Pr RINVOQ®
upadacitinib

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Ease-of-Use Arthritis Society arthritis.ca

Drug Identification Number (DIN): 02495155

THE RINVOQ BOTTLE WAS AWARDED THE ARTHRITIS SOCIETY EASE-OF-USE COMMENDATION[1]*

* The Arthritis Society Ease-of-Use commendation recognizes products that have been independently tested with people living with arthritis and is not intended as a general product endorsement. The Ease-of-Use logo indicates the ease of use only and does not endorse the therapeutic properties of the product.

RINVOQ (upadacitinib) is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate (MTX). RINVOQ may be used as monotherapy or in combination with MTX or other nonbiologic disease-modifying antirheumatic drugs (DMARDs).

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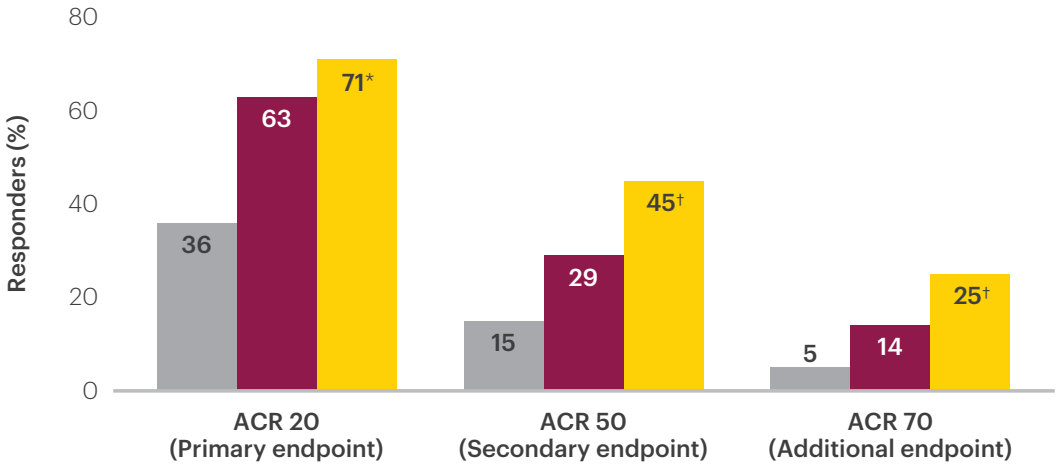
Pr RINVOQ® upadacitinib

THE SELECT-COMPARE TRIAL

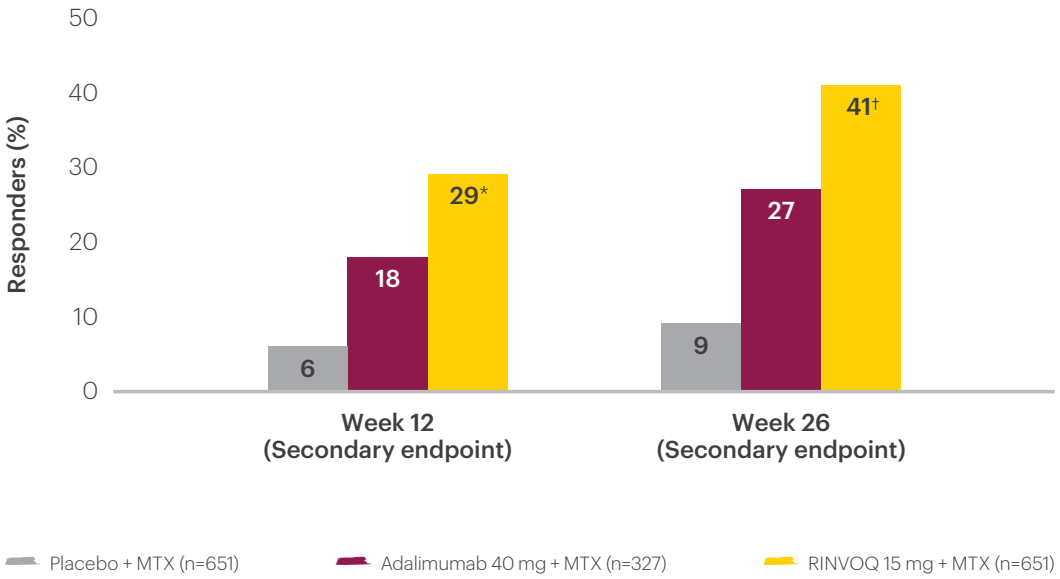
RINVOQ + MTX demonstrated ACR 20, ACR 50, and ACR 70 responses at Week 12 in MTX-IR patients[2,3‡§]



Adapted from the Product Monograph and Fleischmann, *et al.*, 2019[2,3]

Demonstrated remission (DAS28-CRP <2.6) results at Weeks 12 and 26 in MTX-IR patients[2,3‡§]

From Week 14, non-responding patients on RINVOQ could be rescued to adalimumab, and non-responding patients on adalimumab or placebo could be rescued to RINVOQ in a blinded manner.



Adapted from the Product Monograph and Fleischmann, *et al.*, 2019[2,3]

Placebo + MTX (n=651) Adalimumab 40 mg + MTX (n=327) RINVOQ 15 mg + MTX (n=651)

* $p \leq 0.001$, RINVOQ + MTX vs. placebo + MTX; included in multiplicity adjustment for overall type I error control.
† $p \leq 0.001$, RINVOQ + MTX vs. placebo + MTX; not included in multiplicity adjustment for overall type I error control.
‡ No conclusions can be drawn regarding the superiority of upadacitinib + MTX vs. adalimumab + MTX.
§ Patients in SELECT-COMPARE had an inadequate response to MTX; those with prior exposure to ≤1 bDMARD (except adalimumab) were eligible (up to 20% of the total study number of patients) if they had either limited exposure (<3 months) or had to discontinue the bDMARD due to intolerability. Patients with moderate to severe active rheumatoid arthritis (N=1,629) were randomized to receive RINVOQ 15 mg + MTX (n=651), adalimumab 40 mg + MTX (n=327), or placebo + MTX (n=651). The presence of ≥6 tender and 6 swollen joints and evidence of systemic inflammation based on elevated high-sensitivity C-reactive protein was required at baseline.

MTX: methotrexate; ACR: American College of Rheumatology; DAS28-CRP: 28-joint disease activity score using C-reactive protein; IR: inadequate responder; RA: rheumatoid arthritis.

EASY ONCE-DAILY DOSING[2*]

RINVOQ is available as extended-release tablets.

The recommended daily dosing for RINVOQ is 15 mg orally once per day, with or without food. If a dose of RINVOQ is missed, it should be taken as soon as possible. The subsequent dose should be taken at the regularly scheduled time.

HOW TO STORE RINVOQ[2]

RINVOQ should be stored in the original bottle to protect from moisture, between 2 and 25°C. Keep out of reach and sight of children.

SAFETY PROFILE[2]

Adverse reactions reported in ≥1% of RA patients treated with RINVOQ 15 mg in three placebo-controlled studies (SELECT-NEXT, SELECT-COMPARE, SELECT-BEYOND) for up to 12 to 14 weeks

Adverse Reaction	Placebo*	Adalimumab†	RINVOQ 15 mg*
	n=1,042 (%)	n=327 (%)	n=1,035 (%)
Upper respiratory tract infection (URTI)‡	9.5	8.0	13.5
Nausea	2.2	2.4	3.5
Blood creatine phosphokinase (CPK) increased	0.9	0.3	2.5
Cough	1.0	1.2	2.2
Neutropenia	0.2	0.3	1.8
Pyrexia	0	0.3	1.2
Hypercholesterolemia	0.2	1.2	1.1

* SELECT-NEXT, SELECT-COMPARE, SELECT-BEYOND
† SELECT-COMPARE
‡ URTI includes: acute sinusitis, laryngitis, nasopharyngitis, oropharyngeal pain, pharyngitis, pharyngotonsillitis, rhinitis, sinusitis, tonsillitis, viral upper respiratory tract infection.

Adapted from the Product Monograph.

The frequency of herpes zoster, lymphopenia, CPK elevations and ALT/AST elevations were higher with RINVOQ 15 mg compared to adalimumab.

In the placebo-controlled period of SELECT-NEXT, SELECT-COMPARE, and SELECT-BEYOND, serious adverse events were reported in 3.4% of patients who received RINVOQ 15 mg and 1.8% who received placebo.

DRUG INTERACTIONS[2]

- RINVOQ exposure is increased when co-administered with strong CYP3A4 inhibitors (e.g., ketoconazole). RINVOQ should be used with caution in patients receiving chronic treatment with strong CYP3A4 inhibitors.
- RINVOQ exposure is decreased when co-administered with strong CYP3A4 inducers (e.g., rifampin), which may lead to reduced therapeutic effect. Coadministration of RINVOQ with strong CYP3A4 inducers is not recommended.
- RINVOQ should not be used concomitantly with other potent immunosuppressants due to risk of additive immunosuppression. Its combined use with other potent immunosuppressants (e.g., azathioprine, cyclosporine, tacrolimus), other JAK inhibitors, or biologic DMARDs has not been studied in patients with RA and is not recommended.
- RINVOQ should be used with caution when taken with grapefruit juice, as grapefruit juice inhibits CYP3A-mediated metabolism.
- Coadministration of RINVOQ with St. John's Wort is not recommended, as St. John's Wort is a CYP3A inducer and may lead to a reduced therapeutic effect.

* Please see Product Monograph for complete dosing and administration information.

RA: rheumatoid arthritis; ALT: alanine transaminase; AST: aspartate transaminase; CYP: cytochrome P450; JAK: Janus kinase; DMARD: disease-modifying antirheumatic drug.

Clinical use not discussed elsewhere in the piece

RINVOQ should not be used in combination with other Janus kinase (JAK) inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine.

Caution should be used when treating geriatric patients with RINVOQ.

Most serious warnings and precautions

Serious infections: Patients treated with RINVOQ are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. If a serious infection develops, interrupt RINVOQ until the infection is controlled. Reported infections include active tuberculosis (TB), which may present with pulmonary or extrapulmonary disease; invasive fungal infections, including cryptococcosis and pneumocystosis; and bacterial, viral (including herpes zoster), and other infections due to opportunistic pathogens. Test patients for latent TB before RINVOQ use and during therapy. Consider treatment for latent infection prior to RINVOQ use. Do not initiate treatment in patients with active infections including chronic or localized infections. Carefully consider the risks and benefits of treatment prior to initiating therapy in patients with chronic or recurrent infections. Closely monitor patients for signs and symptoms of infection during and after treatment, including the possible development of TB in patients who tested negative for latent infection prior to initiating therapy.

Malignancies: Lymphoma and other malignancies have been observed in patients treated with RINVOQ.

Thrombosis: Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, have occurred in patients treated with JAK inhibitors, including RINVOQ, for inflammatory conditions. Consider the risks and benefits prior to treating patients who may be at increased risk. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately.

Other relevant warnings and precautions

- Increases in lipid parameters, including total, low-density lipoprotein, and high-density lipoprotein cholesterol
- Gastrointestinal perforations
- Hematologic events
- Liver enzyme elevation
- Patients with active hepatitis B or C infection
- Patients with severe hepatic impairment
- Concomitant use with other potent immunosuppressants, biologic DMARDs, or other JAK inhibitors
- Immunizations
- Viral reactivation, including herpes (e.g. herpes zoster) and hepatitis B
- Malignancies
- Increases in creatine phosphokinase
- Monitoring and laboratory tests
- Pregnant women
- Women of reproductive potential
- Breast-feeding
- Sexual health
- Geriatrics (>65 years of age)

For more information

Please consult the Product Monograph at rinvoq.ca/pm for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling us at 1-888-704-8271.

References: 1. AbbVie Corporation. Data on file. **2.** RINVOQ Product Monograph. AbbVie Corporation. **3.** Fleischmann R, Pangan AL, Song IH, *et al.* Upadacitinib versus placebo or adalimumab in patients with rheumatoid arthritis and an inadequate response to methotrexate: Results of a phase 3, double-blind, randomized controlled trial. *Arthritis Rheumatol* 2019;71(11):1788-1800.

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