically during therapy. May require treatment with systemic corticosteroids and mydriatic ophthalmic drops.

Assess patient for rash (mild to moderate rash usually occurs in the 2nd wk of therapy and resolves within 1–2 wk of continued therapy). If rash is severe (extensive eruptions or maculopapular rash with muco-cutaneous or angioedema) or accompanied by systemic symptoms (fever, headache, lethargy, malaise, and nausea), treatment should be discontinued immediately.

Lab Test Considerations: Monitor serum potassium, magnesium, and calcium before starting therapy and after dose modifications.

Monitor AST, ALT, alkaline phosphatase, and bilirubin before starting therapy, monthly during therapy, and as clinically indicated. May require dose reduction, treatment interruption or discontinuation.

Potential Nursing Diagnoses

Impaired skin integrity (Indications)

Implementation

PO: Administer (four 240 mg tablets) twice daily, without regard to food. Take first dose in the morning with second dose about 12 hrs later. Swallow tablets whole, do not crush or chew.

Adverse reactions or QTc prolongation may occur requiring dose modification. If Grade 1 or 2 (tolerable) occur, maintain dose at 480 mg twice daily. If Grade 3 (Intolerable) or Grade 4 (3rd appearance) occurs, discontinue therapy until Grade 0–1. Resume dosing at 360 mg twice daily. If 2nd appearance, discontinue permanently. If Grade 4, 1st appearance occurs, discontinue permanently if 3rd appearance. If Grade 4, 2nd appearance occurs, discontinue permanently if 3rd appearance. Doses below 480 mg twice daily are not recommended.

Patient/Family Teaching

Instruct patient to take vemurafenib as directed. Take missed doses as soon as remembered up to 4 hrs before next dose; do not double dose.

Instruct patient that assessment of BRAF mutation is required for selection of patients.

Instruct patient to stop taking vemurafenib and notify health care professional immediately if signs and symptoms of allergic reaction (rash or redness all over body; feeling faint, difficulty breathing or swallowing; throat tightness or hoarseness; fast heartbeat; swelling of face, lips, or tongue) or severe skin reactions (blisters on skin, blisters or sores in mouth; peeling of skin, fever, redness or swelling of face, hands, or soles of feet) occur.

Advise patient to wear broad spectrum UVA/UVB sunscreen, lip balm (SPF ≥30) and protective clothing, and to avoid sun exposure to prevent photosensitivity reactions. Severe photosensitivity reactions may require dose modifications.

Advise patient to avoid health care professional signs and symptoms of liver dysfunction (yellow skin or whites of eyes; feeling tired; nausea or vomiting; loss of appetite; pain on right side of stomach; eye problems (eye pain, swelling, or redness; blurry vision; vision changes)) occur.

Instruct patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and consult health care professional before taking any new medications.

Instruct patient that regular assessments of skin and assessments for signs and symptoms of other malignancies must be done during and for up to 6 mo after therapy. Advise patient to notify health care professional immediately if any changes in skin occur.

Advise women of childbearing potential and men to use appropriate contraceptive measures during and for at least 2 mo after discontinuation of vemurafenib, and to avoid breast feeding.

Evaluation/Desired Outcomes

Decreased spread of melanoma.

Why was this drug prescribed for your patient?