Ixabepilone (icks-a-hep-i-lone)

Synonyms

Therapeutic: antineoplastics
Pharmacologic: epothilone B analogues

Pregnancy Category D

Indications

Combination use with capecitabine for the treatment of metastatic or locally advanced breast cancer currently resistant to a taxane and anthracycline or resistant to a taxane and cannot tolerate further anthracycline. May also be used as monotherapy for breast cancers that are not responding to anthracyclines, taxanes, or capecitabine.

Action

Binds to β-tubulin subunits on microtubules, the action blocks cells in mitosis, leading to cell death. Also has antiangiogenic activity.

Therapeutic Effects:

Decreased spread of breast cancer.

Pharmacokinetics

Absorption:

IV administration results in complete bioavailability.

Distribution:

Unknown.

Metabolism and Excretion:

Extensively metabolized by the liver, primarily by the CYP3A4 enzyme system. Metabolites are not active and are excreted mainly by the kidneys.

Half-life:

52 hr.

TIME/ACTION PROFILE (blood levels)

ROUTE ONSET PEAK DURATION

IV unknown end of infusion unknown

Contraindications/Precautions

Contraindicated in:

Previous hypersensitivity to any medications containing cremophor EL or similar derivatives (polyoxyethylated castor oil); Neutrophils < 1500 cells/mm³ or platelets < 100,000 cells/mm³; Severe hepatic impairment; Use with capecitabine is contraindicated for hepatic impairment (AST or ALT 2.5 × upper limits of normal or bilirubin > upper limit of normal) due to risk of toxicity and death associated with neutropenia.

OB, Lactation:

Pregnancy or lactation.

Use Cautiously in:

Toxicity; dose adjustments may be required for neuropathy/arthralgia/myalgia/fatigue, mucositis, thrombocytopenia, moderate hepatic impairment or palmar-plantar erythrodysesthesia. Dilute contains methylated alcohol; consider possible CNS effects. Doses high or history of neutropenia (risk of severe neutropenia). History of cardiac disease (may risk of myocardial ischemia or ventricular dysfunction). OB: Patients with childbearing potential; PAL: Discontinue.

Adverse Reactions/Side Effects

CNS:

Fatigue, weakness, dizziness, headache, insomnia.

EENT:

Lacrimation.

CV:

Chest pain, edema, left ventricular dysfunction, myocardial ischemia.

Resp:

Dyspnea.

GI:

Abdominal pain, anorexia, constipation, diarrhea, mucositis, nausea, stomatitis, vomiting, altered taste.

Derm:

Alopecia, hyperpigmentation, nail disorder, palmar-plantar erythrodysesthesia (combination therapy with capecitabine), exfoliation, pruritus, rash, hot flushes.

Hemat:

MYELOSUPPRESSION.

MS:

Arthralgia, musculoskeletal pain, myalgia.

Neuro:

Peripheral neuropathy.

Misc:

Hypersensitivity reactions.

Interactions

Drug-Drug: Strong CYP3A4 inhibitors including ketoconazole, itraconazole, voriconazole, clarithromycin, telithromycin, atazanavir, delavirdine, saquinavir, ritonavir, nefazodone. Blood levels and the risk of serious toxicity, concurrent use should be avoided. If concurrent use is required, dose reduction of ixabepilone is recommended. Inducers of the CYP3A4 enzyme system including dexamethasone, phenytoin, carbamazepine, phenobarbital, rifampin, ritonavir, or rifabutin may ↑ levels and effectiveness, avoid if possible.

Drug-Natural Products: St. John’s wort may ↑ blood levels and should be avoided.

Drug-Food: Grapefruit juice may ↑ blood levels and toxicity; avoid concurrent use.

Route/Dosage

IV (Adults): 40 mg/m² every 3 wk; not to exceed dose greater than that calculated for 2.2 m² (88 mg/dose).

Contraindicated in patient with creatinine clearances ≤ 50 mL/min.

Dosage Adjustments: Neutropenia/platelet dysfunction; indicate most frequent.

Discontinued.
2 Hepatic Impairment

IV (Adults): Moderate Impairment — 20 mg/m² every 3 wk; not to exceed 30 mg/m²

NURSING IMPLICATIONS

Assessment

● Monitor for hypersensitivity reaction (hives, rash, dyspnea, bronchospasm). If severe reactions occur, stop infusion and provide aggressive supportive treatment with epinephrine and corticosteroids. In subsequent cycles, add corticosteroids to the repletion regimen.

● Monitor for myelosuppression frequently during therapy. Assess for signs of neutropenia (neutrophil count is at least 1500 cells/mm³ with bleeding) and target cell count is low.

● Monitor for infection during neutropenia. Assess for signs of infection (temperature >101°F, rash, lymphadenopathy, malaise, and abnormal liver function test results). Possible treatment: if neutropenia is Grade 3 (severe) lasting for 7 days or is disabling; discontinue ixabepilone. If neutropenic fever or if platelet count is <50,000/mm³ with bleeding, stop infusion and provide aggressive supportive treatment with epinephrine and corticosteroids. In subsequent cycles, add corticosteroids to the repletion regimen.

● Monitor for peripheral neuropathy (sensory changes, motor function, reflexes, deep tendon reflexes, autonomic function), may occur early during treatment within the first 3 cycles. Patients experiencing new or worsening symptoms may require a reduction or delay in dose of ixabepilone. If neuropathy is Grade 2 (moderate) lasting for >7 days or Grade 3 (severe) lasting for >7 days decrease dose by 20%. If neuropathy is Grade 3 (severe) lasting >7 days or is disabling discontinue treatment.

● Lab Test Considerations: Monitor CBC and platelets frequently during therapy. If neutrophil count is <5000/mm³ for >7 days or patient has febrile neutropenia or platelet count <25,000/mm³ or platelets are <50,000/mm³ with bleeding decrease the dose by 20%. Begin new treatment cycle only if neutrophil count is at least 5500 cells/mm³ and neutropenia has improved to Grade 1 (mild) or resolved. May also cause leukopenia and anemia.

● Monitor for hyperbilirubinemia (increased AST and ALT >5 x ULN and bilirubin >1.5 x ULN—known.

Implementation

● Premedicate patient with an H₁ and an H₂ antagonist approximately 1 hr before ixabepilone infusion. Patients who experienced a hypersensitivity reaction in a previous ixabepilone cycle should also be premedicated with corticosteroids and extension of the repletion time should be considered.

● To minimize risk of dermal exposure, wear impervious gloves when handling ixabepilone vials regardless of setting (packaging and inspection, transport within a facility, dose preparation and administration).

IV Administration

pH: 6.0–7.5

Intermittent Infusion: Remove Ixempra kit (containing ixabepilone vial and diluent vial) from refrigerator and allow to stand at room temperature for 30 min prior to dilution. Ixempra kit should be stored in refrigerator. When vials are first removed from refrigerator, a white precipitate may be observed in the diluent vial. Precipitate will dissolve to form a clear solution upon standing. If diluent appears cloudy, shake vial prior to administration. Dilute 15 mg/ml with 8 ml and 45 mg/ml with 23.5 ml of diluent. Gently swirl and invert vial until powder is completely dissolved. Diluent: Prior to administration, dilute concentrated solution further with only 10% dextrose in D5W (D5W). Dilute as soon as possible after constitution, but may be stored at room temperature and room light for up to 1 hr. For most doses use 250 ml bag of LR (0.9% NaCl) pH adjusted 6.0–7.0 with sodium bicarbonate) or Plasma-lyte A injection (pH 7.4).

Concentration: If final concentration is not between 0.2 mg/mL and 0.6 mg/mL, adjust pH with sodium bicarbonate or Plasma-lyte A injection (pH 7.4).

Solution contains alcohol and may cause drowsiness or dizziness. Caution patient to avoid driving and other activities requiring alertness until response to medication is known.

Patient/Family Teaching

● Advise patient to avoid grapefruit juice during therapy; may lead to increased levels of ixabepilone and side effects.

● Solution contains alcohol and may cause dizziness or dizziness. Caution patient to avoid driving and other activities requiring alertness until response to medication is known.

CONTINUED
ixabepilone

- Instruct patient to notify health care professional promptly if fever >100.5°F; chills; cough; hoarseness; sore throat; signs of infection; lower back or side pain; burning, painful or difficult urination; bleeding gums; bruising; petechiae; blood in stools, urine, or emesis; increased fatigue; dyspnea; or orthostatic hypotension occurs. Cautions patient to avoid crowds and persons with known infections. Instruct patients to use a soft toothbrush and electric razor and to avoid falls. Caution patient not to drink alcoholic beverages or take medication containing aspirin or NSAIDs that may precipitate bleeding.
- Instruct patient to notify health care professional promptly if signs and symptoms of hyperosmolarity (drowsiness, irritability, seizures, nausea, vomiting, ringing in ears, headache, blurred vision, or fever) occur.
- Advise patient to notify health care professional if signs and symptoms of hypersensitivity (hives, urticaria, pruritus, rash, flushing, swelling, dyspnea, chest tightness), peripheral neuropathy (numbness and tingling in hands and feet), or cardiac adverse reactions (chest pain, difficulty breathing, palpitations, unusual weight gain or edema) occur.
- Advise patient that signs and symptoms of infection may increase risk of bleeding and to delay antibiotic therapy until infection is controlled.
- Advise patient not to receive any vaccinations without advice of health care professional.
- Discuss the possibility of hair loss with patient. Explore methods of coping. Re-growth usually occurs 2–3 mo after discontinuation of therapy.

Evaluation/Desired Outcomes

- Decreased progression of breast cancer.

Why was this drug prescribed for your patient?