Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Emtricitabine (FTC, Emtriva) (Last updated November 1, 2012; last reviewed November 1, 2012)

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

Combination tablets

- *With tenofovir (TDF):* 200 mg FTC + 300 mg TDF (Truvada)
- *With TDF and efavirenz (EFV):* 200 mg FTC + 300 mg TDF + 600 mg EFV (Atripla)
- *With TDF and rilpivirine (RPV):* 200 mg FTC + 300 mg TDF + 25 mg RPV (Complera)
- *With FTC + elvitegravir (EVG) + cobicistat (COBI):* 200 mg FTC + 150 mg EVG + 150 mg COBI + 300 mg TDF (Stribild)

Dosing Recommendations

Neonate/infant dose (aged 0–<3 months):

- *Oral solution:* 3 mg/kg once daily.

Pediatric dose (aged ≥3 months–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 (for children who weigh >33 kg):* 200 mg once daily.

Adolescent (aged ≥18 years)/adult dose:

- *Oral solution:* 240 mg (24 mL) once daily.
- *Capsules:* 200 mg once daily.

Combination Tablets

Truvada

- *Adolescent (aged ≥12 years and ≥35 kg) and adult dose:* 1 tablet once daily.

Atripla

- *Adolescent (aged ≥12 years and ≥40 kg) and adult dose:* 1 tablet once daily.
- See efavirenz section for pregnancy warning.

Complera

- *Adult dose (aged ≥18 years):* 1 tablet once daily.

Selected Adverse Events

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

Special Instructions

- FTC can be given without regard to food; however, administer Atripla on an empty stomach because it also contains EFV.
- FTC 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 FTC, screen patients for HBV.

Metabolism

- Limited metabolism: No cytochrome P (CYP) 450 interactions.
- Renal excretion 86%: Competition with other compounds that undergo renal elimination.
- Dosing of FTC 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

Stribild: • *Adult dose (aged ≥18 years):* 1 tablet once daily in treatment-naive adults. Administer with food.	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. • If using Stribild, please see the elvitegravir section of the drug appendix for additional information.

Drug Interactions (see also the *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*):

- *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.
- *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-co-infected 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://www.iasusa.org/resistance_mutations/index.html) and the Stanford University HIV Drug Resistance Database offers a discussion of each mutation (see http://hivdb.stanford.edu/pages/GRIP/FTC.html).

Pediatric Use: Emtricitabine is Food and Drug Administration (FDA)-approved for once-daily administration in children starting at birth. Owing to its once-a-day dosing, minimal toxicity, and pediatric pharmacokinetic (PK) data, emtricitabine is commonly used as part of a dual-NRTI backbone in antiretroviral therapy (ART).

A single-dose PK study of emtricitabine liquid solution and capsules was performed in 25 HIV-infected children ages 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 to 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.

Based on this dose-finding study, emtricitabine was given at a dose of 6 mg/kg once daily in combination with other antiretroviral (ARV) drugs.[2, 3] PK results were similar to the preceding dose-finding study.[1] 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 (74% of ARV-naive children and 62% of ARV-experienced children at <50 copies/mL). Minimal toxicity was observed in this trial.

In PACTG P1021, 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.[2] 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/mm^3 at Week 96.

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.[4] 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*ug/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 hrs) was similar.[5] Extensive safety data are lacking in this age range.

References

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2. McKinney RE, Jr., Rodman J, Hu C, et al. Long-term safety and efficacy of a once-daily regimen of emtricitabine, didanosine, and efavirenz in HIV-infected, therapy-naive children and adolescents: Pediatric AIDS Clinical Trials Group Protocol P1021. *Pediatrics*. Aug 2007;120(2):e416-423. Available at http://www.ncbi.nlm.nih.gov/pubmed/17646352.
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