

Lamivudine (3TC, Epivir) (Last updated April 14, 2020; last reviewed April 14, 2020)

Formulations

Pediatric Oral Solution:

- [Epivir] 10 mg/mL
- [Epivir HBV]^a 5 mg/mL

Tablets:

- [Epivir] 150 mg (scored) and 300 mg
- [Epivir HBV]^a 100 mg

Generic Formulations:

- 100 mg, 150 mg, and 300 mg tablets
- Fixed-dose combination (FDC) tablet containing lamivudine 150 mg/zidovudine 300 mg

Fixed-Dose Combination Tablets:

- [Cimduo] Lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Combivir and generic] Lamivudine 150 mg/zidovudine 300 mg
- [Delstrigo] Doravirine 100 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Dovato] Dolutegravir 50 mg/lamivudine 300 mg
- [Epzicom] Abacavir 600 mg/lamivudine 300 mg
- [Symfi] Efavirenz 600 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Symfi Lo] Efavirenz 400 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Temixys] Lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg
- [Triumeq] Abacavir 600 mg/dolutegravir 50 mg/lamivudine 300 mg
- [Trizivir] Abacavir 300 mg/lamivudine 150 mg/zidovudine 300 mg

When using FDC tablets, refer to other sections of the [Drug Appendix](#) for 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](#).

For additional information, see [Drugs@FDA](#) or [DailyMed](#).

Dosing Recommendations

Note: See [Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection](#) and [Table 12](#) for information about using lamivudine (3TC) for the prevention of perinatal HIV transmission.

Neonate (≥32 Weeks Gestation at Birth) and Infant (Birth to <4 Weeks) Dose

Oral Solution:

- 3TC 2 mg/kg twice daily

Infant and Child Dose:

- Once-daily dosing of the 3TC oral solution **is not recommended** when initiating 3TC oral solution in infants and young children. Patients can be transitioned to once-daily treatment with the oral solution when they

Selected Adverse Events

- Severe exacerbation of hepatitis can occur in patients with hepatitis B virus (HBV)/HIV coinfection who discontinue 3TC.

Special Instructions

- 3TC can be given without regard to food.
- Store 3TC oral solution at room temperature.
- Screen patients for HBV infection before using 3TC or FDC tablets that contain 3TC. **Hepatic function and hepatitis B viral load should be monitored for several months after patients with HBV infection stop taking 3TC. Patients with HBV/HIV coinfection who receive Dovato will require additional treatment for chronic HBV infection.**

have been stable on twice-daily treatment for 36 weeks and are aged ≥ 3 years. Please see the note below and refer to the text for more detail.

Aged ≥ 4 Weeks to < 3 Months:

- 3TC 4 mg/kg twice daily of the oral solution

Aged ≥ 3 Months to < 3 Years:

- 3TC 5 mg/kg twice daily of the oral solution (maximum 150 mg per dose)

Aged ≥ 3 Years:

- 3TC 5 mg/kg twice daily of the oral solution (maximum 150 mg per dose); *or*
- 3TC 10 mg/kg once daily of the oral solution (maximum 300 mg per dose)

Weight-Band Dosing for the 10 mg/mL Lamivudine Oral Solution in Children Weighing ≥ 3 kg

Weight	Twice-Daily Dose, AM	Twice-Daily Dose, PM
3 kg to 5.9 kg	3 ml	3 ml
6 kg to 9.9 kg	4 ml	4 ml
10 kg to 13.9 kg	6 ml	6 ml

Weighing ≥ 14 kg and Able to Swallow Tablets:

- Weight-band dosing (see table below; dose is approximately 3TC 5 mg/kg per day twice daily or 3TC 10 mg/kg once daily)
- The scored tablet is the preferred formulation for pediatric patients weighing ≥ 14 kg who can swallow a tablet.

Weight-Band Dosing for the Scored, 150-mg Lamivudine Tablet in Children Weighing ≥ 14 kg

Weight	Twice-Daily Dose, AM	Twice-Daily Dose, PM	Once-Daily Dose
14 kg to < 20 kg	$\frac{1}{2}$ tablet (75 mg)	$\frac{1}{2}$ tablet (75 mg)	1 tablet (150 mg)
≥ 20 kg to < 25 kg	$\frac{1}{2}$ tablet (75 mg)	1 tablet (150 mg)	$1\frac{1}{2}$ tablets (225 mg)
≥ 25 kg	1 tablet (150 mg)	1 tablet (150 mg)	2 tablets (300 mg)

Note: The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) supports switching from twice-daily dosing to once-daily dosing of 3TC (using the oral solution or tablets) in children aged ≥ 3 years who have been clinically stable for 36 weeks

Metabolism/Elimination

- Dose adjustment is required for patients with renal insufficiency.
- FDC tablets should not be used in patients who are on dialysis, patients who have creatinine clearance < 50 mL/min, or patients who have impaired hepatic function.

with undetectable viral loads and stable CD4 T lymphocyte counts. Clinicians should choose a once-daily regimen using the once-daily dose of 3TC indicated above (approximately 3TC 10 mg/kg, with a maximum of 3TC 300 mg once daily).

Child and Adolescent (Weighing \geq 25 kg) and Adult Dose:

- 3TC 150 mg twice daily; *or*
- 3TC 300 mg once daily

[Cimduo] Lamivudine/Tenofovir Disoproxil Fumarate (TDF)

Child and Adolescent (Weighing $>$ 35 kg) and Adult Dose:

- One tablet once daily

[Combivir and Generic] Lamivudine/Zidovudine

Child and Adolescent (Weighing \geq 30 kg) and Adult Dose:

- One tablet twice daily

[Delstrigo] Doravirine/Lamivudine/TDF

Adult Dose:

- One tablet once daily
- The use of Delstrigo has not been studied in children or adolescents (see the [Doravirine](#) section for more information).

[Dovato] Dolutegravir/Lamivudine

Adult Dose:

- One tablet once daily with or without food as a complete antiretroviral (ARV) regimen in antiretroviral therapy (ART)-naive adults with no known mutations associated with resistance to the individual components of Dovato.
- Dovato is not approved by the Food and Drug Administration (FDA) or recommended by the Panel for use in children or adolescents **as a complete ARV regimen. However, it could be used as part of a three-drug regimen in patients who meet the minimum body weight requirements for each component drug.**

[Epzicom] Abacavir/Lamivudine

Child and Adolescent (Weighing \geq 25 kg) and Adult Dose:

- One tablet once daily

[Symfi] Efavirenz 600 mg/Lamivudine/TDF

Child and Adolescent (Weighing \geq 40 kg) and Adult Dose:

- One tablet once daily on an empty stomach

[Symfi Lo] Efavirenz 400 mg/Lamivudine/TDF

Child and Adolescent (Weighing ≥ 35 kg) and Adult Dose:

- One tablet once daily on an empty stomach
- Symfi Lo has not been studied in children (sexual maturity ratings [SMRs] 1–3), and major interindividual variability in efavirenz (EFV) plasma concentrations has been found in pediatric patients in a multi-ethnic setting. The 400 mg dose of EFV may be too low in children or adolescents with SMRs 1 to 3 who weigh ≥ 40 kg. The use of therapeutic drug monitoring is suggested by some Panel members when Symfi Lo is used in pediatric patients who weigh ≥ 40 kg. See the [Efavirenz](#) section for more information.

[Temixys] Lamivudine/TDF

Child and Adolescent (Weighing ≥ 35 kg) and Adult Dose:

- One tablet once daily

[Triumeq] Abacavir/Dolutegravir/Lamivudine

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

- One tablet once daily
- This FDC tablet can be used in patients who are ART-naive or ART-experienced (but integrase strand transfer inhibitor-naive) and who are not being treated with uridine diphosphate glucuronosyltransferase 1A1 or cytochrome P450 3A inducers.
- The FDA-approved dose for pediatric patients is one tablet once daily for patients weighing ≥ 40 kg (see the [Dolutegravir](#) section for more information).

[Trizivir and Generic] Abacavir/Lamivudine/Zidovudine

Child and Adolescent (Weighing ≥ 30 kg) and Adult Dose:

- One tablet twice daily

^a Eпивir HBV oral solution and tablets contain a lower amount of 3TC than Eпивir oral solution and tablets. The amount of 3TC in the Eпивir HBV solution and tablet was based on dosing for treatment of HBV infection in people without HIV coinfection. Patients with HIV who are taking Eпивir HBV as part of their ARV regimen should receive the appropriate amount of oral solution or the appropriate number of tablets to achieve the higher doses of 3TC that are used to treat HIV.

Drug Interactions (see also the [Adult and Adolescent Antiretroviral Guidelines](#) and the [HIV Drug Interaction Checker](#))

- Drugs that decrease renal function could decrease clearance of lamivudine (3TC).

- **Do not use** 3TC in combination with emtricitabine (FTC), because these drugs have similar resistance profiles and using them together offers no additional benefit.¹ **Do not use** 3TC with fixed-dose combination (FDC) medications that contain 3TC or FTC. 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 about each individual component of FDC tablets.

Major Toxicities

- *More common:* Headache, nausea.
- *Less common (more severe):* Peripheral neuropathy, lipodystrophy/lipoatrophy.
- *Rare:* Increased levels of liver enzymes. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported.

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

3TC is approved by the Food and Drug Administration (FDA) for the treatment of children aged ≥ 3 months.

Considerations for Use

The efficacy and toxicity of 3TC are equivalent to the efficacy and toxicity of FTC. The oral formulation of FTC has an advantage over the liquid formulation of 3TC, since it can be given once daily at antiretroviral (ARV) initiation while the liquid formulation of 3TC needs to be given twice daily at ARV initiation. When pill formulations of 3TC or FTC are used, they can be administered once daily.

Comparative Clinical Trials

Studies that assess 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 (ABC), than the more static components, such as FTC or 3TC. FTC and 3TC have been considered to be interchangeable, but there is a lack of data to support this conclusion. Investigators studying the ATHENA cohort compared the efficacy of TDF plus FTC to TDF plus 3TC when these drugs were administered with a ritonavir-boosted protease inhibitor (darunavir, atazanavir, or lopinavir) in ART-naïve patients.² The adjusted hazard ratio for the virologic failure of 3TC-containing regimens compared to FTC-containing regimens within 240 weeks of starting therapy was 1.15 (95% confidence interval, 0.58–2.27). There was no difference between these regimens 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 FTC and 3TC; however, the difference disappeared after adjusting for pill burden. Current evidence suggests that FTC and 3TC have equivalent efficacy and toxicity in ARV-naïve patients.³

Efficacy

3TC has been studied in children with HIV both alone and in combination with other ARV drugs. Extensive data have demonstrated the safety of 3TC and have shown that this drug is associated with clinical improvement and virologic response. It is commonly used in children with HIV as a component of a dual-NRTI backbone.⁴⁻¹² In one study that evaluated the efficacy of NRTI background components, the combination of 3TC plus ABC was superior to zidovudine (ZDV) plus 3TC or ZDV plus ABC in achieving long-term virologic efficacy.¹³

Pharmacokinetics in Infants

Because of its safety profile and availability in a liquid formulation, 3TC has been given to infants during the first 6 weeks of life starting at a dose of 2 mg/kg every 12 hours before age 4 weeks.⁹ A population pharmacokinetic (PK) analysis of infants who received 3TC affirms that adjusting the dose from 3TC 2 mg/kg to 3TC 4 mg/kg every 12 hours at age 4 weeks provides optimal 3TC exposure for infants with normal maturation of renal function.¹⁴ For infants, the World Health Organization weight-band dosing (which is up to five times higher than the FDA-approved dose) results in greater plasma concentrations than the 3TC 2 mg/kg dose.¹⁵ In HPTN 040, 3TC was administered with nelfinavir and 6 weeks of ZDV according to a weight-band dosing scheme to prevent perinatal transmission during the first 2 weeks of life. For 2 weeks, all infants weighing >2,000 g received 3TC 6 mg twice daily, and infants weighing ≤2,000 g received 3TC 4 mg twice daily. These doses resulted in 3TC exposure that was similar to the exposure seen in infants who received the standard twice-daily dosing schedule of 3TC 2 mg/kg per dose for neonates.¹⁶

Pharmacokinetics of Liquid versus Tablet Preparations

The PKs of 3TC have been studied after either single or repeat doses in 210 pediatric subjects. Pediatric subjects who received 3TC oral solution according to the recommended dose regimen achieved plasma concentrations of 3TC that were approximately 25% lower than those of adults with HIV who received the oral solution. Pediatric subjects who received 3TC tablets achieved plasma concentrations that were comparable to or slightly higher than those observed in adults who received tablets. In pediatric subjects, the relative bioavailability of 3TC oral solution is approximately 40% lower than the relative bioavailability of tablets that contain 3TC, despite no difference in the bioavailability of these two formulations among adults. The mechanisms for the diminished relative bioavailability of 3TC oral solution are unknown,¹⁷ but results from a study in adults that compared the PKs of 3TC oral solution administered either alone or with increasing concentrations of sorbitol indicates that sorbitol decreases the total exposure of 3TC oral solution.¹⁸ Sorbitol is a component of several ARV solutions, as well as common over-the-counter medications that may be used in infants and young children; this may explain the PK discrepancy between the oral solution and tablet formulations. Modeling of PK data in pediatric patients suggests that increasing the oral solution dose to 3TC 5 mg/kg per dose twice daily or 3TC 10 mg/kg per dose once daily (with a maximum of 3TC 300 mg administered daily) in children aged ≥3 months would provide exposures similar to those seen in adult patients who received tablet formulations. The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) **does not recommend** using a once-daily dose of 3TC until a child is aged ≥3 years. However, this new dosing schedule is now included in the 3TC package insert, even though there are no clinical data from patients who received both 3TC and sorbitol-containing medications.

Dosing Considerations—Once-Daily versus Twice-Daily Administration

The standard adult dose for 3TC is 300 mg once daily, but there is a lack of data on once-daily administration of 3TC in children. Population PK data indicate that once-daily dosing of 3TC 8 mg/kg leads to area under the curve (AUC_{0-24h}) values that are similar to those seen in patients taking 3TC 4 mg/kg twice daily, but C_{min} values are significantly lower and C_{max} values are significantly higher in children aged 1 to 18 years.¹⁹ Intensive PKs of once-daily versus twice-daily dosing of 3TC were evaluated in children with HIV aged 2 to 13 years in the PENTA 13 trial⁴ and in children aged 3 to 36 months in the PENTA 15 trial.²⁰ Both the PENTA 13 and PENTA 15 trials used a crossover design with doses of 3TC 8 mg/kg once daily or 3TC 4 mg/kg twice daily. AUC₀₋₂₄ and clearance values were similar between these two dosing schedules, and most children maintained an undetectable HIV RNA value after the switch. An ARROW trial PK study of 41 children aged 3 to 12 years (median age 7.6 years) in Uganda who were stable on twice-daily 3TC also showed equivalent AUC_{0-24h} and good clinical outcomes (defined by a low disease stage and a high CD4 T lymphocyte [CD4] cell count) after switching to once-daily 3TC. Median follow-up time during this study was 1.15 years.²¹ The larger ARROW trial was a randomized, noninferiority trial that investigated once-daily versus twice-daily doses of 3TC in >600 pediatric patients who had initiated therapy with twice-daily 3TC and who had been receiving therapy for ≥36 weeks. Median follow-up time during the study was 114 weeks.

Rates of plasma HIV RNA suppression and adverse event profiles for once-daily 3TC were similar to (and statistically noninferior to) those of twice-daily 3TC.²²

All four of the studies discussed above enrolled patients who had a low plasma HIV RNA or who were clinically stable on twice-daily 3TC before switching to once-daily dosing. Therefore, the Panel supports switching from twice-daily to once-daily dosing of 3TC in children aged ≥ 3 years who have been clinically stable for 36 weeks with an undetectable viral load and stable CD4 count. Clinicians should use a 10 mg/kg per dose of 3TC oral solution or a weight-based dose of 3TC tablets (neither exceeding 3TC 300 mg) as part of a once-daily regimen.²³ More long-term clinical trials with viral efficacy endpoints are needed to confirm that once-daily dosing of 3TC can be used effectively as part of an initial ARV regimen in children.

3TC undergoes intracellular metabolism to reach its active form, 3TC triphosphate. In adolescents, the mean half-life of intracellular 3TC triphosphate (17.7 hours) is considerably longer than that of unphosphorylated 3TC in plasma (1.5–2 hours). Intracellular concentrations of 3TC triphosphate are equivalent whether 3TC is given once daily or twice daily in adults and adolescents. This supports a recommendation for once-daily 3TC dosing based on FDA recommendations.^{24,25}

Considerations for Use

Weight-band dosing recommendations for 3TC have been developed for children weighing ≥ 3 kg and receiving either the 10 mg/mL oral solution or the 150-mg scored tablets.²⁶⁻²⁸

Both FTC and 3TC have antiviral activity and efficacy against hepatitis B virus. For a comprehensive review of this topic, see the [Hepatitis B Virus](#) section in the [Pediatric Opportunistic Infection Guidelines](#).

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