Upadacitinib (RINVOQ) in Axial Spondyloarthritis
Criteria for Use
November 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

Exclusion Criteria

If ANY of the following criteria are selected, the patient will not meet criteria for upadacitinib in axial spondyloarthritis.

- ☐ Active, serious systemic or localized infection, including undrained abscess (however, upadacitinib may be started / restarted once the infection is controlled).^1
- ☐ Untreated latent or active tuberculosis infection.
- ☐ Hepatitis B surface antigen (HBsAg)-positive and not on antiviral prophylaxis.^2 Upadacitinib may be initiated after starting antiviral prophylaxis.
- ☐ Untreated HIV infection. Treated, well-controlled, asymptomatic HIV-positive patients can be treated with upadacitinib.
- ☐ Malignancy in the previous 5 years other than successfully treated nonmelanoma skin cancer or successfully treated cervical cancer unless the treating rheumatologist (or designated expert) and oncologist agree that risk-benefits favor using the drug.
- ☐ At increased risk of thrombosis or major adverse cardiovascular events where potential harms are expected to outweigh the anticipated benefits.
- ☐ Lymphocytes < 500 cells/mm^3, neutrophils < 1000 cells/mm^3, or hemoglobin < 8 g/dL. (Upadacitinib may be started / restarted once the lymphopenia, neutropenia and/or anemia resolve.)
- ☐ Severe hepatic impairment (Child-Pugh class C).
- ☐ Concomitant JAK inhibitors, biologic immunomodulators, or potent immunosuppressants such as azathioprine and cyclosporine.^3
- ☐ Concomitant strong CYP3A4 inducers (e.g., rifampin).
- ☐ Concomitant live or live-attenuated vaccines or administration of inactivated, live, or live-attenuated vaccines less than 2 weeks before initiation of upadacitinib therapy.^4
- ☐ Pregnancy
- ☐ Breastfeeding

Inclusion Criteria

ALL of the following must be selected in order to meet criteria:

- ☐ Prescribed and monitored by a VA/VA Community Care rheumatologist or locally designated expert.
- ☐ Definite or provisional diagnosis of <u>active</u> axial spondyloarthritis made by a VA / VA Community Care rheumatologist. This diagnosis includes ankylosing spondylitis (aka radiographic axial spondyloarthritis) and nonradiographic axial spondyloarthritis.

- ☐ Completed tuberculosis (TB) test using tuberculin skin test or interferon-gamma release assay [IGRA].
- ☐ Completed hepatitis B screening (at minimum, HBsAg, total antibody-to-hepatitis-B-core-antigen (anti-HBc) and antibody to hepatitis B surface antigen [anti-HBs]).
- ☐ Current or past completion of hepatitis C screening. Upadacitinib may be initiated while waiting for test results.
- ☐ **ONE tumor necrosis factor inhibitor (TNFI)** is medically inadvisable, not tolerated, or not adequate after 3 months.^5

Additional Inclusion Criteria

Select if appropriate.

- ☐ If HBsAg-negative but anti-HBc-positive and patient's practitioner deems consult is indicated: A GI/liver or ID expert has been (e-)consulted for advice on whether to start antiviral prophylaxis or to preemptively monitor for HBV reactivation.
- ☐ For patients who can become pregnant: Pregnancy status verified. Counseling provided on potential risks vs benefits of treatment and the use of effective contraception.

Abbreviations: GI, gastrointestinal; ID, infectious diseases

Other Justification

- ☐ _____

Footnotes

1. Use with extreme caution in people 65 years or older due to higher risks of serious infections, fatal infection and possibly increased mortality.
2. Antiviral prophylaxis for HBV: Agents with high genetic barrier to resistance such as entecavir or tenofovir should be used.
3. Except overlaps during treatment transition. Upadacitinib may be used with methotrexate, leflunomide, sulfasalazine, or hydroxychloroquine.
4. When possible, vaccinations should be updated before the patient initiates upadacitinib. Unless contraindicated, recombinant zoster (SHINGRIX equivalent) vaccine should be completed or at least initiated by the end of the first year of treatment with upadacitinib, preferably when upadacitinib dosage is low, disease is stable, or at other times when a robust immune response to vaccination can be expected.
5. Applies only to new starts on upadacitinib. Patients on upadacitinib who are stable should not be switched to a criteria-required prior drug for nonmedical reasons.

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