Symtuza™ (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) – New drug approval

- On July17, 2018, Janssen announced the FDA approval of Symtuza (darunavir [DRV]/cobicistat [COBI]/emtricitabine [FTC]/tenofovir alafenamide [TAF]), as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults who have no prior antiretroviral (ARV) treatment history or who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable ARV regimen for at least 6 months and have no known substitutions associated with resistance to Prezista® (darunavir) or tenofovir (Vemlidy®, Viread®).

- Symtuza is a four-drug combination of DRV, a HIV-1 protease inhibitor, COBI, a CYP3A inhibitor, and FTC and TAF, both HIV-1 nucleoside analog reverse transcriptase inhibitors.

- The efficacy of Symtuza was demonstrated in two non-inferiority studies: AMBER that enrolled HIV-1 positive adults with no prior ARV therapy, and EMERALD that enrolled virologically-suppressed HIV-1 infected adults. Virologic outcomes were reported at week 48 for both studies.

    - In AMBER, 91% of the Symtuza-treated patients achieved virologic response (HIV-1 RNA < 50 copies/mL) vs. 88% of patients treated with Prezcobix® (DRV/COBI) plus FDC/ tenofovir disoproxil fumarate (treatment difference = 2.7; [95% CI: -1.6; 7.1]).
    - In EMERALD, 0.8% of patients who switched to Symtuza experienced virologic failure vs. 0.5% of patients who maintained their current treatment regimen (treatment difference = 0.3; [95% CI: -0.7; 1.2]).

- Symtuza carries a boxed warning regarding post-treatment acute exacerbation of hepatitis B (HBV).

- Symtuza is contraindicated when co-administered with certain drugs for which altered plasma concentrations are associated with serious and/or life threatening events or which may lead to loss of therapeutic effect of Symtuza and development of resistance.

    - Consult the Symtuza drug label for details on the individual drug interactions.

- Other warnings and precautions of Symtuza include hepatotoxicity, severe skin reactions, risk of serious adverse reactions or loss of virologic response due to drug interactions, immune reconstitution syndrome, new onset or worsening renal impairment, sulfa allergy, lactic acidosis/severe hepatomegaly with steatosis, diabetes mellitus/hyperglycemia, fat redistribution, and hemophilia.

- The most common adverse reactions (≥ 2%, all grades) with Symtuza use were diarrhea, rash, nausea, fatigue, headache, abdominal discomfort, and flatulence.

- The recommended dosage of Symtuza is one tablet orally once daily with food.

    - Prior to or when initiating Symtuza, test patients for HBV infection.
    - Prior to or when initiating Symtuza, and during treatment with Symtuza, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus.

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- Janssen's launch plans for Symtuza are pending. Symtuza will be available as a single tablet containing 800 mg of DRV, 150 mg of COBI, 200 mg of FTC, and 10 mg of TAF.