Delstrigo™ (doravirine/lamivudine/tenofovir disoproxil fumarate) and Pifeltro™ (doravirine) – New drug approvals

- On August 30, 2018, Merck announced the FDA approval of Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) as a complete regimen, and the FDA approval of Pifeltro (doravirine) in combination with other antiretroviral agents, for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adult patients with no prior antiretroviral treatment history.

- Doravirine is a new non-nucleoside reverse transcriptase inhibitor (NNRTI); lamivudine and tenofovir are both nucleoside reverse transcriptase inhibitors (NRTIs).

- The safety and efficacy of Delstrigo were evaluated in the DRIVE-AHEAD clinical trial, enrolling 728 HIV-1 infected adult patients with no antiretroviral treatment history. Patients were randomized to receive either Delstrigo or efavirenz/emtricitabine/tenofovir disoproxil fumarate (EFV/FTC/TDF) once daily. Virologic outcomes were assessed at 48 weeks.

    — HIV-1 RNA < 50 copies/mL was achieved in 84% of the Delstrigo treated patients vs. 81% of EFV/FTC/TDF treated patients (Difference: 3.5% [95% CI: -2.0, 9.0]).

- The safety and efficacy of Pifeltro were evaluated in the DRIVE-FORWARD clinical trial, enrolling 766 HIV-1 infected adult patients with no antiretroviral treatment history. Patients were randomized to receive Pifeltro or darunavir + ritonavir (DRV+r) once daily, each in combination with FTC/TDF or abacavir (ABC)/lamivudine (3TC). Virologic outcomes were assessed at 48 weeks.

    — HIV-1 RNA < 50 copies/mL was achieved in 84% of the Delstrigo treated patients vs. 80% of the DRV+r + 2 NRTIs treated patients (Difference:3.9% [95% CI: -1.6, 9.4]).

- Delstrigo carries a boxed warning regarding the risk of posttreatment acute exacerbations of hepatitis B.

- Delstrigo and Pifeltro are both contraindicated when co-administered with drugs that are strong cytochrome P450 3A enzyme inducers as significant decreases in doravirine plasma concentrations may occur, which may decrease the effectiveness of Delstrigo or Pifeltro. Destrigo is also contraindicated in patients with a previous hypersensitivity reaction to lamivudine.

- Other warnings and precautions of Delstrigo include new onset or worsening renal impairment, risk of adverse reactions or loss of virologic response due to drug interactions, bone loss and mineralization defects, and immune reconstitution syndrome.

- Other warnings and precautions of Pifeltro include risk of adverse reactions or loss of virologic response due to drug interactions and immune reconstitution syndrome.

- The most common adverse reactions (≥ 5%) with Delstrigo use were dizziness, nausea, and abnormal dreams.

- The most common adverse reactions (≥ 5%) with Pifeltro use were nausea, dizziness, headache, fatigue, diarrhea, abdominal pain, and abnormal dreams.

- The recommended dose of Delstrigo in adults is one tablet taken orally once daily with or without food.

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  - — Prior to or when initiating Delstrigo, test patients for hepatitis B infection.
  - — Prior to or when initiating Delstrigo, and during treatment, on a clinically appropriate schedule, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorous.

- The recommended dose of Pifeltro in adults is one tablet taken orally once daily with or without food.

- Merck plans to launch Delstrigo and Pifeltro within one month. Delstrigo will be available in a fixed-dose combination tablet containing 100 mg doravirine, 300 mg 3TC, and 300 mg TDF. Pifeltro will be available as a 100 mg tablet.