PRIOR AUTHORIZATION POLICY

POLICY: Human Immunodeficiency Virus – Rukobia Prior Authorization Policy
- Rukobia™ (fostemsavir extended-release tablets – ViiV/GlaxoSmithKline)

REVIEW DATE: 07/17/2024

OVERVIEW

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

Clinical Efficacy

The efficacy of Rukobia was established in one ongoing, Phase III, multicenter, 96-week pivotal study in heavily treatment-experienced adults with HIV-1 infection failing their current ARV regimen (BRIGHTE; n = 371).[2,5] Eligible patients were ≥ 18 years of age and had failure of their current ARV regimen (baseline HIV-1 RNA ≥ 400 copies/mL), with no viable ARV combination therapy due to exhaustion of a least four of six ARV classes (i.e., nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, integrase inhibitors, protease inhibitors, CCR5 antagonists, and entry inhibitors). Exhaustion was defined as the elimination of all ARVs within a given class as a fully active option to pair with Rukobia because of resistance, previous adverse events, or unwillingness to use Fuzeon® (enfuvirtide subcutaneous injection). Patients were assigned to one of two cohorts, "randomized" or "non-randomized", based on the number of fully active available ARVs with which to construct an optimized background regimen. Patients in the randomized cohort had one or two available fully active ARVs while those in the non-randomized cohort had no available fully active ARVs. There were 15 patients who received Trogarzo® (ibalizumab-uiyk intravenous injection) in combination with Rukobia in the original study (after approval of Rukobia, in 2018, 6 patients in the randomized cohort added Trogarzo to their optimized background therapy). At Week 48 (all patients on Rukobia + optimized background therapy), 54% of patients achieved viral suppression (HIV-1 RNA < 40 copies/mL) and CD4 T-cell count increased to a mean of 139 cells/mm^3 (median baseline 99 cells/mm^3). At Week 96, viral suppression was maintained or improved (60% of patients in the randomized cohort and 37% of patients in the non-randomized cohort).[5] Virologic response rates (in the intent-to-treat population) at Week 240 decreased to 45% in the randomized cohort and to 22% in the non-randomized cohort; however, this included 24 patients (n = 19 in the randomized cohort and n = 5 in the non-randomized cohort) who did not have virologic data due to Coronaviris-19-related disruptions to care. At Week 240, in the observed analysis, HIV-1 RNA was < 40 copies/mL in 82% of patients in the randomized cohort and in 66% of patients in the non-randomized cohort and was < 400 copies/mL in 95% and 80% of patients in the randomized and non-randomized cohorts, respectively. Mean CD4 T-cell count increased through Week 192 in the randomized cohort and remained similar at Week 240; in the non-randomized cohort, CD4 T-cell count increased through Week 240. A safety analysis reported additional findings.[7] At Week 102, 58% of patients with CD4 T-cell count < 200 cells/mm^3 at baseline had on-treatment CD4 T-cell count reported at Week 192, and 75% of these patients had a CD4 T-cell count ≥ 200 cells/mm^2. In addition, acquired immunodeficiency syndrome-defining events were lower among patients with CD4 T-cell count ≥ 200 cells/mm^3 vs. < 200 cells/mm^3.

Guidelines

According to the Department of Health and Human Services Guidelines (February 27, 2024) for the use of antiviral agents in adults and adolescents with HIV infection, treatment-experienced patients with ongoing detectable viremia who lack sufficient treatment options to construct a fully suppressive regimen may be candidates for Trogarzo, Rukobia, or Sunlenca® (lenacapavir tablets/subcutaneous injection).[3] Patients who continue to have detectable viremia and who lack sufficient treatment options to construct a fully suppressive regimen may also be candidates for research studies or expanded access programs, or they may qualify for single-patient access to an investigational new drug as specified in FDA regulations. The goal of therapy is viral resuppression, if possible; otherwise, to keep the viral load as low as possible and CD4 T-cell count as high as possible. CD4 T-cell count is recommended to be monitored at entry into care, when switching or modifying ARVs, and then every 3, 6, or 12 months depending on CD4 T-cell count and the duration of viral suppression. The CD4 count response to ARV therapy varies widely, but a poor CD4 response in a patient with viral suppression is rarely an indication for modifying a treatment regimen.

The International Antiviral Society-USA recommendations (2022) for the treatment and prevention of HIV in adults recognize Rukobia in the setting of integrase strand-transfer inhibitor (INSTI) resistance. If INSTI resistance is relatively limited and a new antiviral regimen is to include an INSTI, the regimen should also include at least one and preferably two other fully active drugs, optimally from drug classes not previously used which may include among other agents, Rukobia.[4]

Consensus recommendations for the use of novel ARVs in individuals with HIV who are heavily treatment-experienced and/or have multidrug-resistant HIV-1 endorsed by the American Academy of HIV Medicine and the American College of Clinical Pharmacology (2024) recommend adding Rukobia to an optimized background regimen that includes at least one other active drug in patients with multidrug resistant HIV-1 who are heavily treatment-experienced and are unable to achieve or maintain viral suppression on their current ARV regimen.[8] If an active drug cannot be included in the optimized background regimen, then the regimen should include partially active agents (preferably several). Prior treatment with Trogarzo should not impact candidacy for Rukobia.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Rukobia. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Rukobia as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Rukobia to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Rukobia is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Human Immunodeficiency Virus (HIV)-1 Infection.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** According to the prescriber, the patient is failing a current antiretroviral regimen for HIV; AND
     - **iii.** According to the prescriber, the patient has exhausted at least FOUR of the following antiretroviral classes defined as elimination of all antiretrovirals within a given class due to demonstrated or projected resistance to the agent(s) in that class OR due to significant intolerance (FOUR of a, b, c, d, e, or f):
       - **a)** Nucleoside reverse transcriptase inhibitor; OR
         Note: Examples of nucleoside reverse transcriptase inhibitors include abacavir, didanosine, emtricitabine, lamivudine, stavudine, tenofovir disoproxil fumarate, tenofovir alafenamide, zidovudine.
       - **b)** Non-nucleoside reverse transcriptase inhibitor; OR
         Note: Examples of non-nucleoside reverse transcriptase inhibitor include delavirdine, efavirenz, etravirine, nevirapine, nevirapine XR, rilpivirine.
       - **c)** Protease inhibitor; OR
         Note: Examples of protease inhibitors include atazanavir, darunavir, fosamprenavir, indinavir, nelfinavir, ritonavir, saquinavir, tipranavir.
       - **d)** Fusion inhibitor; OR
         Note: Examples of fusion inhibitors include Fuzeon (enfuvirtide subcutaneous injection).
       - **e)** Integrase strand transfer inhibitor; OR
         Note: Examples of integrase strand-transfer inhibitors include raltegravir, dolutegravir, elvitegravir.
       - **f)** CCR5 antagonist; AND
         Note: Examples of CCR5 antagonists include Selzentry (maraviroc tablets).
     - **iv.** The medication will be taken in combination with an optimized antiviral background regimen including one or more other antiretroviral agents; AND
     - **v.** The medication is prescribed by or in consultation with a physician who specializes in the treatment of HIV infection.
   - **B)** Patient is Currently Receiving Rukobia. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** The medication will continue to be taken in combination with an optimized antiviral background regimen including one or more other antiretroviral agents; AND
     - **ii.** Patient has responded to a Rukobia-containing regimen, as determined by the prescriber.
       Note: Examples of a response are HIV RNA < 40 cells/mm^3, HIV-1 RNA ≥ 0.5 $\log_{10}$ reduction from baseline in viral load, improvement or stabilization of CD4 T-cell count.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Rukobia is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Rukobia™ extended-release tablets [prescribing information]. Research Triangle Park, NC: ViiV/GlaxoSmithKline; February 2024.
2. Kozal M, Aberg J, Pialoux G, et al. Fostemsavir in adults with multidrug-resistant HIV-1 infection. *N Engl J Med*. 2020;382(13):1232-1243.
3. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. Last Updated: February 24, 2024.Available at: clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf. Accessed on: July 10, 2024.
4. Ghandi RT, Bedimo R, Hoy JF, et al. Antiviral drugs for treatment and prevention of HIV infection in adults. 2022 recommendations of the International Antiviral Society-USA panel. *JAMA.* 2023;329(1):63-84.
5. Lataillade M, Lalezari J, Kozal M, et al. Safety and efficacy of the HIV-1 attachment inhibitor prodrug fostemsavir in heavily treatment-experienced individuals: week 96 results of the phase 3 BRIGHTE study. *Lancet HIV*. 2020; 7(11):e740-e751.
6. Aberg JA, Shepard B, Wang M, et al. Week 240 efficacy and safety of fostemsavir plus optimized background therapy in heavily treatment-experienced adults with HIV-1. *Infect Dis Ther*. 2023;12:2321-2335.
7. llibre JM, Aberg JA, Walmsley S, et al. Long-term safety and impact of immune recovery in heavily treatment-experienced adults receiving fostemsavir for up to 5 years in the phase 3 BRIGHTE study. *Front Immunol*. 2024;15:1394664.
8. Cluck DB, Chastain DB, Murray M, et al. Consensus recommendations for the use of novel antiretrovirals in persons with HIV who are heavily treatment-experienced and/or have multidrug-resistant HIV-1: Endorsed by the American Academy of HIV Medicine, American College of Clinical Pharmacy. *Pharmacotherapy*. 2024;44;360.