Cabenuva (cabotegravir, rilpivirine), Vocabria (cabotegravir) – New drug approvals

- On January 21, 2021, the FDA announced the approval of ViiV Healthcare's Cabenuva (cabotegravir, rilpivirine), as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults to replace the current antiretroviral (ARV) regimen in those who are virologically suppressed (HIV-1 RNA < 50 copies/mL) on a stable ARV regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.

- This is the first FDA-approved injectable, complete regimen for HIV-infected adults that is administered once a month.

- Cabenuva contains two long-acting HIV-1 ARV drugs, cabotegravir and rilpivirine. Cabotegravir is an integrase strand transfer inhibitor (INSTI) and rilpivirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI).

    - In addition to Cabenuva, the FDA also approved a single-ingredient tablet formulation of cabotegravir (Vocabria). Vocabria is to be used in combination with rilpivirine tablets, as a complete regimen for short-term treatment of HIV-1 infection in adults who are virologically stable and suppressed on a stable ARV regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine, for use as an oral lead-in to assess tolerability of cabotegravir prior to initiating Cabenuva and as an oral therapy for patients who will miss planned injection dosing of Cabenuva.
    - An oral tablet formulation of rilpivirine (Edurant®) was already commercially available.

- The efficacy of Cabenuva was established in two randomized, active-controlled, open-label, non-inferiority studies: FLAIR (N = 629) and ATLAS (N = 616). In FLAIR, treatment-naïve patients received a dolutegravir (Tivicay®) INSTI-containing three-drug regimen for 20 weeks. Patients who were virologically suppressed were then randomized to receive either a cabotegravir plus rilpivirine regimen or remain on the current ARV regimen. The primary endpoint was the proportion of patients with plasma HIV-1 RNA ≥ 50 copies/mL at week 48.

    - At week 48, 2% of patients in each treatment arm had a plasma HIV-1 RNA ≥ 50 copies/mL (treatment difference -0.4, 95% CI: -2.8, 2.1).

- In ATLAS, treatment-experienced, virologically suppressed patients were randomized to either a cabotegravir plus rilpivirine regimen or remained on their current ARV regimen. The study had the same primary endpoint as FLAIR.

    - At week 48, 2% of patients in the cabotegravir plus rilpivirine arm had a plasma HIV-1 RNA ≥ 50 copies/mL vs. 1% with patients continuing their current ARV regimen (treatment difference 0.7, 95% CI: -1.2, 2.5).

- Cabenuva is contraindicated in patients with previous hypersensitivity reaction to cabotegravir or rilpivirine and in patients receiving the following co-administered drugs for which significant decreases in cabotegravir and/or rilpivirine plasma concentrations may occur due to UGT1A1 and/or CYP3A enzyme induction, which may result in loss of virologic response:

    - Anticonvulsants: carbamazepine, oxcarbazepine, phenobarbital, phenytoin
    - Antimycobacterials: rifabutin, rifampin, rifapentine
    - Glucocorticoid (systemic): dexamethasone (more than a single-dose treatment)
    - Herbal product: St John's wort

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- Warnings and precautions for Cabenuva include hypersensitivity reactions, post-injection reactions, hepatotoxicity, depressive disorders, risk of adverse reactions or loss of virologic response due to drug interactions, and long-acting properties and potential associated risks with Cabenuva.

- The most common adverse reactions (≥ 2%) with Cabenuva use were injection site reactions, pyrexia, fatigue, headache, musculoskeletal pain, nausea, sleep disorders, dizziness, and rash.

- Prior to initiating treatment with Cabenuva, oral lead-in dosing should be used for approximately 1 month to assess the tolerability of cabotegravir and rilpivirine. The recommended oral lead-in daily dose is one 30-mg tablet of Vocabria and one 25-mg tablet of rilpivirine.

- Injections with Cabenuva should be initiated on the last day of oral lead-in. The recommended initial injection doses of Cabenuva in adults are a single 600-mg gluteal intramuscular (IM) injection of cabotegravir and a single 900-mg gluteal IM injection of rilpivirine. After the initiation injections, the recommended monthly continuation injection doses of Cabenuva in adults are a single 400-mg gluteal IM injection of cabotegravir and a single 600-mg gluteal IM injection of rilpivirine at each visit.

    — Cabenuva must be administered by a healthcare professional.
    — Prior to starting Cabenuva, healthcare professionals should carefully select patients who agree to the required monthly injection dosing schedule and counsel patients about the importance of adherence to scheduled dosing visits to help maintain viral suppression and reduce the risk of viral rebound and potential development of resistance with missed doses.

- ViiV Healthcare plans to launch Cabenuva and Vocabria in February 2021. Cabenuva will be available as a co-packaged kit containing either: 400 mg/2 mL cabotegravir and 600 mg/2 mL rilpivirine single-dose vials; or 600 mg/3 mL cabotegravir and 900 mg/3 mL rilpivirine single-dose vials. Vocabria will be available as a 30 mg tablet containing cabotegravir.