

# Zidovudine-Lamivudine (*Combivir*)

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## Drug Summary

Zidovudine-lamivudine is a nucleoside reverse transcriptase inhibitor combination tablet that was used as the backbone component of combination antiretroviral therapy for years, but now is rarely used due to short-term and long-term toxicity. Lamivudine is usually well-tolerated. Zidovudine, however, frequently causes gastrointestinal side effects, headache, and malaise. Patients taking zidovudine for a prolonged period can develop neutropenia, anemia, myopathy, lactic acidosis, lipoatrophy, and hepatomegaly with steatosis. In addition, the zidovudine-lamivudine combination requires twice-daily dosing. Patients who currently take zidovudine-lamivudine should be strongly encouraged to change to a recommended agent.

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## Key Clinical Trials

In the early years of antiretroviral therapy, before three-drug antiretroviral therapy became the standard of care, zidovudine-lamivudine was studied as dual therapy for treatment of HIV infection, and this strategy demonstrated immunologic benefit as compared to zidovudine or stavudine monotherapy, even in individuals with lamivudine resistance [[NUCA 3001](#)], [[ACTG 306](#)], [[ACTG 298](#)]. Subsequently, zidovudine-lamivudine was shown to be effective as part of various 3-drug combinations, including with indinavir [[ACTG 320](#)], [[ACTG 343](#)], [[054/069](#)], ritonavir [[ACTG 315](#)], amprenavir [[ACTG 347](#)], and efavirenz [[GESIDA 3903](#)]. Later, three-drug combinations that included zidovudine-lamivudine were compared to combinations with newer NRTIs such as tenofovir disoproxil fumarate-emtricitabine; the combinations with newer NRTIs demonstrated superior efficacy with less toxicity [[GS-934](#)]. Also, switching from zidovudine-lamivudine to tenofovir disoproxil fumarate-emtricitabine (each combined with efavirenz) was shown to produce equivalent HIV control but less adverse impact on hematologic parameters, lipids, and limb fat, as compared to continuing zidovudine-lamivudine [[SWEET](#)].

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## Adverse Effects

Zidovudine commonly causes gastrointestinal side effects, such as nausea, vomiting, and loss of appetite. It can cause headache, weakness, dizziness, and other general symptoms, as well as peripheral neuropathy, bone marrow toxicity, including anemia and neutropenia, lipoatrophy, and lactic acidosis. Overall, lamivudine tends to be well tolerated. It may rarely cause side effects such as headache, diarrhea, nausea, or rash. It may be difficult to distinguish the cause of these side effects, since they are more commonly caused by zidovudine.

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## Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), **zidovudine-lamivudine** is designated as an Alternative Two-NRTI backbone combination in the category Alternative Initial Regimens in Pregnancy.

- For additional information regarding the safety and toxicity of zidovudine-lamivudine in pregnancy see the HHS Perinatal Guidelines summaries on [Zidovudine](#) and [Lamivudine](#).
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## Resistance

For a listing of the most common clinically significant mutations associated with zidovudine-lamivudine (ZDV-3TC) resistance, see the [NRTI Resistance Notes on the Stanford University HIV Drug Resistance Database](#).

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## Key Drug Interactions

For complete information on zidovudine-lamivudine-related drug interactions, see the [Drug Interactions section in the Zidovudine-Lamivudine \(Combivir\) Prescribing Information](#).

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