Abbott Virology
100 Abbott Park Road
Abbott Park, IL 60064

KALETRA 100/25 mg tablets
NDC #0074-0522-60

Dear Healthcare Provider:

Introducing a new strength of KALETRA® (lopinavir/ritonavir): 100/25 mg tablets[1]

Abbott is pleased to introduce the new lower-strength KALETRA 100/25 mg tablet. Recently approved by the FDA, this new formulation is now available and contains 100 mg of lopinavir and 25 mg of ritonavir for adults and children weighing ≥15 kg who are able to swallow the intact tablet.

The new lower-strength tablets offer these same benefits as the original-strength KALETRA tablets:

- May be taken with or without food
- May be stored at room temperature with no need for refrigeration before or after dispensing (please see storage information on following pages)

KALETRA oral solution, available as 400 mg lopinavir and 100 mg ritonavir per 5 mL (80 mg lopinavir and 20 mg ritonavir per mL), will remain available for patients who cannot or prefer not to swallow tablets. Additionally, original-strength KALETRA 200/50 mg tablets will remain available.

Body weight dosing guidelines[1]

Dosing the new lower-strength KALETRA 100/25 mg tablets for pediatric patients weighing ≥15 kg who are able to swallow the lower-strength tablet intact is based on patient body weight. Dosing for pediatric patients is outlined in the chart below.

Once-daily dosing in pediatric patients has not been evaluated. KALETRA tablets and oral solution should not be administered once daily in pediatric patients <18 years of age. Please see full Prescribing Information for complete dosing guidelines.

Recommended dosing for pediatric patients (6 months to 12 years of age)[1]

Weight (kg)	Dose based on lopinavir component*	Volume of oral solution twice daily (80 mg lopinavir/ 20 mg ritonavir per mL)	Number of 100/25 mg tablets twice daily
Without nevirapine, efavirenz, or (fos)amprenavir†			
7 to <15 kg	**12 mg/kg BID‡**		
7 to 10 kg		1.25 mL	Tablets are not recommended. Use oral solution
>10 to <15 kg		1.75 mL	Tablets are not recommended. Use oral solution
15 to 40 kg	**10 mg/kg BID‡**		
15 to 20 kg		2.25 mL	2§
>20 to 25 kg		2.75 mL	2§
>25 to 30 kg		3.5 mL	3
>30 to 35 kg		4 mL	3
>35 to 40 kg		4.75 mL	4 (or two 200/50 mg tablets)
>40 kg	400 mg BID	5 mL	4 (or two 200/50 mg tablets)

*Dosing based on the lopinavir component of lopinavir/ritonavir solution (80/20 mg per mL). The safety, efficacy, and pharmacokinetic profiles of KALETRA in pediatric patients below the age of 6 months have not been established.

†A dose increase of KALETRA is needed when co-administered with efavirenz, nevirapine, or (fos)amprenavir. Please see full Prescribing Information for recommended dosing in pediatric patients taking these medications with KALETRA.

‡Dose is approximately equivalent to lopinavir/ritonavir 230/57.5 mg/m^2.

§Alternatively, one 200/50 mg tablet may be used for this dose in those patients who can swallow the larger tablet.

For patients weighing greater than 40 kg, see adult dosing recommendations.

KALETRA is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection.

Please see full Indication and Important Safety Information on following pages

Please see accompanying full Prescribing Information about KALETRA in combination HIV therapy

Abbott

KALETRA® (lopinavir/ritonavir) 100/25 mg tablets should be swallowed whole and should not be chewed, broken, or crushed[1]

Although new lower-strength KALETRA 100/25 mg tablets are not scored, there is potential for parents, caretakers, or healthcare workers to cut or crush the tablets for dosing in children. However, anyone administering the drug should be advised against this method. A preclinical study using crushed KALETRA tablets found that crushing the tablet is likely to significantly reduce lopinavir bioavailability.[2] The KALETRA label states that KALETRA tablets should be swallowed whole and not chewed, broken, or crushed. Reduced lopinavir/ritonavir bioavailability caused by crushing could reduce the efficacy of the tablets. KALETRA 200/50 mg tablets should also be swallowed whole and not chewed, broken, or crushed.

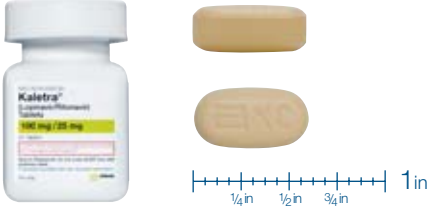
Before prescribing lopinavir/ritonavir 100/25 mg tablets, children should be assessed for the ability to swallow intact tablets. If a child is unable to reliably swallow a lopinavir/ritonavir tablet, the lopinavir/ritonavir oral solution formula should be prescribed.

Key differences between 200/50 mg tablets and 100/25 mg tablets[1]

The new lower-strength KALETRA 100/25 mg tablets are small and pale yellow in color, as compared with the larger, darker yellow 200/50 mg tablets. Key differences between the new lower-strength KALETRA 100/25 mg tablet and the original-strength KALETRA 200/50 mg tablet are listed in the chart and illustrated in the photographs below.

KALETRA 200/50 mg tablet	New KALETRA 100/25 mg tablet
• Dark yellow tablet	• Pale yellow tablet
• Embossed with the Abbott “A” and “KA”	• Embossed with the Abbott “A” and “KC”
• Supplied in a 250-mL bottle	• Supplied in a 100-mL bottle
• Bottle is labeled with a blue bar	• Bottle is labeled with a green bar
• National Drug Code (NDC) #0074-6799-22	• NDC #0074-0522-60
• 120 tablets per bottle	• 60 tablets per bottle
• One tablet is 0.75 inches long	• One tablet is 0.6 inches long
• One tablet weighs 1,242 mg	• One tablet weighs 625 mg

Tablets are shown actual size.



Tablets are shown actual size.

Please see full Indication and Important Safety Information on following pages

Please see accompanying full Prescribing Information about KALETRA in combination HIV therapy

Avoiding dosing errors

Medication errors may potentially occur because KALETRA® (lopinavir/ritonavir) tablets are now available in 2 dosage strengths. To avoid errors, it is important to make note of the dosage strength on all prescriptions for KALETRA. Also, anyone administering the drug should be advised to check the medication after receiving it from the pharmacy to ensure that he or she has received the correct dose.

- Healthcare professionals should pay special attention to accurate calculation of the dose of KALETRA, transcription of the medication order, dispensing information, and dosing instructions to minimize the risk of medication errors, overdose, and underdose

Not all local pharmacies will have KALETRA 100/25 mg tablets in stock. To ensure that patients receive their prescriptions at their pharmacy, healthcare providers are encouraged to call the prescription into the pharmacy in advance. In most cases, pharmacies will be able to order KALETRA 100/25 mg tablets and have them available for patients within 24 to 48 hours of receiving the prescription.

If you have any questions or need additional information about new lower-strength KALETRA 100/25 mg tablets, please contact your Abbott sales representative or call Abbott Medical Information at 1-800-633-9110.

Sincerely,

Robert Hoff MD

Robert Hoff, MD
Senior Medical Director
Global Medical Communications
Abbott Laboratories

Please see full Indication and Important Safety Information on following pages

Please see accompanying full Prescribing Information about KALETRA in combination HIV therapy

Indication and Important Safety Information

Indication[1]

KALETRA® (lopinavir/ritonavir) is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection.

Important Safety Information[1]

KALETRA is contraindicated in patients with known hypersensitivity to any of its ingredients.

Co-administration of KALETRA is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening reactions, and with potent CYP3A inducers where significantly reduced lopinavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance and cross-resistance. These contraindicated drugs include: cisapride, dihydroergotamine, ergonovine, ergotamine, methylergonovine, midazolam, pimozide, triazolam, rifampin, St. John's wort *(Hypericum perforatum)*, lovastatin, and simvastatin.

Consider drug-drug interaction potential to reduce risk of serious or life-threatening adverse reactions. Alteration in dose or regimen, drug level monitoring, or increased observations for adverse events may be recommended during co-administration of KALETRA with tenofovir, abacavir, zidovudine, indinavir, saquinavir, tipranavir, amiodarone, bepridil, lidocaine (systemic), quinidine, warfarin, trazodone, ketoconazole, itraconazole, voriconazole, rifabutin, dihydropyridine (eg, felodipine, nifedipine, nicardipine), dexamethasone, disulfiram/metronidazole, sildenafil, tadalafil, vardenafil, atorvastatin, rosuvastatin, cyclosporine, tacrolimus, rapamycin, fluticasone, methadone, and ethinyl estradiol.

KALETRA once-daily should not be administered in combination with efavirenz, nevirapine, (fos)amprenavir, nelfinavir, carbamazepine, phenobarbital, phenytoin, in therapy-experienced patients or in pediatric patients <18 years of age.

Pancreatitis, including some fatalities, has been observed in patients receiving KALETRA; suspend therapy as clinically appropriate.

Hepatotoxicity, including some fatalities, has been observed in patients receiving KALETRA. Monitor liver function before and during therapy, especially in patients with underlying hepatic disease or marked transaminase elevations.

Patients receiving protease inhibitor therapy may develop new onset or exacerbations of diabetes mellitus or hyperglycemia.

Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy, including KALETRA.

Redistribution/accumulation of body fat have been observed in patients receiving antiretroviral therapy. The mechanism and long-term consequences of these events are currently unknown.

Treatment with KALETRA has resulted in large increases in concentrations of total cholesterol and triglycerides. Monitor lipids prior to therapy and periodically thereafter.

There have been reports of increased bleeding in patients with hemophilia treated with protease inhibitors.

Various degrees of cross-resistance among protease inhibitors have been observed.

The safety, efficacy and pharmacokinetic profiles of KALETRA in pediatric patients below the age of 6 months have not been established. KALETRA once-daily has not been evaluated in pediatric patients.

Healthcare professionals should pay close attention to accurate calculation of the dose of KALETRA, transcription of the medication order, dispensing information, and dosing instructions to minimize the risk for medication errors, overdose, and underdose. The appropriate dose must be carefully calculated for each pediatric patient, based on the mg/kg recommendations in the full Prescribing Information.

Before being prescribed lopinavir/ritonavir 100/25 mg tablets, children should be assessed for the ability to swallow intact tablets. If unable to reliably swallow an intact tablet, the lopinavir/ritonavir oral solution formulation should be prescribed.

In KALETRA clinical trials, the most common adverse reactions of moderate to severe intensity reported in ≥5% of adult patients were diarrhea, nausea, abdominal pain, asthenia, vomiting, headache, and dyspepsia. In children receiving KALETRA oral solution, the most common adverse reactions of any severity were taste aversion, vomiting, and diarrhea.

Please see accompanying full Prescribing Information about KALETRA in combination HIV therapy

Important Adult Dosing Information[1]

Do not administer once-daily KALETRA tablets or oral solution in therapy-experienced patients.

When initiating treatment with KALETRA in therapy-naïve patients, it should be noted the incidence of diarrhea was greater for KALETRA capsules once-daily compared to KALETRA capsules twice-daily in Study 418 (57% vs. 35%-reactions of all grades; 16% vs. 5%-reactions of at least moderate severity).

The recommended adult dose of KALETRA tablets and oral solution is 400/100 mg (two 200/50 mg tablets or 5 mL of oral solution) twice daily. KALETRA also may be dosed 800/200 mg (four 200/50 mg tablets or 10 mL of oral solution) once daily for therapy-naïve adult patients only.

- KALETRA tablets may be taken with or without food
- KALETRA tablets should be swallowed whole and not chewed, broken, or crushed
- KALETRA oral solution must be taken with food
- KALETRA can be taken with acid-reducing agents (such as omeprazole and ranitidine) with no dose adjustment
- KALETRA oral solution contains 42.4% alcohol

Concomitant therapy with efavirenz, nevirapine, (fos)amprenavir, or nelfinavir:

- –KALETRA tablets and oral solution should not be administered as a once-daily regimen in combination with efavirenz, nevirapine, (fos)amprenavir, or nelfinavir
- –KALETRA 400/100 mg (two 200/50 mg tablets) can be used twice-daily in combination with these drugs with no dose adjustment in antiretroviral-naïve patients
- –A dose increase of KALETRA tablets to 600/150 mg (three 200/50 mg tablets) twice-daily may be considered when used in combination with efavirenz, nevirapine, (fos)amprenavir without ritonavir, or nelfinavir in treatment-experienced patients where decreased susceptibility to lopinavir is clinically suspected (by treatment history or laboratory evidence)
- –A dose increase is recommended for all patients who use KALETRA oral solution to 533/133 mg (6.5 mL) twice-daily, taken with food, when used in combination with efavirenz, nevirapine, (fos)amprenavir, or nelfinavir

Important Pediatric Dosing Information[1]

Do not administer KALETRA once-daily in pediatric patients <18 years of age.

- The recommended dosage of KALETRA in patients 6 months to 12 years of age should be calculated based on body weight (kg) and should not exceed the recommended adult dose
- Healthcare professionals should pay special attention to accurate calculation of the KALETRA dose, transcription of the medication order, dispensing information, and dosing instructions to minimize the risk for medication errors, overdose, and underdose
- Prescribers should calculate the appropriate dose (based on mg/kg recommendations in the pediatric dosing tables in the full Prescribing Information) for each individual child and determine the corresponding volume of oral solution
- Alternatively, dosing with the 100/25 mg tablets can be based on body weight ranges in the pediatric dosing tables in the full Prescribing Information. Before prescribing lopinavir/ritonavir 100/25 mg tablets, children should be assessed for the ability to swallow intact tablets. If a child is unable to reliably swallow a lopinavir/ritonavir tablet, the oral solution formulation should be prescribed

Storage Conditions

- –KALETRA tablets: Store at 68°-77°F (20°-25°C), excursions permitted to 59°-86°F (15°-30°C). Dispense in original container or USP equivalent tight container. For patient use: Exposure of this product to high humidity outside the original container or USP equivalent tight container for longer than 2 weeks is not recommended
- –KALETRA oral solution: Store at 36°-46°F (2°-8°C) until dispensed. Avoid exposure to excessive heat. For patient use, refrigerated KALETRA oral solution remains stable until the expiration date printed on the label. If stored at room temperature up to 77ºF (25ºC), oral solution should be used within 2 months

References: 1. KALETRA Prescribing Information. **2.** Liu W, Klein CE, Marsh K, et al. Predicted pharmacokinetics of lopinavir after multiple-dose administration of lopinavir/ritonavir tablet to pediatric patients. Presented at: 8th International Congress on Drug Therapy in HIV Infection; November 2006; Glasgow, UK. Poster 366.

Please see accompanying full Prescribing Information about KALETRA in combination HIV therapy