Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Emtricitabine (FTC, Emtriva) (Last updated May 22, 2018; last reviewed May 22, 2018)

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

**Formulations**

**Pediatric Oral Solution:** 10 mg/mL  
**Capsules:** 200 mg  
**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  
- [Biktarvy] Bictegravir 50 mg plus emtricitabine 200 mg plus TAF 25 mg

**Dosing Recommendations**

**Note:** See Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV for information about the prevention of perinatal transmission.

**Neonatal and Infant (Aged 0 to <3 Months) Dose**  
**Oral Solution:**  
- 3 mg/kg once daily

**Pediatric (Aged ≥3 Months to 17 Years) Dose**  
**Oral Solution:**  
- 6 mg/kg (to a maximum dose of 240 mg) once daily; the maximum dose of oral solution is higher than the capsule dose because the oral solution has 20% lower plasma exposure in pediatric pharmacokinetic analysis.

**Capsules (Patients Weighing >33 kg):**  
- 200 mg once daily

**Adolescent (Aged ≥18 Years) and Adult Dose**  
**Oral Solution for Those Unable to Swallow Capsules:**  
- 240 mg (24 mL) once daily

**Capsules:**  
- 200 mg once daily

**Selected Adverse Events**

- Severe acute exacerbation of hepatitis can occur in patients with hepatitis B virus (HBV) and HIV who discontinue emtricitabine.
- Hyperpigmentation/skin discoloration on palms and/or soles

**Special Instructions**

- Although emtricitabine can be administered without regard to food, there are food requirements for some fixed-dose combination (FDC) tablet formulations that contain emtricitabine.
- When using FDC tablets, see other sections of the drug appendix for special instructions and additional information about the individual components of the FDC.
- 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.
- Before using emtricitabine, screen patients for HBV

**Metabolism/Elimination**

- No cytochrome P (CYP) 450 interactions
- Renal excretion of emtricitabine is 86%.
[Truvada] Emtricitabine plus TDF (FTC/TDF)

Pediatric Dose:

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>FTC/TDF Tablet Once Daily</th>
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<tbody>
<tr>
<td>17 kg to &lt;22 kg</td>
<td>One FTC/TDF 100 mg/150 mg tablet</td>
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<tr>
<td>22 kg to &lt;28 kg</td>
<td>One FTC/TDF 133 mg/200 mg tablet</td>
</tr>
<tr>
<td>28 kg to &lt;35 kg</td>
<td>One FTC/TDF 167 mg/250 mg tablet</td>
</tr>
<tr>
<td>≥35 kg</td>
<td>One FTC/TDF 200 mg/300 mg tablet</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Dosing Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescent (Weighing ≥35 kg) and Adult</td>
<td>One FTC/TDF 200 mg/300 mg tablet once daily</td>
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</tbody>
</table>

[Descovy] Emtricitabine plus TAF

Pediatric and Adolescent (Weighing ≥25 kg) and Adult Dose:

- **Body Weight 25 to <35 kg:** 1 tablet once daily in combination with other antiretroviral (ARV) agents, except for protease inhibitors (PIs) that require a CYP3A inhibitor (i.e., emtricitabine/TAF [Descovy]) can be used in combination with an integrase strand transfer inhibitor [INSTI] or a non-nucleoside reverse transcriptase inhibitor [NNRTI], but not a boosted PI
- **Body Weight ≥35 kg:** 1 tablet once daily in combination with an INSTI, NNRTI, or boosted PI

[Complera] Emtricitabine plus Rilpivirine plus TDF

Adolescent (Weighing ≥35 kg) and Adult Dose:

- 1 tablet once daily in antiretroviral treatment (ART)-naive patients who have baseline plasma HIV-1 RNA <100,000 copies/mL. This Complera dose can also be used to replace a stable ARV regimen in patients who are currently on their first or second regimen and who have been virologically suppressed (HIV-1 RNA <50 copies/mL) for at least 6 months with no history of virologic failure or resistance to the individual components of Complera.
- Administer with a meal of at least 500 calories.

Emtricitabine may compete with other compounds that undergo renal elimination.

Emtricitabine Dosing in Patients with Renal Impairment:

- Decrease dose in patients with impaired renal function. Consult manufacturer’s prescribing information.
- Do not use the FDC Atripla in patients with creatinine clearance (CrCl) <50 mL/min or in patients who require dialysis.
- Do not use the FDCs Truvada or Biktarvy in patients with CrCl <30 mL/min. Do not use Truvada in patients who require 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 increase in patients with severe renal impairment or end-stage renal disease.
- Striibild 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 for patients with estimated CrCl <30 mL/min.
[Odefsey] Emtricitabine plus Rilpivirine plus TAF
Adolescent (Weighing ≥35 kg) and Adult Dose:

- 1 tablet once daily as initial therapy in ART-naive patients with HIV-1 RNA ≤100,000 copies per mL. This Odefsey dose can also be used to replace a stable ART regimen in patients who have been 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
Adolescent (Weighing ≥35 kg with a Sexual Maturity Rating of 4 or 5) and Adult Dose:

- 1 tablet once daily with food in ART-naive patients. This Stribild dose can also be used to replace a stable ARV regimen in patients who have been 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 Stribild.

[Genvoya] Elvitegravir plus Cobicistat plus Emtricitabine plus TAF
Child and Adolescent (Weighing ≥25 kg) and Adult Dose:

- 1 tablet once daily with food in ART-naive patients. This Genvoya dose can also be used to replace the current ART regimen in patients who have been virologically suppressed (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.

[Biktarvy] Bictegravir plus Emtricitabine plus TAF
Pediatric and Adolescent Dose (Aged <18 Years):

- Biktarvy has not been Food and Drug Administration-approved for use in patients aged <18 years.
- Children aged <12 years: No data on appropriate dose of Biktarvy in children aged <12 years.
- Children and adolescents (aged ≥12 to 18 years and weighing ≥35 kg): 1 tablet once
Drug Interactions (see also the Adults and Adolescent Guidelines and HIV Drug Interaction Checker)

- **Other nucleoside reverse transcriptase inhibitors (NRTIs):** Do not use emtricitabine in combination with lamivudine because these agents share similar resistance profiles and lack additive benefit. Do not use emtricitabine separately with Combivir, Epzicom, or Trizivir because lamivudine is a component of these fixed-dose combinations. Do not use emtricitabine separately when prescribing Truvada, Atripla, Complera, Biktarvy, Strivpit, Genvoa, Descovy, or Odefsey because emtricitabine is a component of these fixed-dose combinations. Please see other sections of the drug appendix for drug interaction information about each individual component when using these fixed-dose combinations.

- **Renal elimination:** Emtricitabine competes with other compounds that undergo renal elimination (possible competition for renal tubular secretion). Drugs that decrease renal function could decrease clearance of emtricitabine.

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 and hepatitis B virus (HBV) 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 and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation.

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 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, such as tenofovir or abacavir, than the more static components, such as emtricitabine or lamivudine. Emtricitabine and lamivudine have been considered interchangeable, but there are little data to support this perspective in antiretroviral (ARV)-naive patients. Investigators studying the ATHENA cohort compared the efficacy of tenofovir disoproxil fumarate (TDF) plus emtricitabine or TDF plus lamivudine in combination with a ritonavir-boosted protease inhibitor (darunavir, atazanavir, or lopinavir) in ARV-naive patients. The adjusted hazard ratio for virologic failure of lamivudine-containing regimens compared to emtricitabine-containing regimens 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 time to virologic failure after attaining suppression. Yang et al. in the Swiss cohort found a potential difference in efficacy that disappeared after adjusting for pill burden. Current evidence suggests that emtricitabine and lamivudine have equivalent efficacy and toxicity in ARV-naive patients.

**Efficacy**

Based on a dose-finding study by Wang et al. (described in the Pharmacokinetics: Liquid Versus Capsule subsection below), emtricitabine 6 mg/kg once daily in combination with other ARV drugs was studied in 116 patients aged 3 months to 16 years. The study used a maximum dosage of 240 mg of the emtricitabine liquid formulation. PK results showed that plasma exposures were similar to those in adults receiving emtricitabine 200 mg once daily. Follow-up data extending to Week 96 indicated that 89% of the ARV-naive children and 76% of the ARV-experienced children maintained plasma HIV RNA <400 copies/mL (75% of ARV-naive children and 67% of ARV-experienced children had HIV RNA <50 copies/mL). Minimal toxicity was observed in this trial. PACTG P1021 studied ARV-naive children aged 3 months to 21 years using emtricitabine 6 mg/kg (with a maximum of emtricitabine 200 mg/day of the liquid formulation) in combination with didanosine and efavirenz, all given once daily. Eighty-five percent of children achieved HIV RNA <400 copies/mL, and 72% of children maintained HIV RNA suppression at <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 enrolled 25 children with HIV aged 2 to 17 years. 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 emtricitabine 6 mg/kg once-daily dose were approximately equivalent to those seen in adults receiving the standard emtricitabine 200-mg dose. However, plasma concentrations of emtricitabine after administration of the capsule formulation were slightly higher (approximately 20%) that those observed with the liquid solution in this small cohort of children.

**Pharmacokinetics in Infants**

A study in South Africa evaluated the PKs of emtricitabine in 20 infants aged <3 months with perinatal HIV exposure. The participants received a dose of emtricitabine 3 mg/kg once daily for two 4-day courses, separated by an interval of ≥2 weeks. Emtricitabine exposure (area under the curve [AUC]) in neonates receiving emtricitabine 3 mg/kg once daily was in the range of pediatric patients aged >3 months receiving the recommended dose of emtricitabine 6 mg/kg once daily and adults receiving the once-daily recommended dose of emtricitabine 200 mg (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. Extensive safety data are lacking for this age range.

**Considerations for Use**

Formulations favor liquid emtricitabine over liquid lamivudine, since 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, lamivudine and emtricitabine are equivalent.
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 Infection Guidelines.

References


