Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Emtricitabine (FTC, Emtriva) (Last updated September 12, 2019; last reviewed September 12, 2019)

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

Formulations

Pediatric Oral Solution: 10 mg/mL
Capsule: 200 mg

Fixed-Dose Combination Tablets:
- [Atripla and Generic] Efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate (TDF) 300 mg
- [Biktarvy] Bictegravir 50 mg/emtricitabine 200 mg/tenofovir alafenamide (TAF) 25 mg
- [Complera] Emtricitabine 200 mg/rilpivirine 25 mg/TDF 300 mg
- [Descovy] Emtricitabine 200 mg/TAF 25 mg
- [Genvoya] Elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/TAF 10 mg
- [Odefsey] Emtricitabine 200 mg/rilpivirine 25 mg/TAF 25 mg
- [Stribild] Elvitegravir 150 mg/cobicistat 150 mg/emtricitabine 200 mg/TDF 300 mg
- [Symtuza] Darunavir 800 mg/cobicistat 150 mg/emtricitabine 200 mg/TAF 10 mg
- [Truvada low-strength tablets]
  - Emtricitabine 100 mg/TDF 150 mg
  - Emtricitabine 133 mg/TDF 200 mg
  - Emtricitabine 167 mg/TDF 250 mg
- [Truvada] Emtricitabine 200 mg/TDF 300 mg

When using fixed-dose combination (FDC) tablets, refer to other sections of the Drug Appendix for special instructions, drug interaction information, and additional information about the individual components of the FDC. See also Appendix A, Table 2, Antiretroviral Fixed-Dose Combination Tablets: Minimum Body Weights and Considerations for Use in Children and Adolescents.

Dosing Recommendations

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

Child (Aged ≥3 Months) and Adolescent Dose
Oral Solution:
- Emtricitabine 6 mg/kg once daily (maximum 240 mg per dose). The maximum dose of oral solution is higher than the capsule dose because the oral solution showed 20% lower plasma exposure during pediatric pharmacokinetic analysis.

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

Adult Dose
Oral Solution for Those Unable to Swallow Capsules:
- Emtricitabine 240 mg (24 mL) once daily

Selected Adverse Events

- Severe acute exacerbation of hepatitis can occur in patients with hepatitis B virus (HBV) and HIV coinfection 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 FDC tablet formulations that contain emtricitabine.
- Emtricitabine oral solution can be kept at room temperature, up to 77°F (25°C), if used within 3 months; refrigerate for long-term storage.
- Before using emtricitabine, screen patients for HBV.
**Capsules:**
- Emtricitabine 200 mg once daily

**[Atripla and Generic] Efavirenz/Emtricitabine/TDF**

**Child and Adolescent (Weighing ≥40 kg) and Adult Dose:**
- One tablet once daily
- Take on an empty stomach.

**[Biktarvy] Bictegravir/Emtricitabine/TAF**

**Child (Weighing <25 kg) Dose:**
- There are currently no data available on the appropriate dose of Biktarvy in children aged <6 years and weighing <25 kg. Studies are currently being conducted to identify the appropriate dose for this age and weight group.

**Child and Adolescent (Weighing ≥25 kg) and Adult Dose:**
- One tablet once daily with or without food in antiretroviral therapy (ART)-naive patients. This dose of Biktarvy can also be used to replace the current antiretroviral (ARV) regimen in patients who have been virologically suppressed (HIV RNA <50 copies/mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of Biktarvy.
- See the bictegravir section for additional information.

**[Complera] Emtricitabine/Rilpivirine/TDF**

**Child and Adolescent (Aged ≥12 Years and Weighing ≥35 kg) and Adult Dose:**
- One tablet once daily in ART-naive patients who have baseline plasma HIV RNA ≤100,000 copies/mL. This dose of Complera 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 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.

**[Descovy] Emtricitabine/TAF**

**Child and Adolescent (Weighing ≥25 kg) and Adult Dose:**
- Body Weight 25 to <35 kg: One tablet once

**Metabolism/Elimination**
- No cytochrome P450 interactions
- Eighty-six percent of emtricitabine is excreted in urine. Emtricitabine may compete with other compounds that undergo renal elimination.

**Emtricitabine Dosing in Patients with Renal Impairment:**
- Decrease the dose of emtricitabine in patients with impaired renal function. Consult the manufacturer’s prescribing information for recommended dose adjustments.
- 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. Monitor frequently 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 use in patients with estimated CrCl <30 mL/min.
daily in combination with other ARV agents, except for protease inhibitors (PIs) that require a cytochrome P450 3A inhibitor (i.e., 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:** One tablet once daily in combination with an INSTI, NNRTI, or boosted PI.

**[Genvoya] Elvitegravir/Cobicistat/Emtricitabine/TAF**

*Child and Adolescent (Weighing ≥ 25 kg) and Adult Dose:*

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

**[Odefsey] Emtricitabine/Rilpivirine/TAF**

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

- One tablet once daily in ART-naive patients with HIV RNA ≤100,000 copies per mL. This dose of Odefsey can also be used to replace a stable ARV regimen in patients who have been virologically suppressed (HIV 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/Cobicistat/Emtricitabine/TDF**

*Child and Adolescent (Weighing ≥ 35 kg with a Sexual Maturity Rating of 4 or 5) and Adult Dose:*

- One tablet once daily with food in ART-naive patients. This dose of Stribild can also be used to replace a stable ARV regimen in patients who have been virologically suppressed (HIV 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.

[Symtuza] Darunavir/Cobicistat/Emtricitabine/TAF

Child and Adolescent (Aged <18 Years) Dose:
- Symtuza has not been approved by the FDA for use in patients aged <18 years.

Adult (Aged ≥18 Years) Dose:
- One tablet taken once daily with food in ARV-naive patients or in patients who have been virologically suppressed for at least 6 months with no known substitutions associated with resistance to darunavir or tenofovir.

[Truvada] Emtricitabine/TDF (FTC/TDF):

Child, Adolescent, and Adult Dose:

Truvada Dosing Table

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Truvada Tablet Once Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 kg to &lt;22 kg</td>
<td>FTC/TDF 100 mg/150 mg tablet</td>
</tr>
<tr>
<td>22 kg to &lt;28 kg</td>
<td>FTC/TDF 133 mg/200 mg tablet</td>
</tr>
<tr>
<td>28 kg to &lt;35 kg</td>
<td>FTC/TDF 167 mg/250 mg tablet</td>
</tr>
<tr>
<td>≥35 kg and Adults</td>
<td>FTC/TDF 200 mg/300 mg tablet</td>
</tr>
</tbody>
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Drug Interactions (see also the Adult and Adolescent Antiretroviral 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 with combination medications that contain lamivudine or emtricitabine. Please see Appendix A, Table 1: Antiretrovirals Available in Fixed-Dose Combination Tablets and refer to other sections of the Drug Appendix for drug interaction information for each individual component of a fixed-dose combination tablet.

- Renal elimination: Emtricitabine may compete with other compounds that undergo renal tubular secretion. Drugs that decrease renal function could decrease clearance of emtricitabine.

Major Toxicities

- More common: Headache, insomnia, diarrhea, nausea, rash. Hyperpigmentation/skin discoloration, which may be more common in children than in adults.

- 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) coinfection who switched from regimens that included emtricitabine to regimens that did not include emtricitabine.

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 approved by the Food and Drug Administration for once-daily administration in children, starting at birth. Emtricitabine is often used as part of a dual-NRTI backbone in antiretroviral (ARV) regimens for children and adolescents due to its once-daily dosing, minimal toxicity, and favorable pediatric pharmacokinetic (PK) data.

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 disoproxil fumarate (TDF), tenofovir alafenamide (TAF), or abacavir, than the more static components, such as emtricitabine or lamivudine. Emtricitabine and lamivudine have been considered interchangeable, but data supporting the ability to switch between these two drugs was lacking. Investigators studying the ATHENA cohort compared the efficacy of TDF plus emtricitabine to TDF plus lamivudine when these drugs were administered with a ritonavir-boosted protease inhibitor (darunavir, atazanavir, or lopinavir) in ARV-naive patients.1 The adjusted hazard ratio for the virologic failure of lamivudine-containing regimens compared to emtricitabine-containing regimens within 240 weeks of starting therapy was 1.15 (95% confidence interval, 0.58–2.27). There was no difference in time to virologic suppression during the first 48 weeks of therapy or time to virologic failure after attaining suppression. In a Swiss cohort, Yang et al. found a potential difference in efficacy between emtricitabine and lamivudine; however, the difference disappeared after adjusting for pill burden.2 Current evidence suggests that emtricitabine and lamivudine have equivalent efficacy and toxicity in ARV-naive patients.

Efficacy

Following a dose-finding study by Wang et al. (described in the Pharmacokinetics: Liquid Versus Capsule section below),3 a once-daily dose of emtricitabine 6 mg/kg administered in combination with other ARV drugs was studied in 116 patients aged 3 months to 16 years.4 The study used a maximum dosage of 240 mg of the emtricitabine liquid formulation. PK results showed that the plasma exposures seen in these children and adolescents were similar to those seen in adults who received emtricitabine 200 mg once daily. Follow-up data extending to Week 96 indicated that 89% of ARV-naive children and 76% of 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 P10215 evaluated the use of emtricitabine 6 mg/kg (with a maximum dose of emtricitabine 200 mg/day of the liquid formulation) in combination with didanosine and efavirenz, all given once daily to ARV-naive children aged 3 months to 21 years. 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.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 who received the emtricitabine 6 mg/kg once-daily dose were approximately equivalent to those seen in adults who received the standard emtricitabine 200-mg dose. However, plasma concentrations of emtricitabine after administration of the capsule formulation were approximately 20% higher than those observed after administration of 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,
Emtricitabine exposure (area under the curve [AUC]) in neonates receiving emtricitabine 3 mg/kg once daily was within the range of exposures seen in pediatric patients aged >3 months who received the recommended dose of emtricitabine 6 mg/kg once daily and adults who received the once-daily recommended dose of emtricitabine 200 mg. 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) who received a single dose of emtricitabine 3 mg/kg and whose mothers received a single dose of emtricitabine 600 mg during delivery, the emtricitabine AUC exceeded the AUC seen in adults and older children. However, emtricitabine had a half-life of 9.2 hours in these neonates, which is similar to that observed in adults and older children. Extensive safety data are lacking for this age range.

Considerations for Use

Liquid emtricitabine has an advantage over liquid lamivudine, since it can be given once daily at ARV initiation while liquid lamivudine needs to be given twice daily at ARV initiation. When pill formulations of lamivudine or emtricitabine are used, they can be administered once daily.

Both emtricitabine and lamivudine have antiviral activity and efficacy against HBV. For a comprehensive review of this topic, see the Hepatitis B Virus section of the Pediatric Opportunistic Infection Guidelines.

References


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