

Prior Authorization DRUG Guidelines

KALETRA (Lopinavir and ritonavir)

Effective Date: 1/28/14

Date Developed: 1/28/14 by Catherine Sanders, MD

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Kaletra is an Antiretroviral Agent, Protease Inhibitor, coformulation of lopinavir and ritonavir, used in the treatment of HIV-1 infections. The lopinavir component binds to the site of HIV-1 protease activity and inhibits the cleavage of viral Gag-Pol polyprotein precursors into individual functional proteins required for infectious HIV. This results in the formation of immature, noninfectious viral particles. The ritonavir component inhibits the CYP3A metabolism of lopinavir, allowing increased plasma levels of lopinavir.

Pre-Authorization Criteria:

Kaletra is to be used for treatment of HIV infection in combination with other antiretroviral agents for therapy-naïve and therapy-experienced patients.

VCHCP requires that Kaletra be prescribed by an Immunology Clinic physician with current American Academy of HIV Medicine (AAHIVM) certification or a physician boarded in Infectious Disease.

Medication Guide:

An FDA-approved patient medication guide, which is available with the product information and at <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM143461.pdf>, must be dispensed with this medication.

Dosing: Adult:

HIV infection (as a component of combination therapy): Oral:

Twice-daily dosing:

Therapy-naïve or therapy-experienced: Lopinavir 400 mg/ritonavir 100 mg twice daily.

Therapy-naïve or therapy-experienced patients receiving efavirenz, fosamprenavir, nelfinavir, nevirapine: Lopinavir 500 mg/ritonavir 125 mg twice daily or lopinavir 533 mg/ritonavir 133 mg solution twice daily

Once-daily dosing: Therapy-naïve or experienced patients with <3 lopinavir resistance-associated substitutions: Lopinavir 800 mg/ritonavir 200 mg once daily

Dosage adjustment for combination therapy with efavirenz, fosamprenavir, nelfinavir, or nevirapine:
Oral:

Twice-daily dosing: Therapy-naïve and therapy-experienced patients:

Solution: Lopinavir 533 mg/ritonavir 133 mg (6.5 mL) twice daily

Tablet: Lopinavir 500 mg/ritonavir 125 mg twice daily

Once-daily dosing: Not recommended in those receiving efavirenz, fosamprenavir, nevirapine, nelfinavir, carbamazepine, phenobarbital, phenytoin.

Dosing: Pediatric:

HIV infection (component of combination therapy): Oral: Dosage based on weight or body surface area (BSA), presented based on lopinavir component (maximum dose: Lopinavir 400 mg/ritonavir 100 mg).

14 days to 6 months: 16 mg/kg or 300 mg/m² twice daily; Note: Should not be administered to neonates age <14 days (defined as postmenstrual age of 42 weeks [first day of mother's last menstrual period to birth plus postnatal age]) and a postnatal age of at least 14 days

6 months to 18 years: Note: FDA-approved dose is approximately equivalent to lopinavir 230 mg/m² per dose.

<15 kg: 12 mg/kg twice daily

15-40 kg: 10 mg/kg twice daily

>40 kg: Lopinavir 400 mg/ritonavir 100 mg twice daily

Dosage adjustment for combination therapy with efavirenz, fosamprenavir, nelfinavir, or nevirapine:

Oral:

Twice-daily dosing:

Children 14 days to 6 months: Combination therapy with these agents is not recommended due to lack of data.

Children 6 months to 18 years: Solution or tablet (based on mg of lopinavir component): FDA-approved dose is approximately equivalent to lopinavir 300 mg/m² per dose:

<15 kg: 13 mg/kg twice daily (Note: Tablets are not recommended)

15-45 kg: 11 mg/kg twice daily

>45 kg: Refer to adult dosing.

Once-daily dosing: Not recommended in children.

Administration:

Solution: Must be administered with food; if using didanosine, take didanosine 1 hour before or 2 hours after lopinavir/ritonavir. Administer using calibrated dosing syringe.

Tablet: May be taken with or without food. Swallow whole, do not break, crush, or chew. May be taken with didanosine when taken without food. Tablets are not recommended in patients <15 kg.

Dosing: Geriatric:

Initial studies did not include enough elderly patients to determine effects based on age. Use with caution due to possible decreased hepatic, renal, and cardiac function.

Dosing: Renal Impairment:

Has not been studied in patients with renal impairment; however, a decrease in clearance is not expected.

Hemodialysis: Do not use once-daily dosing in hemodialysis patients (DHHS, 2013)

Dosing: Hepatic Impairment:

Use caution in hepatic impairment (metabolized primarily by the liver).

Mild-to-moderate impairment: Lopinavir AUC may be increased ~30%

Severe impairment: No data available

Dosage Forms: U.S.:

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, oral:

Kaletra®: Lopinavir 80 mg and ritonavir 20 mg per 1 mL (160 mL) [contains ethanol 42.4%, menthol, propylene glycol; cotton candy flavor]

Tablet:

Kaletra®:

Lopinavir 100 mg and ritonavir 25 mg

Lopinavir 200 mg and ritonavir 50 mg

Generic Equivalent Available: U.S.-No

Exceptions:

Kaletra is not to be used in neonates <42 week postmenstrual age and <14 days old.

Once-daily dosing is not recommended in patients with ≥ 3 of the following lopinavir-resistance-associated amino acid substitutions in protease (L10F/I/R/V, K20M/N/R, L24I, L33F, M36I, I47V, G48V, I54L/T/V, V82A/C/F/S/T, and I84V); those receiving efavirenz, fosamprenavir, nevirapine, or nelfinavir, carbamazepine, phenobarbital, phenytoin, or in children <18 years of age.

Adverse Reactions:

>10%: rash, hypercholesterolemia, hypertriglyceridemia, diarrhea, abnormal tast/taste perversion, vomiting, nausea, abdominal pain, GGT increased, ALT increased.

Other severe less common reactions: QT prolongation, torsades de pointes, PR prolongation, AV block, hyperglycemia, diabetes mellitus, pancreatitis, hepatotoxicity, fat redistribution, hypersensitivity reaction, exfoliative dermatitis, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, immune reconstitution syndrome, autoimmune disorders.

References:

1. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents, "Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, Department of Health and Human Services," February 12, 2013;1-267. Available at <http://www.aidsinfo.nih.gov>
2. Working Group on Antiretroviral Therapy and Medical Management of HIV-Infected Children, "Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection," August 16, 2010. Available at <http://www.aidsinfo.nih.gov>
3. www.uptodate.com: Lopinavir and ritonavir: Drug Information
4. www.epocrates.com: Kaletra Drug Information

REVISION HISTORY:

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