RXADVANCE
2 Park Central Drive
Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	RUKOBIA
Generic Name	fostemsavir
Drug Manufacturer	ViiV Healthcare

New Drug Approval

RUKOBIA, a human immunodeficiency virus type 1 (HIV-1) gp120-directed attachment inhibitor, in combination with other antiretroviral(s), is indicated for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.

FDA Approval date: Jul 2, 2020

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

HIV stands for human immunodeficiency virus. It weakens a person's immune system by destroying important cells that fight disease and infection. No effective cure exists for HIV. But with proper medical care, HIV can be controlled. Some groups of people in the United States are more likely to get HIV than others because of many factors, including their sex partners, their risk behaviors, and where they live.

At the end of 2018, an estimated 1.2 million people aged 13 and older had HIV in the United States, including an estimated 161,800 (14%) people whose infections had not been diagnosed. The highest rate for HIV infection was for blacks/African Americans (45.4), followed by Hispanic/Latinos (22.4) and persons of multiple races.

According to the latest estimates from the Centers for Disease Control and Prevention, approximately 36,400 new HIV infections occurred in the United States in 2018 and there were 15,820 deaths among adults and adolescents with diagnosed HIV in the United States and 6 dependent areas. These deaths may be due to any cause.

Efficacy

Efficacy of RUKOBIA in heavily treatment-experienced adult subjects with HIV-1 infection is based on 96-week data from a Phase 3, partially-randomized, international, double-blind, placebo-controlled trial (BRIGHTE [NCT02362503]). It was conducted in 371 heavily treatment-experienced subjects with multiclass HIV-1 resistance. All subjects were required to have a viral load ≥400 copies/mL and ≤2 classes of antiretroviral medications remaining at baseline due to resistance, intolerability, contraindication, or other safety concerns. Subjects were enrolled in either a randomized or nonrandomized cohort.

Randomized Cohort: Primary efficacy endpoint was the adjusted mean decline in HIV-1 RNA from Day 1 to

Day 8 with RUKOBIA versus placebo. Primary endpoint analysis demonstrated superiority of RUKOBIA compared with placebo.

Nonrandomized Cohort: HIV-1 RNA <40 copies/mL was achieved in 37% of subjects at Weeks 24 and 96. At these timepoints, the proportion of subjects with HIV-1 RNA <200 copies/mL was 42% and 39%, respectively. Mean changes in CD4+ cell count from baseline increased over time: 41 cells/mm3 at Week 24 and 119 cells/mm3 at Week 96.

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Safety

ADVERSE EVENTS

The most common adverse reaction (all grades) observed in ≥5% of subjects was nausea.

WARNINGS & PRECAUTIONS

- Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapies.
- QTc prolongation: Use RUKOBIA with caution in patients with a history of QTc prolongation or with relevant pre-existing cardiac disease or who are taking drugs with a known risk of Torsade de Pointes.
- Elevations in hepatic transaminases in patients with hepatitis B or C virus co-infection: Elevations in hepatic transaminases were observed in a greater proportion of subjects with HBV and/or HCV co-infection compared with those with HIV mono-infection.

CONTRAINDICATIONS

- Hypersensitivity to fostemsavir or any of the components of the formulation.
- Coadministration with strong cytochrome P450 (CYP)3A inducers as significant decreases in temsavir plasma concentrations may occur, which may result in loss of virologic response

Clinical Pharmacology

MECHANISMS OF ACTION

Fostemsavir is a prodrug without significant biochemical or antiviral activity. It hydrolyzed to the active moiety, temsavir, which is an HIV-1 attachment inhibitor. Temsavir binds directly to the gp120 subunit within the HIV-1 envelope glycoprotein gp160 and selectively inhibits the interaction between the virus and cellular CD4 receptors, thereby preventing attachment. Additionally, temsavir can inhibit gp120-dependent post-attachment steps required for viral entry into host cells.

Dose & Administration

ADULTS

One tablet taken twice daily with or without food.

PEDIATRICS

The safety and effectiveness of RUKOBIA have not been established.

GERIATRICS

Clinical trials of RUKOBIA did not include sufficient numbers of subjects aged 65 and older to determine whether they respond differently from younger subjects. In general, caution should be exercised in administration of RUKOBIA in elderly patients reflecting greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

RENAL IMPAIRMENT

No dosage adjustment is required for patients with renal impairment or those on hemodialysis.

HEPATIC IMPAIRMENT

No dosage adjustment is required in patients with mild to severe hepatic impairment.

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Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Extended-release tablets: 600 mg