



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Emtricitabine (FTC, Emtriva) (Last updated July 10, 2017; last reviewed July 10, 2017)

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

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
- *[Truvada tablet]* Emtricitabine 200 mg plus TDF 300 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.

Note: Please see [Special Considerations for Neonates](#) section.

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)/Adult Dose

Oral Solution for Those Unable to Swallow Capsules:

- 240 mg (24 mL) once daily.

Capsules:

- 200 mg once daily.

Combination Tablets

[Truvada tablet] Emtricitabine plus TDF

Selected Adverse Events

- Severe acute exacerbation of hepatitis can occur in hepatitis B virus (HBV)-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 ARV drugs 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 HBV.

Metabolism/Elimination

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

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

[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-naïve 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 antiretroviral treatment (ART) history with HIV-1 RNA $\leq 100,000$ copies per mL; or to replace a stable ART regimen in those who are virologically-suppressed (HIV-1 RNA <50 copies/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-naïve or virologically suppressed adults.
- Administer with a meal.

[Genvoya] Elvitegravir plus Cobicistat plus Emtricitabine plus TAF

- **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 events 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 CrCl below 30 mL per minute.

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

- 1 tablet once daily with food in ART-naïve patients or to replace the current ART regimen in those who are virologically suppressed (i.e., HIV-1 RNA < 50 copies/mL) on a stable ART 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.

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, Stribild, Genvoya, Descovy, and Odefsey because emtricitabine is a component of these formulations. Please see the appropriate section of the drug appendix when using these fixed-dose combinations.
- *Renal elimination*: Competition with other compounds that undergo renal elimination (possible competition for renal tubular secretion). Drugs that decrease renal function could decrease clearance.

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 patients with HIV/hepatitis B (HBV) coinfection 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 used as part of a dual-NRTI backbone in combination antiretroviral therapy.

Efficacy and Pharmacokinetics

Comparative Clinical Trials

Studies assessing the efficacy and/or potency of nucleoside/nucleotide analogues have been more concerned with the dynamic components of the regimen (e.g., tenofovir or abacavir versus the more static components like emtricitabine or lamivudine). Emtricitabine and lamivudine have been considered interchangeable, but little data exist to make this recommendation in antiretroviral (ARV)-naïve patients. Investigators in the ATHENA cohort

compared naive patients who started tenofovir plus emtricitabine or tenofovir plus lamivudine in combination with a ritonavir-boosted protease inhibitor (darunavir, atazanavir, or lopinavir).¹ The adjusted hazard ratio for virologic failure of lamivudine compared to emtricitabine within 240 weeks of starting therapy was 1.15 (95% CI; 0.58–2.27). There was also no difference in time to virologic suppression in the first 48 weeks of therapy or the time to virologic failure after attaining suppression. Yang et al. in the Swiss cohort found a potential difference in efficacy which disappeared after adjusting for pill burden.² Current evidence suggests that emtricitabine and lamivudine have equivalent efficacy and toxicity in ARV-naïve patients.

Efficacy

Based on a dose-finding study described below,³ emtricitabine was studied at a dose of 6 mg/kg once daily in combination with other 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-naïve and 76% of the ARV-experienced children maintained suppression of plasma HIV RNA <400 copies/mL (75% of ARV-naïve children and 67% of ARV-experienced children at <50 copies/mL). Minimal toxicity was observed in this trial. The Saez-Lorens study used a maximum of 240 mg of the liquid formulation. In PACTG P1021,⁴ emtricitabine at a dose of 6 mg/kg (maximum 200 mg/day as liquid) in combination with didanosine and efavirenz, all given once daily, was studied in 37 ARV-naïve children with HIV 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.

Pharmacokinetics Liquid Versus Capsule

A single-dose PK study of emtricitabine liquid solution and capsules was performed in 25 children with HIV aged 2 to 17 years.³ 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. However, plasma concentrations of emtricitabine after administration of the capsule formulation were slightly higher (approx. 20%) in this small cohort.

Pharmacokinetics in Infants

A study in South Africa evaluated the PKs of emtricitabine in 20 infants with perinatal HIV exposure aged <3 months, given emtricitabine as 3 mg/kg once daily for two, 4-day courses, separated by an interval of ≥2 weeks.⁶ 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* µg/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.⁷ Extensive safety data are lacking in this age range.

Considerations for Use

Formulations favor liquid emtricitabine over liquid lamivudine, since the liquid emtricitabine can be given once daily at ARV initiation but liquid lamivudine needs to be given twice daily at ARV initiation. When pill formulations can be administered, again lamivudine and emtricitabine are equivalent.

Both emtricitabine and lamivudine have antiviral activity and efficacy against hepatitis B virus. 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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