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

- On March 22, 2018, the FDA approved Mylan's Symfi (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 ≥ 40 kg.

- Symfi is three-drug, fixed-dose combination of EFV, a non-nucleoside reverse transcriptase inhibitor, and 3TC and TDF, both nucleo(t)side reverse transcriptase inhibitors.

- Mylan recently launched Symfi Lo™, which is also a three-drug, fixed-dose combination product containing EFV 400 mg, 3TC 300 mg, and TDF 300 mg. Symfi Lo is indicated as a complete regimen for the treatment of HIV-1 infection in adult and pediatric patients weighing ≥ 35 kg.

- The safety and effectiveness of Symfi as a fixed-dose tablet in pediatric patients infected with HIV-1 and weighing ≥ 40 kg have been established based on clinical studies using the individual components.

- The efficacy of Symfi was based on data from a clinical study of 600 treatment-naïve adult patients with HIV-1 infection. Patients were randomized to a triple drug regimen of EFV/3TC/TDF vs. EFV/3TC/stavudine (d4T).

    — Seventy-nine percent 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.

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

- Symfi 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 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 with Symfi use were impaired concentration, abnormal dreams, headache, nausea, malaise and fatigue, nasal signs and symptoms, diarrhea, rash, dizziness, insomnia, pain, depression, asthenia, and cough.
- The recommended dose of Symfi is one tablet taken orally once daily on an empty stomach, preferably at bedtime. Dosing at bedtime may improve the tolerability of nervous system symptoms.

    — Prior to initiation of Symfi, 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 and during therapy in all patients as clinically appropriate.
    — Hepatic function should be monitored prior to and during treatment with Symfi.

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- Mylan's launch plans for Symfi are pending. Symfi is a three-drug, fixed-dose combination tablet containing EFV 600 mg, 3TC 300 mg, and TDF 300 mg.