Doravirine-Tenofovir DF-Lamivudine (Delstrigo)

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Drug Summary

Doravirine-tenofovir DF-lamivudine is a single-tablet regimen dosed once daily with or without food that is approved for use in persons with no antiretroviral history. The non-nucleoside reverse transcriptase inhibitor (NNRTI) anchor drug in this regimen—doravirine—retains activity in the presence of common NNRTI drug-resistant mutations (e.g. K103N, Y181C, G190A) and thus may have clinical utility for individuals with resistance to other NNRTI’s. Treatment failure with doravirine can result in emergence of resistance associated substitutions that may confer cross-resistance resistance to efavirenz, etravirine, nevirapine, and rilpivirine. Unlike the NNRTI rilpivirine, there are no CD4 count or HIV RNA level criteria for the use of doravirine. In addition, doravirine does not have restrictions for use in combination with proton pump inhibitors. The single-tablet regimen doravirine-tenofovir DF-lamivudine is a potent and well-tolerated NNRTI single-tablet regimen, but its use may be somewhat limited by the since current recommendations to use integrase strand transfer inhibitors as the anchor drug when initiating antiretroviral therapy.

Key Clinical Trials

- **DRIVE AHEAD**: This phase 3, randomized-controlled trial compared doravirine-tenofovir DF-lamivudine to efavirenz-tenofovir DF-emtricitabine as therapy for treatment-naïve individuals. Investigators randomized 364 individuals to each arm and at 48 weeks results demonstrated non-inferiority of the doravirine regimen by FDA snapshot (proportion of participants with HIV RNA below 50 copies/mL was 84.3% in the doravirine arm versus 80.8% in the efavirenz arm by intention-to-treat analysis). Results also showed that less rash, central nervous side effects, and lipid changes occurred in the doravirine arm and there were overall fewer treatment discontinuations due to adverse effects as compared to the efavirenz arm.
- **DRIVE FORWARD**: In this phase 3 study, doravirine was compared to ritonavir-boosted darunavir as initial antiretroviral therapy, each with two NRTIs. In the primary analysis, there were 383 participants in each arm; at 48 weeks, doravirine was non-inferior to ritonavir-boosted darunavir (HIV RNA less than 50 copies/mL in 83.8% versus 79.9%, respectively). Overall rates of drug-related adverse events were similar between the two arms, though lipid parameters were more favorable in the doravirine group.
- **DRIVE SHIFT**: In this open-label, active-controlled, non-inferiority trial, investigators enrolled 670 adults who had suppressed HIV RNA levels for at least 6 months and randomized them...
(2:1) to switch to once-daily single-tablet regimen of doravirine plus tenofovir DF plus lamivudine or to continue on their current antiretroviral regimen. Participants enrolled were taking two nucleoside reverse transcriptase inhibitors (NRTIs) plus either (1) a boosted protease inhibitor, (2) boosted elvitegravir, or (3) a non-nucleoside reverse transcriptase inhibitor.

**Adverse Effects**

The adverse effects that occurred in trials in more than 5% of participants consisted of dizziness, nausea, and abnormal dreams. Tenofovir DF may cause nephrotoxicity and decreases in bone mineral density. Doravirine-tenofovir DF-lamivudine should not be used in persons with a creatinine clearance less than 50 mL/min.

**Key Drug Interactions**

For complete information on doravirine-tenofovir df-lamivudine-related drug interactions, see the Drug Interactions section in the Doravirine-Tenofovir DF-Lamivudine (Delstrigo) Prescribing Information.

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