Dovato™ (dolutegravir and lamivudine) – New drug approval

- On April 8, 2019, the FDA announced the approval of ViiV Healthcare's Dovato (dolutegravir and lamivudine), as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults with no antiretroviral treatment history and with no known substitutions associated with resistance to the individual components of Dovato.

- Dovato is the first FDA-approved two-drug, fixed-dose, complete regimen for HIV-infected adults who have never received treatment for HIV.

    — Currently, the standard of care for patients who have never been treated is a three-drug regimen.

- Dovato is a fixed-dose combination of lamivudine, a nucleoside analogue reverse transcriptase inhibitor (NRTI), and dolutegravir, the active ingredient in Tivicay®, an integrase strand transfer inhibitor.

- The efficacy of Dovato was established in two identical, double-blind, non-inferiority studies (GEMINI-1 and GEMINI-2) in 1,433 HIV-1 infected adults with no antiretroviral treatment history. Patients were randomized to receive a 2-drug regimen of Tivicay 50 mg plus lamivudine 300 mg administered once daily or Tivicay 50 mg plus fixed-dose Truvada (tenofovir disoproxil fumarate and emtricitabine) administered once daily. The primary efficacy endpoint for each GEMINI trial was the proportion of subjects with plasma HIV-1 RNA < 50 copies/mL at week 48. Non-inferiority was assessed using a margin of 10%.

    — The percentage of patients achieving the primary endpoint in the pooled analysis was 91% with Tivicay plus lamivudine vs. 93% with Tivicay plus Truvada. The treatment difference was -1.7% (95% CI: -4.4, -1.1).
    — At week 48, no patients had any detectable treatment-emergent substitutions associated with resistance to dolutegravir or NRTIs.

- Dovato carries a boxed warning for patients co-infected with hepatitis B virus (HBV) and HIV-1 due to the emergence of lamivudine-resistant HBV and exacerbations of HBV.

- Dovato is contraindicated in patients with prior hypersensitivity reaction to dolutegravir or lamivudine and in patients receiving dofetilide, due to the potential for increased dofetilide plasma concentrations and the risk for serious and/or life-threatening events.

- Additional warnings and precautions of Dovato include hypersensitivity reactions, hepatotoxicity, embryo-fetal toxicity, lactic acidosis and severe hepatomegaly with steatosis, risk of adverse reactions or loss of virologic response due to drug interactions, and immune reconstitution syndrome.

- The most common adverse reactions (≥ 2%) with Dovato use were headache, diarrhea, nausea, insomnia, and fatigue.

- The recommended dosage regimen of Dovato in adults is one tablet taken orally once daily with or without food.

    — Prior to or when initiating Dovato, patients should be tested for HBV infection

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- ViiV Healthcare plans to launch Dovato in late April. Dovato will be available as a 50 mg of dolutegravir and 300 mg of lamivudine fixed-dose combination tablet.