EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Rinvoq (upadacitinib extended-release tablets – AbbVie)

TAC APPROVAL DATE: 08/21/2019

OVERVIEW

Rinvoq is a Janus kinase (JAK) inhibitor. It is indicated for treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate (MTX), either as monotherapy or in combination with MTX or other nonbiologic disease-modifying antirheumatic drugs (DMARDs). Rinvoq is not recommended for use in combination with other JAK inhibitors, biologics, or potent immunosuppressants such as azathioprine or cyclosporine.

The efficacy of Rinvoq over placebo was established in five pivotal studies that included a variety of clinical scenarios, including Rinvoq as monotherapy or in combination with MTX or other conventional synthetic DMARDs and in patients who had previously failed a biologic.

Disease Overview

Inflammatory conditions are chronic, systemic, autoimmune, inflammatory disorders of unknown origin characterized by inflammation.[2] RA causes joint swelling, stiffness, and tenderness which may lead to cartilage damage, bone erosions, and joint destruction, and is often associated with significant activity limitations and disability. Compared with patients who do not have RA, mortality is increased in patients with established RA with approximately 40% of deaths in the RA population attributed to cardiovascular causes such as ischemic heart disease or stroke.[3] RA is associated with a decreased quality of life and can contribute to reduced employment rates and increased costs of care.[2] In RA, Rinvoq inhibits JAK, an intracellular enzyme that transmits signals on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function.[1] JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STAT) which then modulate intracellular activity such as gene expression. Inhibition of JAK block multiple cytokines resulting in modulation of the immune response involved in RA.

Guidelines

Guidelines from the American College of Rheumatology (ACR) [2015], updated prior to the approval of Rinvoq, have tumor necrosis factor (TNF) inhibitors and non-TNF biologics, administered with or without MTX, equally positioned as a recommended therapy following a trial of a conventional synthetic DMARD (e.g., MTX, leflunomide, hydroxychloroquine, sulfasalazine).[4] Although Rinvoq and Olumiant (baricitinib tablets) [another approved JAK inhibitor] are not yet addressed, another JAK inhibitor (Xeljanz/Xeljanz XR [tofacitinib tablets, tofacitinib extended release tablets]) is not recommended for early RA; in established RA, Xeljanz/XR is most frequently recommended for patients with moderate or high disease activity despite use of multiple biologics.

Safety

Rinvoq has Boxed Warnings regarding increased risk of developing serious infections which may lead to hospitalization or death.[1] Patients who develop a serious infection should interrupt treatment with Rinvoq until infection is controlled. Patients should be tested for tuberculosis (TB) prior to starting therapy and monitored during treatment with Rinvoq. There is also a Boxed Warning for lymphoma

and other lymphoproliferative disorders which have been observed in patients taking Rinvoq. Viral reactivation, including cases of herpes virus reactivation, have been reported. Rinvoq also has a Boxed Warning regarding thrombosis, including deep vein thrombosis and pulmonary embolism which occurred in patients treated with other JAK inhibitors used to treat inflammatory conditions.

POLICY STATEMENT

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

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Rheumatoid Arthritis (RA).** Approve Rinvoq for the duration noted if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** The patient is greater than or equal to 18 years of age; AND
     - **ii.** The patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months.
       Note: Examples include methotrexate [oral or injectable], leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already has a 3-month trial at least one biologic (e.g., Cimzia [certolizumab pegol SC injection], an etanercept product [e.g., Enbrel], an adalimumab product [e.g., Humira], an infliximab product [e.g., Remicade, Inflectra, Renflexis], Simponi [golimumab SC injection], Simponi Aria [golimumab IV infusion], Actemra [tocilizumab IV infusion, tocilizumab SC injection], Kevzara [sarilumab SC injection], Kineret [anakinra SC injection], Orencia [abatacept IV infusion, abatacept SC injection], or a rituximab product [e.g., Rituxan, Truxima]). These patients who have already tried a biologic for RA are not required to "step back" and try a conventional synthetic DMARD); AND
     - **iii.** The agent is prescribed by or in consultation with a rheumatologist.
   - **B)** Patients Currently Receiving Rinvoq. Approve for 3 years if the patient has had a response, as determined by the prescriber.
     Note: Examples of a response to therapy include less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids. The patient may not have a full response, but there should have been a recent or past response to Rinvoq.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Rinvoq has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Ceularonditions Not Recommended for Approval.)

1. **Concurrent Use with a Biologic or with a Targeted Synthetic DMARD.** Rinvoq should not be administered in combination with a biologic used for an inflammatory condition (see APPENDIX for examples).[1] Combination therapy is generally not recommended due to a potential for a higher rate of adverse effects with combinations and lack of evidence supporting additive efficacy. There are no data evaluating combination of Rinvoq with other targeted synthetic DMARD (e.g., Otezla, Xeljanz/XR, Olumiant); therefore, safety and efficacy of this combination is unknown.

2. **Concurrent use with Other Potent Immunosuppressants** (e.g., azathioprine, cyclosporine).[1] Coadministration with other potent immunosuppressive drugs has the risk of added immunosuppression and has not been evaluated in RA. Note: This does NOT exclude use of Rinvoq with MTX; Rivnoq has been evaluated with background MTX or other conventional synthetic DMARDs.

3. 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. Rinvoq [prescribing information]. North Chicago, IL: AbbVie; August 2019.
2. Smolen JS, Aletaha D, Bijlsma JW, et al; T2T Expert Committee. Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis*. 2010;69:631-637.
3. Singh JA, Cameron DR. Summary of AHRQ's comparative effectiveness review of drug therapy for rheumatoid arthritis (RA) in adults--an update. *J Manag Care Pharm*. 2012;18(4 Supp C):S1-18.
4. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.
5. Furst DE, Keystone EC, So AK, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2012. *Ann Rheum Dis*. 2013;72 Suppl 2:ii2-34.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	--	08/21/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee; RA – Rheumatoid arthritis.

APPENDIX

Brand (generic name)	Mechanism of Action
Cimzia® (certolizumab pegol for SC injection)	Inhibition of TNF
Enbrel® (etanercept for SC injection)	Inhibition of TNF
Erelzi™ (etanercept-szzs for SC injection)	Inhibition of TNF
Humira® (adalimumab for SC injection)	Inhibition of TNF
Amjevita® (adalimumab-atto for SC injection)	Inhibition of TNF
Cyltezo® (adalimumab-adbm for SC injection)	Inhibition of TNF
Simponi® (golimumab for SC injection)	Inhibition of TNF
Simponi® Aria™ (golimumab for IV infusion)	Inhibition of TNF
Remicade® (infliximab for IV infusion)	Inhibition of TNF
Inflectra™ (infliximab-dyyb for IV infusion)	Inhibition of TNF
Renflexis® (infliximab-abda for IV infusion)	Inhibition of TNF
Actemra® (tocilizumab for IV infusion)	Inhibition of IL-6
Actemra® (tocilizumab for SC injection)	Inhibition of IL-6
Kevzara® (sarilumab for SC injection)	Inhibition of IL-6
Orencia® (abatacept for IV infusion)	T-cell costimulation modulator
Orencia® (abatacept for SC injection)	T-cell costimulation modulator
Rituxan® (rituximab for IV infusion)	CD20-directed cytolytic antibody
Truxima® (rituximab-abbs IV injection)	CD20-directed cytolytic antibody
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1
Stelara® (ustekinumab for SC injection)	Inhibition of IL-12/23
Stelara® (ustekinumab for IV infusion)	Inhibition of IL-12/23
Siliq™ (brodalumab SC injection)	Inhibition of IL-17
Cosentyx™ (secukinumab for SC injection)	Inhibition of IL-17A
Taltz® (ixekizumab for SC injection)	Inhibition of IL-17A
Skyrizi™ (risankizumab SC injection)	Inhibition of IL-23
Tremfya™ (guselkumab for SC injection)	Inhibition of IL-23
Ilumya™ (tildrakizumab-asmn for SC injection)	Inhibition of IL-23
Otezla® (apremilast tablets)	Inhibition of PDE4
Olumiant® (baricitib tablets)	Inhibition of the JAK pathways
Rinvoq™ (upadacitinib extended-release tablets)	Inhibition of the JAK pathways
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways

SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin;PDE4 – Phosphodiesterase 4; JAK – Janus kinase.