Janssen Seeks FDA Approval for Darunavir-Based Combo HIV Tablet

The combo tablet contains Janssen's darunavir and Gilead Sciences cobicistat, emtricitabine and tenofovir alafenamide.

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Janssen has applied to the Food and Drug Administration (FDA) for approval of the fixed-dose combination tablet of the company's antiretroviral (ARV) darunavir plus Gilead Sciences' cobicistat, emtricitabine and tenofovir alafenamide. According to Janssen, research indicates that the tablet has demonstrated a high barrier to the development of drug resistance to darunavir, while also boasting the high kidney and bone safety profile of emtricitabine and tenofovir alafenamide.

The combination tablet has already been approved under the brand name Symtuza in Europe for use in adults and adolescents age 12 and older.

Darunavir, marketed individually under the brand name Prezista, is a protease inhibitor. Emtricitabine and tenofovir alafenamide, which are marketed as a fixed-dose combination tablet under the brand name Descovy, are nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs). Cobicistat, which is marketed individually as Tybost, is a boosting agent used in this case to raise the level of darunavir in the body. Darunavir and cobicistat are marketed together as a fixed-dose combination tablet under the brand name Prezcobix.

Tenofovir alafenamide, or TAF, is an updated version of the drug tenofovir disoproxil fumarate, or TDF, which is marketed individually under the brand name Viread and is included in numerous combination tablets, including Truvada (tenofovir disoproxil fumarate/emtricitabine) and Complera (rilpivirine/tenofovir disoproxil fumarate/emtricitabine). Numerous studies have indicated that TAF is safer for the bones and kidneys than TDF. Gilead has released TAF-containing versions of all its TDF-containing combination tablets, with the exception of Atripla (efavirenz/tenofovir disoproxil fumarate/emtricitabine), which is no longer a preferred regimen.

Janssen's new drug application to the FDA is based on two Phase III studies.

The Phase III AMBER study is a randomized, active-controlled, double-blind, international, multicenter, parallel-group noninferiority study evaluating the efficacy and safety of darunavir/cobicistat/emtricitabine/tenofovir alafenamide, known by the shorthand D/C/F/TAF, in

people with HIV who are new to ARV treatment. The trial's main purpose is to look at the difference in the rates of full viral suppression after 48 weeks of treatment between 362 people randomly assigned to receive D/C/F/TAF and a control group of 363 people assigned to receive Prezcobix plus Truvada. The experimental combination tablet will be considered noninferior (as effective as) Prezcobix plus Truvada if the difference in viral suppression rates is no greater than 10 percent.

The Phase III EMERALD study is a randomized, open-label, international, multicenter, parallel-group noninferiority 48-week study evaluating the efficacy and safety of switching to D/C/F/TAF compared with staying on a boosted protease inhibitor plus Truvada (the control regimen). The participants included people with HIV who upon entry into the study had a fully suppressed viral load for at least two months and who had no more than one viral load of 50 or higher during the previous 12 months. The study is looking primarily at the proportion of participants who experience a virologic rebound—those who either experience a viral load of 50 or above or who stop the study drug early—through week 48 of the study. To be considered noninferior to the control regimen, those receiving D/C/F/TAF must have a virologic rebound rate with a difference no greater than 4 percent. A total of 1,141 people were randomized in the trial, 763 of them to D/C/F/TAF and 378 of them to the control.

Janssen will present the EMERALD 48-week data at ID Week 2017, which will take place form October 4 to 8 in San Diego, and the AMBER 48-week data at the European AIDS Conference, which takes place from October 25 to 27 in Milan, Italy.

To read a press release about the FDA application, click here.
