



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Emtricitabine (FTC, Emtriva) (Last updated April 26, 2016; last reviewed April 26, 2016)

For additional information see Drugs@FDA: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>

Formulations

Pediatric Oral Solution: 10 mg/mL

Capsules: 200 mg

Generic Formulations: None available

Fixed-Dose Combination Tablets:

- [Truvada low strength tablet]
 - Emtricitabine 100 mg plus tenofovir disoproxil fumarate (TDF) 150 mg
 - Emtricitabine 133 mg plus TDF 200 mg
 - Emtricitabine 167 mg plus TDF 250 mg
- [Descovy] Emtricitabine 200 mg plus tenofovir alafenamide (TAF) 25 mg
- [Atripla] Efavirenz 600 mg plus emtricitabine 200 mg plus TDF 300 mg
- [Complera] Emtricitabine 200 mg plus rilpivirine 25 mg plus TDF 300 mg
- [Odefsey] Emtricitabine 200 mg plus rilpivirine 25 mg plus TAF 25 mg
- [Stribild] Elvitegravir 150 mg plus cobicistat 150 mg plus emtricitabine 200 mg plus TDF 300 mg
- [Genvoya] Elvitegravir 150 mg plus cobicistat 150 mg plus emtricitabine 200 mg plus TAF 10 mg

Dosing Recommendations

Neonatal/Infant Dose (Aged 0 to <3 Months)

Oral Solution:

- 3 mg/kg once daily.

Pediatric Dose (Aged ≥3 Months to 17 Years)

Oral Solution:

- 6 mg/kg (maximum dose 240 mg) once daily; higher maximum dose because the oral solution has 20% lower plasma exposure in pediatric pharmacokinetic analysis.

Capsules (Weight >33 kg):

- 200 mg once daily.

Adolescent (Aged ≥18 Years) and Adult Dose

Oral Solution:

- 240 mg (24 mL) once daily.

Capsules:

- 200 mg once daily.

Combination Tablets

[Truvada tablet] Emtricitabine plus TDF

Truvada Tablets Dosing Table

Body Weight kg	FTC/TDF Tablet Once Daily
17 to <22	One 100 mg/150 mg tablet
22 to <28	One 133 mg/200 mg tablet
28 to <35	One 167 mg/250 mg tablet
Adolescent (Weighing ≥35 kg) and Adult Dose	One 200 mg/300 mg tablet

Selected Adverse Events

- Minimal toxicity
- Severe acute exacerbation of hepatitis can occur in hepatitis B virus-coinfected patients who discontinue emtricitabine.
- Hyperpigmentation/skin discoloration on palms and/or soles

Special Instructions

- Although emtricitabine can be administered without regard to food, food requirements vary depending on the other antiretrovirals contained in a combination tablet. For Atripla (administer without food) and Complera (administer with a meal of at least 500 calories), refer to efavirenz or rilpivirine special instructions.
- Emtricitabine oral solution can be kept at room temperature up to 77° F (25° C) if used within 3 months; refrigerate for longer-term storage.
- If using Stribild, please see the elvitegravir section of the drug appendix for additional information.
- Before using emtricitabine, screen patients for hepatitis B virus.

Metabolism/Elimination

- Limited metabolism: No cytochrome P (CYP) 450 interactions.

[Descovy] Emtricitabine plus TAF

Adolescent (Weighing >35 kg) and Adult Dose:

- 1 tablet once daily

[Atripla] Efavirenz plus Emtricitabine plus TDF 300 mg

Adolescent (Weighing ≥40 kg) and Adult Dose:

- 1 tablet once daily.
- Administer without food
- See efavirenz section for pregnancy warning.

[Complera] Emtricitabine plus Rilpivirine plus TDF

Adolescent (Weighing ≥35 kg) and Adult Dose:

- 1 tablet once daily in treatment-naive patients with baseline plasma RNA <100,000 copies/mL or virologically suppressed patients with no history of virologic failure, resistance to rilpivirine and other antiretroviral (ARV) drugs, and who are currently on their first or second regimen.
- Administer with a meal of at least 500 calories.

[Odefsey] Emtricitabine plus Rilpivirine plus (TAF)

Adolescent (Weighing ≥35 kg) and Adult Dose:

- 1 tablet once daily with a meal as initial therapy in those with no ARV treatment history with HIV-1 RNA less than or equal to 100,000 copies per mL; or to replace a stable ARV regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL) for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Odefsey.
- Administer with a meal of at least 500 calories.

[Stribild] Elvitegravir plus Cobicistat plus Emtricitabine plus TDF

Adult Dose (Aged ≥18 Years):

- 1 tablet once daily in treatment-naive or virologically suppressed adults
- Administer with a meal.

[Genvoya] Elvitegravir plus Cobicistat plus Emtricitabine plus TAF

Adolescent (Aged ≥12 Years and Weighing ≥35 kg) and Adult Dose:

- 1 tablet once daily with food in ARV treatment-naive patients or to replace the current ARV regimen in those who are virologically suppressed (i.e., HIV-1 RNA <50 copies/mL) on a stable ARV regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Genvoya.

- **Renal excretion 86%:** Potential competition with other compounds that undergo renal elimination.
- **Dosing of emtricitabine in patients with renal impairment:** Decrease dosage in patients with impaired renal function. Consult manufacturer's prescribing information.
- Do not use Atripla (fixed-dose combination) in patients with creatinine clearance (CrCl) <50 mL/min or in patients requiring dialysis.
- Do not use Truvada (fixed-dose combination) in patients with CrCl <30 mL/min or in patients requiring dialysis.
- Use Complera with caution in patients with severe renal impairment or end-stage renal disease. Increase monitoring for adverse effects because rilpivirine concentrations may be increased in patients with severe renal impairment or end-stage renal disease.
- Stribild should not be initiated in patients with estimated CrCl <70 mL/min and should be discontinued in patients with estimated CrCl <50 mL/min.
- TAF-containing formulations are not recommended in patients with estimated creatinine clearance (CrCl) below 30 mL per minute.

Drug Interactions (see also the [Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents](#) and <http://www.hiv-druginteractions.org/>)

- *Other nucleoside reverse transcriptase inhibitors (NRTIs)*: Do not use emtricitabine in combination with lamivudine because the agents share similar resistance profiles and lack additive benefit. Do not use separately with Combivir, Epzicom, or Trizivir because lamivudine is a component of these combinations. Do not use separately when prescribing Truvada, Atripla, Complera, or Stribild because emtricitabine is a component of these formulations.
- *Renal elimination*: Competition with other compounds that undergo renal elimination (possible competition for renal tubular secretion). Drugs that decrease renal function could decrease clearance.
- *Use with Stribild*: If using Stribild, please see the elvitegravir section of the drug appendix for additional information.

Major Toxicities

- *More common*: Headache, insomnia, diarrhea, nausea, rash, and hyperpigmentation/skin discoloration (possibly more common in children).
- *Less common (more severe)*: Neutropenia. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported. Exacerbations of hepatitis have occurred in HIV/hepatitis B virus (HBV)-coinfected patients who changed from emtricitabine-containing to non-emtricitabine-containing regimens.

Resistance

The International Antiviral Society-USA (IAS-USA) maintains a list of updated resistance mutations (see http://iasusa.org/sites/default/files/tam/october_november_2015.pdf#page=10) and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation (see <http://hivdb.stanford.edu/DR/>).

Pediatric Use

Approval

Emtricitabine is Food and Drug Administration-approved for once-daily administration in children, starting at birth. Owing to its once-daily dosing, minimal toxicity, and pediatric pharmacokinetic (PK) data, emtricitabine is commonly used as part of a dual-nucleoside reverse transcriptase inhibitor backbone in combination antiretroviral therapy.

Efficacy and Pharmacokinetics

Pharmacokinetics

A single-dose PK study of emtricitabine liquid solution and capsules was performed in 25 HIV-infected children aged 2 to 17 years.¹ Emtricitabine was found to be well absorbed following oral administration, with a mean elimination half-life of 11 hours (range 9.7–11.6 hours). Plasma concentrations in children receiving the 6 mg/kg emtricitabine once-daily dose were approximately equivalent to those in adults receiving the standard 200-mg dose.

A study in South Africa evaluated the PKs of emtricitabine in 20 HIV-exposed infants aged <3 months, given emtricitabine as 3 mg/kg once daily for two, 4-day courses, separated by an interval of ≥ 2 weeks.² Emtricitabine exposure (area under the curve [AUC]) in neonates receiving 3 mg/kg emtricitabine once daily was in the range of pediatric patients aged >3 months receiving the recommended emtricitabine dose of 6 mg/kg once daily and adults receiving the once-daily recommended 200-mg emtricitabine dose (AUC approximately 10 hr* μ g/mL). Over the first 3 months of life, emtricitabine AUC decreased with increasing age, correlating with an increase in total body clearance of the drug. In a small group of neonates (N = 6) receiving a single dose of emtricitabine 3 mg/kg after a single maternal dose of 600 mg during delivery, the AUC exceeded that seen in adults and older children, but the half-life (9.2 hours) was similar.³ Extensive safety data are lacking in this age range.

Efficacy

Based on the aforementioned dose-finding study,¹ emtricitabine was studied at a dose of 6 mg/kg once daily in combination with other antiretroviral (ARV) drugs in 116 patients aged 3 months to 16 years.^{4,5} PK results were similar, and follow-up data extending to Week 96 indicated that 89% of the ARV-naive and 76% of the ARV-experienced children maintained suppression of plasma HIV RNA <400 copies/mL (75% of ARV-naive children and 67% of ARV-experienced children at <50 copies/mL). Minimal toxicity was observed in this trial. In PACTG P1021,⁴ emtricitabine at a dose of 6 mg/kg (maximum 240 mg/day as liquid or 200 mg/day as capsules) in combination with didanosine and efavirenz, all given once daily, was studied in 37 ARV-naive HIV-infected children aged 3 months to 21 years. Eighty-five percent of children achieved HIV RNA <400 copies/mL and 72% maintained HIV RNA suppression to <50 copies/mL through 96 weeks of therapy. The median CD4 T lymphocyte count rose by 329 cells/mm³ at Week 96.

Both emtricitabine and lamivudine have antiviral activity and efficacy against HBV. For a comprehensive review of this topic, please see the [Hepatitis B Virus section of the Pediatric Opportunistic Infections Guidelines](#).

References

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2. Blum M, Ndiweni D, Chittick G, et al. Steady state pharmacokinetic evaluation of emtricitabine in neonates exposed to HIV in utero. Paper presented at: 13th Conference on Retroviruses and Opportunistic Infections. 2006. Denver, CO.
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