Fosamprenavir (FPV, Lexiva)

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Formulations

Tablets: 700 mg

Oral Suspension: 50 mg/mL

For additional information, see Drugs@FDA.

Dosing Recommendations

Pediatric Dose (Aged >6 Months to 18 Years)

- Unboosted fosamprenavir (without ritonavir) is Food and Drug Administration (FDA)-approved for antiretroviral (ARV)-naive children aged 2 to 5 years, but **not recommended** by the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) because of low exposures (see text below).
- Boosted fosamprenavir (with ritonavir) is FDA-approved for ARV-naive infants ≥4 weeks and for treatment-experienced infants ≥6 months; however, the Panel **does not recommend** use in infants aged <6 months because of similarly low exposures (see text below). If used in infants as young as 4 weeks, it should only be administered to infants born at 38 weeks' gestation or greater.

Note: Once-daily dosing **is not recommended** for any pediatric patient.

Pediatric Dose (Aged ≥6 Months to 18 Years)

Twice-Daily Dose Regimens by Weight for Pediatric **Patients ≥6 Months Using Fosamprenavir Oral Suspension** with Ritonavir

Weight	Dose (Both Drugs Twice Daily[a] with Food)
<11 kg	Fosamprenavir 45 mg/kg/dose plus ritonavir 7 mg/kg/dose
11 kg to <15 kg	Fosamprenavir 30 mg/kg/dose plus ritonavir 3 mg/kg/dose
15 kg to <20 kg	Fosamprenavir 23 mg/kg/dose plus ritonavir 3 mg/kg/dose
≥20 kg	Fosamprenavir 18 mg/kg/dose plus ritonavir 3 mg/kg/dose

Selected Adverse Events

- Diarrhea, nausea, vomiting
- Skin rash (fosamprenavir has a sulfonamide moiety. Stevens-Johnson syndrome and erythema multiforme have been reported.)
- Headache
- Hyperlipidemia, hyperglycemia
- Nephrolithiasis
- Transaminase elevation
- Fat maldistribution
- Possible increased bleeding episodes in patients with hemophilia

Special Instructions

- Fosamprenavir tablets with ritonavir should be taken with food. Children should take the suspension with food.
- Patients taking antacids should take fosamprenavir at least 1 hour before or after antacid use.
- Fosamprenavir contains a sulfonamide moiety. The potential for cross sensitivity between fosamprenavir and other drugs in the sulfonamide class is unknown. Fosamprenavir should be used with caution in patients with sulfonamide allergy.
- Shake oral suspension well before use. Refrigeration is not required.

[a] Not to exceed the adult dose of fosamprenavir 700 mg plus ritonavir 100 mg twice daily. Note: When administered with ritonavir, the adult regimen of 700 mg fosamprenavir tablets plus 100 mg ritonavir, both given twice daily, can be used in patients weighing ≥39 kg. Ritonavir tablets can be used in patients weighing ≥33 kg. Adolescent and Adult Dose • Dosing regimen depends on whether the patient is ARV-naive or ARV-experienced. *ARV-Naive Patients* • Fosamprenavir 700 mg plus ritonavir 100 mg, both twice daily • Fosamprenavir 1400 mg plus ritonavir 100–200 mg, both once daily *Protease-Inhibitor-Experienced Patients* • Fosamprenavir 700 mg plus ritonavir 100 mg, both twice daily. Note: Once-daily administration of fosamprenavir plus ritonavir is not recommended.	Metabolism/Elimination • The prodrug fosamprenavir is rapidly and almost completely hydrolyzed to amprenavir by cellular phosphatases in the gut as it is absorbed. • Amprenavir is a cytochrome P (CYP) 450 3A4 inhibitor, inducer, and substrate. Fosamprenavir Dosing in Patients with Hepatic Impairment • Specific dose adjustments are recommended for adults with mild, moderate, and severe hepatic impairment. However, there are no data to support dosing recommendations for pediatric patients with hepatic impairment. Please refer to the package insert. Fosamprenavir Dosing in Patients with Renal Impairment • No dose adjustment is required in patients with renal impairment.

Drug Interactions

Additional information about drug interactions is available in the Adult and Adolescent Guidelines and the HIV Drug Interaction Checker.

- Fosamprenavir may interact with a number of other drugs, and using ritonavir as a boosting agent increases the potential for drug interactions. Before administration, a patient's medication profile should be carefully reviewed for potential drug interactions with fosamprenavir.

Major Toxicities

- *More common:* Vomiting, nausea, diarrhea, perioral paresthesia, headache, rash, lipid abnormalities
- *Less common (more severe):* Life-threatening rash, including Stevens-Johnson syndrome, in <1% of patients. Fat maldistribution, neutropenia, and elevated serum creatinine kinase levels.
- *Rare:* New-onset diabetes mellitus, hyperglycemia, ketoacidosis, exacerbation of preexisting diabetes mellitus, spontaneous bleeding in hemophiliacs, hemolytic anemia, elevation in serum transaminases, angioedema, and nephrolithiasis.
- *Pediatric-specific:* Vomiting was more frequent in children than in adults during clinical trials of fosamprenavir with ritonavir (20% to 36% vs. 10%, respectively) and in trials of fosamprenavir without ritonavir (60% vs. 16%, respectively). Neutropenia was also more common in children across all the trials (15% vs. 3%, respectively).[1]

Resistance

The International AIDS Society–USA maintains a list of updated resistance mutations and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation.

Pediatric Use

Approval

Fosamprenavir is Food and Drug Administration (FDA)-approved for use in children as young as age 4 weeks, but the Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) recommends use only in children aged ≥6 months. Although unboosted fosamprenavir has been approved by the FDA for antiretroviral-naive children aged 2 to 5 years, the Panel **does not recommend** unboosted fosamprenavir for this—or any other—age group because of low exposures and also because unboosted fosamprenavir may select for mutations associated with resistance to darunavir.[2]

Efficacy and Pharmacokinetics

Dosing recommendations for fosamprenavir are based on three pediatric studies that enrolled more than 200 children aged 4 weeks to 18 years. In two, open-label trials in both treatment-experienced and treatment-naive children aged 2 to 18 years,[3,4] fosamprenavir was well-tolerated and effective in suppressing viral load and increasing CD4 T lymphocyte count. However, data were insufficient to support a once-daily dosing regimen of fosamprenavir/ritonavir in children; therefore, once-daily dosing **is not recommended** for pediatric patients.

Pharmacokinetics in Infants

In a study of infants, higher doses of both fosamprenavir and ritonavir were used in treatment-naive infants as young as age 4 weeks and in treatment-experienced infants as young as age 6 months.[1,5] Exposures in those aged <6 months were much lower than those achieved in older children and adults and comparable to those seen with unboosted fosamprenavir (see table below). Given these low exposures, limited data, large dosing volumes, unpleasant taste, and the availability of alternatives for infants and young children, the Panel **does not recommend** fosamprenavir use in infants aged <6 months.

Table A. Fosamprenavir Dose and Amprenavir Exposure by Age Group

Population	Dose	$AUC_{0\text{-}24h}$ (mcg*hr/mL) Except Where Noted	C_{min} (mcg/mL)
Infants Aged <6 Months	FPV 45 mg/kg plus RTV 10 mg/kg twice daily	26.6[a]	0.86
Children Aged 2 Years to <6 Years	FPV 30 mg/kg twice daily (no RTV)	22.3[a]	0.513
Children Weighing <11 kg	FPV 45 mg/kg plus RTV 7 mg/kg twice daily	57.3	1.65
Children Weighing 15 kg to <20 kg	FPV 23 mg/kg FPV plus RTV 3 mg/kg twice daily	121.0	3.56
Children Weighing **≥20 kg**	FPV 18 mg/kg plus RTV 3 mg/kg twice daily (maximum 700/100 mg)	72.3–97.9	1.98–2.54
Adults	FPV 1400 mg twice daily (no RTV)	33	0.35
Adults	FPV 1400 mg plus RTV 100–200 mg RTV once daily	66.4–69.4	0.86–1.45
Adults	FPV 700 mg plus RTV 100 mg twice daily	79.2	2.12

[a] $AUC_{0\text{-}12}$ (mcg*hr/mL)

Key: $AUC_{0\text{-}24h}$ = area under the curve for 24 hours post-dose; C_{min} = minimum plasma concentration; FPV = fosamprenavir; RTV = ritonavir

Note: Dose for those weighing 11 kg to <15 kg is based on population pharmacokinetic studies; therefore, AUC and C_{min} are not available.

References

1. Fosamprenavir [package insert]. Food and Drug Administration. 2016. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/022116s023_21548-s39lbl.pdf.

2. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. 2022. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/guidelines-adult-adolescent-arv.pdf.

3. Chadwick E, Borkowsky W, Fortuny C, et al. Safety and antiviral activity of fosamprenavir/ritonavir once daily regimens in HIV-infected pediatric subjects ages 2 to 18 years (48-week interim data, study apv20003). Presented at: 14th Conference on Retroviruses and Opportunistic Infections. 2007. Los Angeles, CA.

4. Fortuny C, Duiculescu D, Cheng K, et al. Pharmacokinetics and 48-week safety and antiviral activity of fosamprenavir-containing regimens in HIV-infected 2- to 18-year-old children. *Pediatr Infect Dis J.* 2014;33(1):50-56. Available at http://www.ncbi.nlm.nih.gov/pubmed/23811744.

5. Cotton M, Cassim H, Pavia-Ruz N, et al. Pharmacokinetics, safety and antiviral activity of fosamprenavir/ritonavir-containing regimens in HIV-infected children aged 4 weeks to 2 years-48-week study data. *Pediatr Infect Dis J.* 2014;33(1):57-62. Available at http://www.ncbi.nlm.nih.gov/pubmed/23811743.