

## lamivudine/nevirapine/zidovudine – New drug approval

- On August 13, 2018, the FDA approved Micro Labs' [lamivudine/nevirapine/zidovudine](#), for use alone as a complete regimen or in combination with other antiretroviral drugs for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults and pediatric patients weighing at least 35 kg.
  - Based on serious and life-threatening hepatotoxicity observed in controlled and uncontrolled trials, lamivudine/nevirapine/zidovudine is not recommended to be initiated, unless the benefit outweighs the risks, in adult females with CD4+ cell counts > 250 cells/mm<sup>3</sup> or adult males with CD4+ cell counts > 400 cells/mm<sup>3</sup>.
- [Lamivudine](#) and [zidovudine](#) are both nucleoside reverse transcriptase inhibitors and [nevirapine](#) is a non-nucleoside reverse transcriptase inhibitor (NNRTI).
- The safety and efficacy of lamivudine plus zidovudine was evaluated in a placebo-controlled study of 1,816 HIV-1 infected adults, comparing continued current therapy (zidovudine alone or zidovudine with [didanosine](#) or zalcitabine) + lamivudine or lamivudine + an investigational NNRTI.
  - A greater percentage of patients who continued on current therapy alone experienced at least one HIV-1 disease-progression event or death vs. patients who had lamivudine or lamivudine + NNRTI added to their current therapy (19.6% vs. 9.6% and 8.9%, respectively).
- The safety and efficacy of nevirapine was established in two placebo-controlled studies that enrolled 2,400 HIV-1 infected adult patients. The first study compared treatment with nevirapine + lamivudine + background therapy vs. lamivudine + background therapy. The second study compared treatment with nevirapine + zidovudine + didanosine vs. nevirapine + zidovudine and zidovudine + didanosine.
  - In the first study, a greater proportion of patients in the nevirapine group were treatment responders (HIV-1 RNA < 50 copies/mL) vs. the lamivudine + background therapy group (18% vs. 2%, respectively).
  - In the second study, a greater proportion of patients treated with nevirapine + zidovudine + didanosine experienced treatment response (HIV-1 RNA < 400 copies/mL) vs. the zidovudine + didanosine group and the nevirapine + zidovudine group (45% vs. 19% and 0%, respectively.)
- Lamivudine/nevirapine/zidovudine carries a boxed warning for the risk of life-threatening (including fatal) hepatotoxicity, skin reactions, hematologic toxicity, myopathy, lactic acidosis and severe hepatomegaly with steatosis, and exacerbations of hepatitis B.
- Lamivudine/nevirapine/zidovudine is contraindicated in patients with a previous hypersensitivity reaction, patients with moderate or severe (Child-Pugh Class B or C, respectively) hepatic impairment, and for use as part of occupational and non-occupational post-exposure prophylaxis regimens, an unapproved use.
- Other warnings and precautions of lamivudine/nevirapine/zidovudine include use with interferon-and [ribavirin](#)-based regimens, pancreatitis, lipodystrophy, drug interactions, resistance, and immune reconstitution syndrome.
- The most common adverse reactions ( $\geq 15\%$ ) with lamivudine and zidovudine use were nausea, headache, malaise and fatigue, nasal signs and symptoms, diarrhea, and cough.

- The most common adverse reaction (15% vs. 6% with placebo) with nevirapine use was rash. In pediatric patients, the incidence of rash was 21%.
- The recommended dose of lamivudine/nevirapine/zidovudine in adults and pediatric patients weighing at least 35 kg is as follows:

Regimen timing	Dosage
First 14 days	One lamivudine/nevirapine/zidovudine fixed-dose tablet administered orally once daily followed by a daily oral dose of lamivudine and zidovudine 12 hours later.
After 14 days	One lamivudine/nevirapine/zidovudine fixed-dose tablet administered orally twice daily.

- Intensive clinical and laboratory monitoring, including liver enzyme tests, is essential at baseline and during the first 18 weeks of treatment. After the initial 18 week period, frequent clinical and laboratory monitoring should continue throughout treatment.
  - The 14-day lead-in period with nevirapine 200 mg once daily must be strictly followed; it has been demonstrated to reduce the frequency of rash.
- Micro Labs' launch plans for lamivudine/nevirapine/zidovudine are pending. Lamivudine/nevirapine/zidovudine will be available in a fixed-dose combination tablet containing 150 mg lamivudine, 200 mg nevirapine, and 300 mg zidovudine.



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