

Dolutegravir-Lamivudine (*Dovato*)

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Drug Summary

Dolutegravir-lamivudine is a two-drug antiretroviral combination tablet approved for initial therapy for treatment-naïve individuals who have no known or suspected resistance to the two components (dolutegravir, an integrase strand transfer inhibitor, and lamivudine, a nucleoside reverse transcriptase inhibitor). This two-drug antiretroviral tablet was studied as a complete regimen for treatment-naïve adults in two small single arm studies and then in a randomized controlled trial that compared dolutegravir-lamivudine initial therapy to dolutegravir plus tenofovir DF-emtricitabine. In these trials, dolutegravir-lamivudine was found to be effective first-line therapy. Potential advantages of this option for first-line therapy include avoidance of the NRTI's tenofovir DF, tenofovir alafenamide, and abacavir. This may be beneficial for individuals with contraindications to those NRTI's (such as significant renal insufficiency, ischemic cardiovascular disease, or positive HLA-B*5701 testing). Optimal candidates for two-drug initial ART have not been established. It is important to note that dolutegravir-lamivudine is not adequate treatment for hepatitis B coinfection. In addition, all of the trials of dolutegravir-lamivudine as initial therapy excluded individuals with very high screening HIV RNA levels.

Key Clinical Trials

For treatment-naïve individuals, dolutegravir-lamivudine was studied in a small, single-arm, pilot study that enrolled 20 adults with screening HIV RNA below 100,000 copies/mL and 90% (18 of 20) of the participants achieved suppressed HIV RNA levels at week 48 [[PADDLE](#)]. Another single arm trial enrolled 120 treatment-naïve adults with HIV RNA below 500,000 copies/mL to receive dolutegravir plus lamivudine and 85% achieved HIV RNA below 50 copies/mL at 48 weeks; there was no significant difference in viral suppression rates between those with a baseline HIV RNA below 100,000 copies/mL versus those between 100,000 and 500,000 copies/mL [[ACTG 5353](#)]. Two identical, double-blind, randomized controlled trials enrolled treatment-naïve adults with HIV RNA less than 500,000 copies/mL to receive a two-drug regimen of dolutegravir plus lamivudine or a three-drug regimen of dolutegravir plus tenofovir DF-emtricitabine triple antiretroviral therapy [[GEMINI-1](#) and [GEMINI-2](#)]. At 48 weeks, HIV RNA levels were less than 50 copies/mL in 91% of (655 of 716) individuals in the dolutegravir-lamivudine arm versus 93% of (669 of 717) in the dolutegravir plus emtricitabine-tenofovir DF arm. Markers of renal proximal tubulopathy and bone mineral density were better in the two-drug regimen. Of note, all of these trials excluded individuals with chronic hepatitis B infection.

Dolutegravir plus lamivudine dual therapy has also been studied for maintenance antiretroviral therapy (a simplification strategy after an individual with no past virologic failure or resistance has a routinely suppressed HIV RNA for at least 6 months [[LAMIDOL](#) and [ASPIRE](#)]).

Adverse Effects

Overall, lamivudine tends to be well tolerated. It may rarely cause side effects such as headache, diarrhea, nausea, or rash. Adverse effects to dolutegravir are uncommon, and usually mild. Headaches, insomnia, and psychiatric symptoms have been reported, as have rash and hypersensitivity reaction. Dolutegravir inhibits tubular secretion of creatinine and may increase serum creatinine (average increase of 0.12 mg/dL); it has no effect on actual (measured) glomerular filtration rate (GFR). Creatinine elevation may occur in the early weeks after initiation of dolutegravir and does not worsen with time.

Dolutegravir Safety Alert: On May 18, 2018, an [FDA Safety Alert](#) was posted that warned of potential serious neural tube birth defects in infants born to mothers who received dolutegravir at the time of becoming pregnant or early in the first trimester. On May 30, 2018, the HHS Antiretroviral Guideline Panels issued [Recommendations Regarding Dolutegravir](#) that address the use of dolutegravir in adults and adolescents with HIV who are pregnant or of child-bearing potential.

Key Drug Interactions

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