Lopinavir/ritonavir

(loe-pi-nav-ir/ri-to-na-veer)

Safati

Classification

Therapeutic: antiretrovirals

Pharmacologic: protease inhibitors, metabolic inhibitors

Pregnancy Category C

Indications

HIV infection (with other antiretrovirals).

Action

Lopinavir: Inhibits HIV viral protease.

Ritonavir: Although ritonavir has antiretroviral activity of its own (inhibits the action of HIV protease and prevents the cleavage of viral polyproteins), it is combined with lopinavir to inhibit the metabolism of lopinavir thus increasing its plasma levels.

Therapeutic Effects:

Increased CD4 cell counts and decreased viral load with subsequent slowed progression of HIV infection and its sequelae.

Pharmacokinetics

Absorption:

Well absorbed following oral administration; food enhances absorption.

Distribution:

Ritonavir—poor CNS penetration.

Protein Binding:

Lopinavir—98–99% bound to plasma proteins.

Metabolism and Excretion:

Lopinavir—completely metabolized in the liver by cytochrome P450 3A (CYP450 3A); ritonavir is a potent inhibitor of this enzyme.

Ritonavir—highly metabolized by the liver (by CYP450 3A and CYP2D6 enzymes); one metabolite has antiretroviral activity; 3.5% excreted unchanged in urine.

Half-life:

Lopinavir—5–6 hr

Ritonavir—3–5 hr.

TIME/ACTION PROFILE (blood levels)

ROUTE ONSET PEAK DURATION

Lopinavir PO rapid 4 hr 12 hr

Ritonavir PO rapid 4 hr* 12 hr

*Non-fasting

Contraindications/Precautions

Contraindicated in:

Hypersensitivity (including toxic epidermal necrolysis, Stevens-Johnson syndrome, or erythema multiforme); Concurrent use of dihydroergotamine, ergotamine, ergonovine, lovastatin, methylprednisolone, milrinone (PPI), phenytoin, sildenafil (Revatio), allopurinol, statins, and ranitidine (may result in serious and/or life-threatening events). Concurrent use with 9 (beta)- receptor/alpha receptor-blockers (may result in hypotension, bradycardia, and chest pain).

Use Cautionally in:

Hypersensitivity or intolerance to alcohol or castor oil (present in liquid); Congenital long QT syndrome; Concurrent use of QF (urea) neutralizing drops, or histamine H2 blockers; Risk of QT interval prolongation.

Pedi:

Preterm infants (should be avoided until 14 days after their due date) or full-term infants 14 days old (risk of toxicity from alcohol and propylene glycol in oral solution).

Adverse Reactions/Side Effects

CNS:

Headache, insomnia, weakness.

CV:

Torsades de Pointes, prolongation of the PR interval, heart block, QT interval prolongation.

GI:

Hepatotoxicity, pancreatitis, diarrhea (in children), abdominal pain, nausea, taste aversion (in children), vomiting (in children).

Derm:

Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, rash.

Misc:

Immune reconstitution syndrome.

Interactions

Drug-Drug:

Avoid concomitant use of ergot derivatives (dihydroergotamine, ergotamine, ergonovine, methylergonovine) pimozide, sildenafil (Revatio), alfuzosin, simvastatin, and lovastatin; use lowest possible dose of statin; do not exceed rosuvastatin dose of 10 mg/day. Concurrent use with efavirenz or nevirapine prolongs lopinavir/ritonavir levels and effectiveness; dose recommended.

Delavirdine decreases lopinavir levels.

Drug-Food:

No impact on pharmacokinetics.

Drug-Lifestyle:

No impact on pharmacokinetics.

Monitoring:

CBC, liver function tests.

Lopinavir/ritonavir:

Platelet count, fasting lipid profile, hepatitis panel, HCV tests, HIV RNA level.

Ritonavir:

Platelet count, fasting lipid profile, hepatitis panel, HCV tests, HIV RNA level.

Patient Preparation:

Inform patient that lopinavir/ritonavir is used for long-term management of HIV infection. Will not cure HIV. Must take as directed and as prescribed. Failure to comply will lead to virologic and clinical failure.

Laboratory Considerations:

Avoid concomitant use of ergot derivatives (dihydroergotamine, ergotamine, ergonovine, methylergonovine) pimozide, sildenafil (Revatio) alfuzosin, simvastatin, and lovastatin; use lowest possible dose of statin; do not exceed rosuvastatin dose of 10 mg/day. Concurrent use with efavirenz or nevirapine prolongs lopinavir/ritonavir levels and effectiveness; dose recommended.
The text on the page discusses drug interactions and dosing information for lopinavir/ritonavir. It mentions monitoring blood levels of these drugs and provides guidance on how to adjust dosages when co-administered with other medications. The page also includes information on the use of lopinavir/ritonavir in various patient populations and highlights the importance of blood level monitoring to prevent toxicity and ensure efficacy.
CONTINUED

lopinavir/ritonavir

PO (Children ages 6 mo and ≥5 kg): 10/3.25 mg/kg lopinavir/ritonavir content twice daily.

NURSING IMPLICATIONS

Assessment

- Assess for change in severity of HIV symptoms and for symptoms of opportunistic infections during therapy.
- Assess patient for signs of pancreatitis (nausea, vomiting, abdominal pain, increased serum lipase or amylase) periodically during therapy. May require discontinuation of therapy.
- 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 (cotton mouth or maculopapular rash with moist desquamation or impetigo) or accompanied by severe symptoms (serum sickness-like reaction, Stevens-Johnson syndrome, toxic epidermal necrolysis), therapy must be discontinued immediately.
- Lab Test Considerations: Monitor renal and liver function tests regularly during therapy.
- Monitor triglyceride and cholesterol levels prior to initiating therapy and periodically during therapy.
- May cause hyperglycemia.
- Monitor liver function before and during therapy, especially in patients with underlying hepatic disease, including hepatitis B and hepatitis C, or marked transaminase elevations. May cause serum AST, ALT, GGT, and total bilirubin concentrations.

Potential Nursing Diagnoses

Risk for infection (Indications)
Noncompliance (Patient/Family Teaching)

Implementation

- Do not confuse Kaletra (lopinavir/ritonavir) with Keppra (levetiracetam).
- Patients taking didanosine with Kaletra solution should take didanosine 1 hr before or 2 hr after taking lopinavir/ritonavir.
- PO: Tablets may be administered with or without food. Swallow whole, do not break, crush, or chew.
- Oral solution must be taken with food. Oral solution is light yellow to orange. Solution is stable if refrigerated until expiration date on label or 2 mo at room temperature.
- Oral solution should be avoided in premature babies until 14 days after birth due to altered serum osmolality, serum creatinine, and other signs of toxicity.

Patient/Family Teaching

- Emphasize the importance of taking lopinavir/ritonavir as directed, at evenly spaced times throughout day. Do not take more than prescribed amount, and do not stop taking this or other antiretrovirals without consulting health care professional. Take missed doses as soon as remembered; do not double doses. Advise patient to read the Patient Information prior to taking this medication and with each Rx refill in case of changes.
- Instruct patient to notify health care professional immediately if rash, symptoms of lactic acidosis (tiredness or weakness, unusual muscle pain, trouble breathing, stomach pain with nausea and vomiting, cold especially in arms or legs, dizziness, fast or irregular heartbeat) or if signs of hepatotoxicity (yellow skin or whites of eyes, dark urine, light-colored stools, lack of appetite for several days or longer, nausea, abdominal pain) occur.
Inform patient that lopinavir/ritonavir may cause hyperglycemia. Advise patient to notify health care professional if increased thirst or hunger, unexplained weight loss, or increased urination occurs.

Caution patients taking sildenafil, vardenafil, or tadalafil of increased risk of associated side effects (hypotension, visual changes, sustained erection). Notify health care professional promptly if these occur.

Inform patient that redistributions and accumulations of body fat may occur causing central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, breast enlargement, and altered appearance. The cause and long-term effects are not known.

Advise patients taking oral contraceptives to use a nonhormonal method of birth control during lopinavir/ritonavir therapy. Instruct patient to notify health care professional if pregnancy is planned or suspected if breastfeeding an infant. Breast feeding should be avoided during therapy. Encourage pregnant women exposed to lopinavir/ritonavir to enroll in the Antiretroviral Pregnancy Registry by calling 1–800–258–4263 to monitor maternal/fetal outcomes.

Emphasize the importance of regular follow-up exams and blood counts to determine progress and monitor for side effects.

Evaluation/Desired Outcomes
- Delayed progression of AIDS and decreased opportunistic infections in patients with HIV.
- Decrease viral load and improvement in CD4 cell counts.

Why was this drug prescribed for your patient?