Symfi Lo™ (efavirenz/lamivudine/tenofovir disoproxil fumarate) – New drug approval

- On February 7, 2018, the FDA announced the approval of Mylan's Symfi Lo (efavirenz [EFV]/lamivudine [3TC]/tenofovir disoproxil fumarate [TDF]) as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adult and pediatric patients weighing at least 35 k.

- The approval of Symfi Lo was based on data from two clinical studies of 1,230 treatment-naïve adult patients with HIV-1 infection. The first study evaluated the efficacy of a triple drug regimen of EFV/3TC/TDF vs. EFV/3TC/stavudine (d4T). The second study compared 400 mg of EFV to a 600 mg dose of EFV in a triple drug regimen.

    - In the first study, 79% of patients were responders (HIV-1 RNA < 400 copies/mL) in the EFV/3TC/TDF group vs. 82% in the EFV/3TC/d4T group at week 48, and 68% of patients were responders in the EFV/3TC/TDF group vs.62% in the EFV/3TC/d4T group at week 144.
    - Through 144 weeks of therapy, 62% and 58% of subjects in the TDF and d4T groups, respectively, achieved and maintained confirmed HIV-1 RNA < 50 copies/mL.
    - In the second study, achievement of plasma HIV-1 RNA < 50 copies/mL at week 48 was similar between the EFV 400 mg and EFV 600 mg groups (86% vs. 84%, respectively).

- Symfi Lo carries a boxed warning for post-treatment acute exacerbations of hepatitis B.

- Symfi Lo is contraindicated in patients with a previous hypersensitivity reaction (eg, Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions) to any of the components contained in the formulation, and when coadministered with Zepatier® (elbasvir/grazoprevir).

- Other warnings and precautions of Symfi Lo include lactic acidosis and severe hepatomegaly with steatosis, risk of adverse reactions or loss of virologic response due to drug interactions, new onset or worsening renal impairment, psychiatric symptoms, nervous system symptoms, embryo-fetal toxicity, skin and systemic hypersensitivity reaction, hepatotoxicity, risk of hepatic decompensation when used with interferon- and ribavirin-based regimens, pancreatitis, convulsions, lipid elevations, bone effects, immune reconstitution syndrome, fat redistribution, and QTc prolongation.

- The most common adverse reactions (> 5%) with Symfi Lo use were rash and dizziness.

- The recommended dosage of Symfi Lo is one tablet taken orally once daily preferably at bedtime. Dosing at bedtime may improve tolerability of nervous system symptoms.

    - Prior to initiation of Symfi Lo, patients should be tested for hepatitis B virus infection.
    - Serum creatinine, serum phosphorus, estimated creatinine clearance, urine glucose, and urine protein should be assessed before initiating Symfi Lo and during therapy in all patients as clinically appropriate.
    - Hepatic function should be monitored prior to and during treatment with Symfi Lo.

- Mylan plans to launch Symfi Lo in 4 to 6 weeks. Symfi Lo is a three-drug, fixed-dose combination product containing 400 mg of EFV, 300 mg of 3TC, and 300 mg of TDF.