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רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

אבוט מעבדות רפואיות בע"מ מודיעה כי העלון לצרכן והעלון לרופא של התכשירים הבאים עודכנו.
בהודעה זו מצוינים סעיפים בהם נעשה שינוי אשר מהווה החמרה או שינוי מהותי.
עדכונים נוספים אשר אינם מהווים החמרה או שאינם מהותיים, אינם נכללים בהודעה זו (שינוי שהינו הוספה מסומן בקו תחתון, מחיקה מסומנת בקו אמצעי).

Kaletra Oral Solution
Kaletra 200mg/50mg Tablets
Kaletra 100mg/25mg Tablets
קלטרה תמיסה
קלטרה 200 מ"ג/50 מ"ג טבליות
קלטרה 100 מ"ג/25 מ"ג טבליות
Lopinavir & Ritonavir 80mg+20mg / ml
Lopinavir & Ritonavir 200mg/50mg
Lopinavir & Ritonavir 100mg/25mg

ההתוויות המאושרות לתכשיר:
KALETRA is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection

העלון לצרכן עודכן בסעיפים:

- **תגובות בין תרופתיות:**

מהות השינוי:

אם הינך נוטל/ת תרופה נוספת, או אם גמרת זה עתה טיפול בתרופה אחרת, עליך לדווח לרופא המטפל כדי למנוע סיכונים או אי-יעילות הנובעים מתגובות בין-תרופתיות, במיוחד לגבי תרופות מהקבוצות הבאות: תרופות אנטיוויראליות (כגון: אפאביראנז, נביראפין, טנופוביר, אמפרנאביר, פוסאמפרנאביר, אינדינאביר, נלפינאביר, סקוינאביר, מראבירוק, בוספרויר), תרופות ליתר לחץ דם ריאתי (בוסנטן).

- **אחסנה:**

מהות השינוי:

טבליות: ~~יש לאחסן את התכשיר בטמפרטורת החדר~~. יש לאחסן באריזה המקורית. אין להעביר את הטבליות למיכל אחר.
קלטרה 25/100 מ"ג טבליות: יש לאחסן מתחת ל - 25°C.
קלטרה 50/200 מ"ג טבליות: יש לאחסן את התכשיר בטמפרטורת החדר.

העלון לרופא עודכן בסעיפים:

2. DOSAGE AND ADMINISTRATION

מהות השינוי:

2.1 Adult Patients

Once daily administration of KALETRA is not recommended for adult patients with three or more of the following lopinavir resistance-associated substitutions: L10F/I/R/V, K20M/N/R, L24I, L33F, M36I, I47V, G48V, I54L/T/V, V82A/C/F/S/T, and I84V [see Clinical Pharmacology (12.4)].

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2.2 Pediatric Patients

Dosing recommendations using tablets

Table 2. Pediatric Dosing Recommendations for Patients 6 Months to 18 Years of Age Based on Body Weight or Body Surface Area for KALETRA Tablets With Concomitant Efavirenz†, Nevirapine, amprenavir† or Nelfinavir†

Body Weight (kg)	Body Surface Area (m^2)*	Recommended number of 100/25 mg Tablets Twice Daily
15 to 20	≥0.6 to < 0.8	2
>20 to 30	≥0.8 to < 1.2	3
>30 to 45	≥1.2 to <1.7	4 (or two 200/50 mg tablets)
>45	≥1.7	~~4 or 6~~ 5 ~~(or two or three 200/50 mg tablets)~~ {*see Dosage and Administration*, Adult Patients (2.1)}
* KALETRA oral solution is available for children with a BSA less than 0.6 m^2 or those who are unable to reliably swallow a tablet. † Please refer to the individual product labels for appropriate dosing in children.		

5. WARNINGS AND PRECAUTIONS

מהות השינוי:

5.8 Immune Reconstitution Syndrome

Autoimmune disorders (such as Graves' disease, polymyositis, and Guillain-Barré syndrome) have also been reported to occur in the setting of immune reconstitution, however, the time to onset is more variable, and can occur many months after initiation of treatment.

6. ADVERSE REACTIONS

מהות השינוי:

6.1 Adults - Clinical Trials Experience

Blood and Lymphatic System Disorders

neutropenia

Gastrointestinal Disorders

rectal hemorrhage

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7. DRUG INTERACTIONS

מהות השינוי:

7.3 Established and Other Potentially Significant Drug Interactions

Table 9. Established and Other Potentially Significant Drug Interactions

Concomitant Drug Class: Drug Name	Effect on Concentration of Lopinavir or Concomitant Drug	Clinical Comment
HIV CCR5 – antagonist	↓ Boceprevir	Concomitant administration of boceprevir and lopinavir/ritonavir resulted in reduced boceprevir and lopinavir steady-state exposure. It is not recommended to co-administer opinavir/ritonavir and boceprevir
Endothelin receptor anagonists: bosentan	↑ bosentan	Co-administration of bosentan in patients on KALETRA: In patients who have been receiving KALETRA for at least 10 days, start bosentan at 62.5 mg once daily or every other day based upon individual tolerability. Co-administration of KALETRA in patients on bosentan: Discontinue use of bosentan at least 36 hours prior to initiation of KALETRA. After at least 10 days following the initiation of KALETRA, resume bosentan at 62.5 mg once daily or every other day based upon individual tolerability
HMG-CoA Reductase Inhibitors: atorvastatin* rosuvastatin	↑atorvastatin ↑ rosuvastatin	Use lowest possible dose of atorvastatin or rosuvastatin with careful monitoring ,*do not exceed rosuvastatin 10 mg/day*, or consider other HMG-CoA reductase inhibitors such as pravastatin or fluvastatin in combination with KALETRA.
Long-acting beta-adrenoceptor agonist: salmeterol	↑ salmeterol	Concurrent administration of salmeterol and KALETRA is not recommended. The combination may result in increased risk of cardiovascular adverse events associated with salmeterol, including QT prolongation, palpitations and sinus tachycardia.

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8.USE IN SPECIFIC POPULATIONS

מהות השינוי:

8.4 Pediatric Use

An open-label, multi-center, dose-finding trial was performed to evaluate the pharmacokinetic profile, tolerability, safety and efficacy of KALETRA oral solution containing lopinavir 80 mg/mL and ritonavir 20 mg/mL at a dose of with 300/75 mg/m2 twice daily plus two NRTIs in HIV-infected infants ≥14 days and < 6 months of age. Results revealed that infants younger than 6 months of age generally had lower lopinavir AUC12 than older children (6 months to 12 years of age), however, despite the lower lopinavir drug exposure observed, antiviral activity was demonstrated as reflected in the proportion of subjects who achieved HIV-RNA <400 copies/mL at Week 24 *[see Adverse Reactions (6.2), Clinical Pharmacology (12.3), Clinical Studies (14.4)].*

~~In HIV-1 infected patients age 6 months to 12 years, the adverse reaction profile seen during the clinical trial was similar to that for adult patients. The evaluation of the antiviral activity of KALETRA in other pediatric patient populations is ongoing.~~

12. CLINICAL PHARMACOLOGY

מהות השינוי:

12.3 Pharmacokinetics

Once-Daily Dosing

The pharmacokinetics of once daily KALETRA has also been evaluated in treatment experienced HIV-1 infected subjects. Lopinavir exposure (Cmax, AUC[0-24h], Ctrough) with once daily KALETRA administration in treatment experienced subjects is comparable to the once daily lopinavir exposure in treatment naïve subjects.

Drug Interactions

Table 10. Drug Interactions: Pharmacokinetic Parameters for Lopinavir in the Presence of the Co-administered Drug for Recommended Alterations in Dose or Regimen

Co-administered Drug	Dose of Co-administered Drug (mg)	Dose of KALETRA (mg)		Ratio (in combination with co-administered drug/alone) of Lopinavir Pharmacokinetic Parameters (90% CI); No Effect = 1.00		
			n	C_{max}	AUC	C_{min}
Boceprevir	*800 mg q8h, 6 d*	*400/100 tablet BID, 22d*	*39*	*0.70 (0.65, 0.77)*	*0.66 (0.60, 0.72)*	*0.57 (0.49, 0.65)*

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Table 11. Drug Interactions: Pharmacokinetic Parameters for co-administered Drug in the Presence of KALETRA for Recommended Alterations in Dose or Regimen

Co-administered Drug	Dose of Co-administered Drug (mg)	Dose of KALETRA (mg)		Ratio (in combination with KALETRA/alone) of co-administered Drug Pharmacokinetic Parameters (90% CI); No Effect = 1.00		
			n	C_{max}	AUC	C_{min}
Boceprevir	*800 mg q8h, 6 d*	*400/100 tablet BID, 22 d*	*39*	*0.50 (0.45, 0.55)*	*0.55 (0.49, 0.61)*	*0.43 (0.36, 0.53)*

12.4 Microbiology

Clinical Studies - Antiviral Activity of KALETRA in Patients with Previous Protease Inhibitor Therapies

Once daily administration of KALETRA for adult patients with three or more of the above substitutions is not recommended.

14. CLINICAL STUDIES

מהות השינוי:

14.2 Patients With Prior Antiretroviral Therapy

Through 48 weeks of treatment, the mean change from baseline for CD4 + cell count was 135 cells/mm3 for the once daily group and 122 cells/mm3 for the twice daily group.

14.4 Pediatric Studies

Among patients 14 days to 6 months of age receiving 300/75 mg/m2 twice daily without nevirapine, plasma concentrations were lower than those observed in adults or in older children. This dose resulted in HIV-1 RNA < 400 copies/mL in 55% of patients (70% in those initiating treatment at <6 weeks of age).

16. HOW SUPPLIED/STORAGE AND HANDLING

מהות השינוי:

16.2 KALETRA Tablets, 100 mg lopinavir/25 mg ritonavir

~~This medicinal product does not require any special storage conditions.~~ Store below 25°C

העלונים המעודכנים לרופא ולצרכן נשלחו למאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום, אבוט מעבדות רפואיות בע"מ, קריית עתידים בניין 4, ת.ד. 58099 תל אביב או בטלפון 03-7691037.

בברכה,

אורית פוקס
רוקחת ממונה

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A Promise for Life