RINVOQ® upadacitinib | RINVOQ® LQ upadacitinib 1 mg/mL oral solution

RINVOQ/RINVOQ LQ is indicated for pediatric TNFi-IR patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (pJIA) or active psoriatic arthritis (PsA)[1]

APPROVED IN AGES 2+

THE FIRST AND ONLY JAKi FOR THE TREATMENT OF *pJIA* AND *JPsA*[2,a]

[a]JPsA=juvenile psoriatic arthritis in pediatric patients aged 2 to less than 18 years.

Not an actual patient.

INDICATIONS[1]

RINVOQ is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers.

Limitations of Use: RINVOQ is not recommended for use in combination with other Janus kinase (JAK) inhibitors, biologic disease-modifying antirheumatic drugs (bDMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine.

RINVOQ/RINVOQ LQ is indicated for the treatment of patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis (pJIA) who have had an inadequate response or intolerance to one or more TNF blockers.

RINVOQ/RINVOQ LQ is indicated for the treatment of adults and pediatric patients 2 years of age and older with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers.

Limitations of Use: RINVOQ/RINVOQ LQ is not recommended for use in combination with other JAK inhibitors, bDMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine.

IMPORTANT SAFETY INFORMATION FOR RINVOQ/RINVOQ LQ[1]

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. Test patients for latent TB before RINVOQ use and during therapy. Consider treatment for latent TB infection prior to RINVOQ use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis.**
- **Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.**

Carefully consider the risks and benefits of treatment with RINVOQ prior to initiating therapy in patients with chronic or recurrent infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with RINVOQ, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

*Unless otherwise stated, "RINVOQ" in the IMPORTANT SAFETY INFORMATION refers to RINVOQ and RINVOQ LQ.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

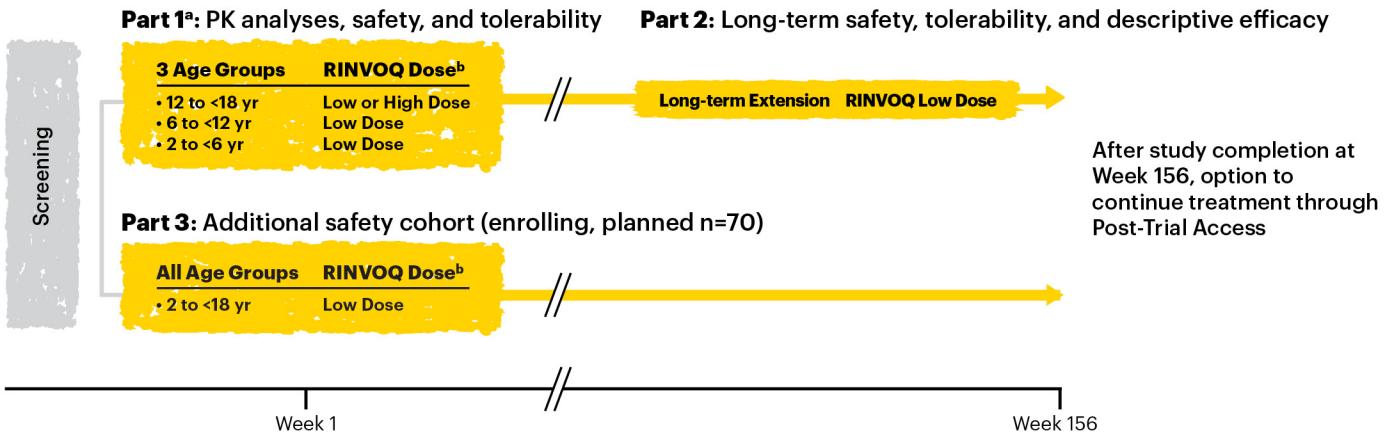
Please see accompanying full Prescribing Information, including Boxed Warning.

Visit RinvoqHCP.com to explore PsA data for RINVOQ

IR=intolerance or inadequate response; TNFi=tumor necrosis factor inhibitor.

OVERVIEW OF THE SELECT-YOUTH TRIAL IN pJIA

Open-Label, 3-Part, Phase 1 Study[3]



Select Endpoints[3,c]

- TEAEs
- JIA ACR30/50/70/90/100 response
- C-HAQ
- JADAS27-CRP

Statistical Analyses[3]

- TEAEs coded using MedDRA v25.0 for all patients who received ≥1 dose of the study drug
- Efficacy endpoints were reported using observed data without imputation of missing values
- All endpoints are presented with descriptive statistics for overall patients and by age groups

[a]Part 1 is completed.[3]
[b]Low dose is the only approved dose; see page 10 for more dosing information.[1]
[c]Efficacy was evaluated in Parts 1 and 2; safety was assessed in Parts 1, 2, and 3.[1]

IMPORTANT SAFETY INFORMATION (cont'd)[1]

MORTALITY

In a large, randomized, postmarketing safety study comparing another Janus kinase (JAK) inhibitor with tumor necrosis factor (TNF) blockers in rheumatoid arthritis (RA) patients ≥50 years old with at least one cardiovascular (CV) risk factor, a higher rate of all-cause mortality, including sudden CV death, was observed with the JAK inhibitor.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with RINVOQ.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

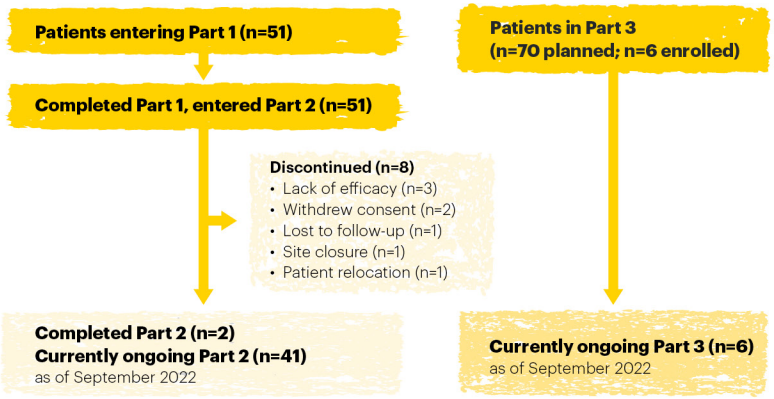
Please see accompanying full Prescribing Information, including Boxed Warning.

ACR=American College of Rheumatology; ACR30/50/70/90/100=improvement of at least 30%, 50%, 70%, 90%, 100% from baseline in 3 of 6 ACR core criteria for JIA; C-HAQ=Childhood Health Assessment Questionnaire; JADAS27-CRP=Juvenile Arthritis Disease Activity Score 27 C-reactive protein; MedDRA=Medical Dictionary of Regulatory Activities; PK=pharmacokinetic; TEAE=treatment-emergent adverse event.

OVERVIEW OF THE SELECT-YOUTH TRIAL IN pJIA

Patient Selection Criteria[3]

- Age: 2 to <18 years
- Weight: ≥10 kg
- Active pJIA: ≥5 active joints[a]; ERA or JPsA excluded
- 31 sites: North America, Europe, and Asia
- Prior exposure: No JAKis
- Allowed concomitant medications: methotrexate and glucocorticoids (stable doses)



Baseline Demographics[3]

	Age cohort, years					
	Parts 1 and 2				Part 3	Overall
Parameter	2 to <6, Low Dose[c] (n=14)	6 to <12, Low Dose[c] (n=19)	12 to <18, Low Dose[c] (n=9)	12 to <18, High Dose (n=9)	2 to <18 (n=6)	All ages (n=57)
Female, n (%)	11 (78.6)	15 (78.9)	7 (77.8)	8 (88.9)	4 (66.7)	45 (78.9)
Age (years), mean (SD)	3.6 (1.5)	9.5 (1.6)	14.9 (1.5)	13.9 (1.2)	9.2 (3.3)	9.5 (4.4)
pJIA types,[b] n (%)						
Extended oligoarticular	3 (21.4)	3 (15.8)	0	0	1 (16.7)	7 (12.3)
RF negative	10 (71.4)	13 (68.4)	8 (88.9)	7 (77.8)	4 (66.7)	42 (73.7)
RF positive	0	3 (15.8)	1 (11.1)	2 (22.2)	1 (16.7)	7 (12.3)
Weight (kg), mean (SD)	15.1 (3.2)	37.8 (14.4)	61.3 (14.6)	51.7 (13.0)	37.1 (22.0)	38.1 (20.4)
Total active joints, mean (SD)	8.0 (3.1)	11.6 (7.2)	11.6 (5.5)	11.9 (7.5)	15.3 (16.5)	11.1 (7.74)
Prior therapy exposure, n (%)						
csDMARDs	6 (42.9)	9 (47.4)	9 (100)	6 (66.7)	4 (66.7)	34 (59.6)
bDMARDs	1 (7.1)	1 (5.3)	9 (100)	3 (33.3)	0	14 (24.6)
Current methotrexate therapy, n (%)	5 (35.7)	7 (36.8)	5 (55.6)	3 (33.3)	3 (50.0)	23 (40.4)

Data as of September 2022

[a]Active joints are defined as those with the presence of swollen joints (not due to deformity); if there is no swelling, then joints with LOM plus pain on motion and/or tenderness with palpation, with LOM present in ≥3 active joints.[3]
[b]1 patient (aged 2 to <6 years) had systemic pJIA type of active arthritis without active systemic features.[3]
[c]Low dose is the only approved dose; see page 10 for more dosing information.[1]

IMPORTANT SAFETY INFORMATION (cont'd)[1]

MALIGNANCIES

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

In a large, randomized, postmarketing safety study comparing another JAK inhibitor with TNF blockers in RA patients, a higher rate of malignancies (excluding non-melanoma skin cancer [NMSC]), lymphomas, and lung cancer (in current or past smokers) was observed with the JAK inhibitor. Patients who are current or past smokers are at additional increased risk.

With RINVOQ, consider the benefits and risks for the individual patient prior to initiating or continuing therapy, particularly in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy when on treatment, and patients who are current or past smokers. NMSCs have been reported in patients treated with RINVOQ. Periodic skin examination is recommended for patients who are at increased risk for skin cancer. Advise patients to limit sunlight exposure by wearing protective clothing and using sunscreen.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

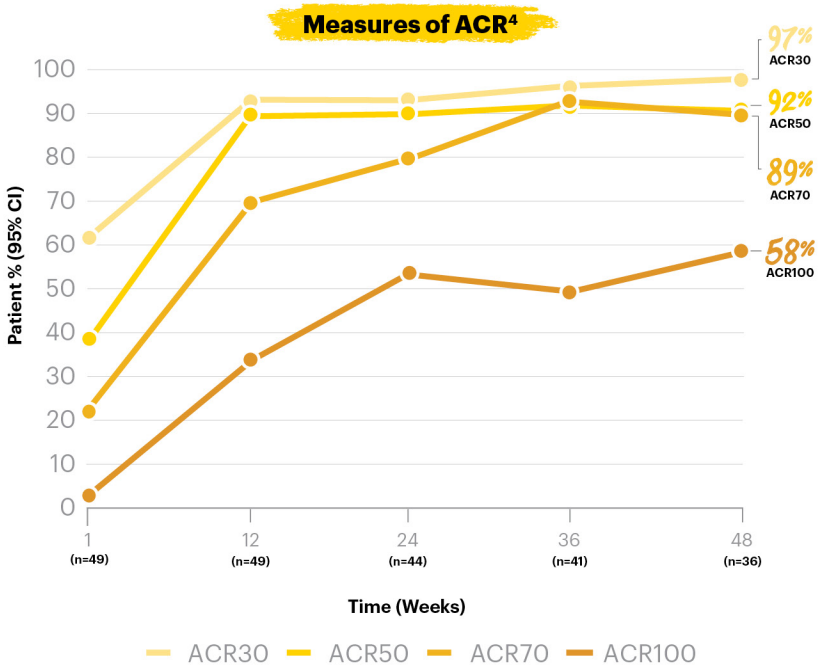
Please see accompanying full Prescribing Information, including Boxed Warning.

csDMARD=conventional synthetic DMARD; DMARD=disease-modifying antirheumatic drug; ERA=enthesitis-related arthritis; LOM=limitation of movement; RF=rheumatoid factor; SD=standard deviation.

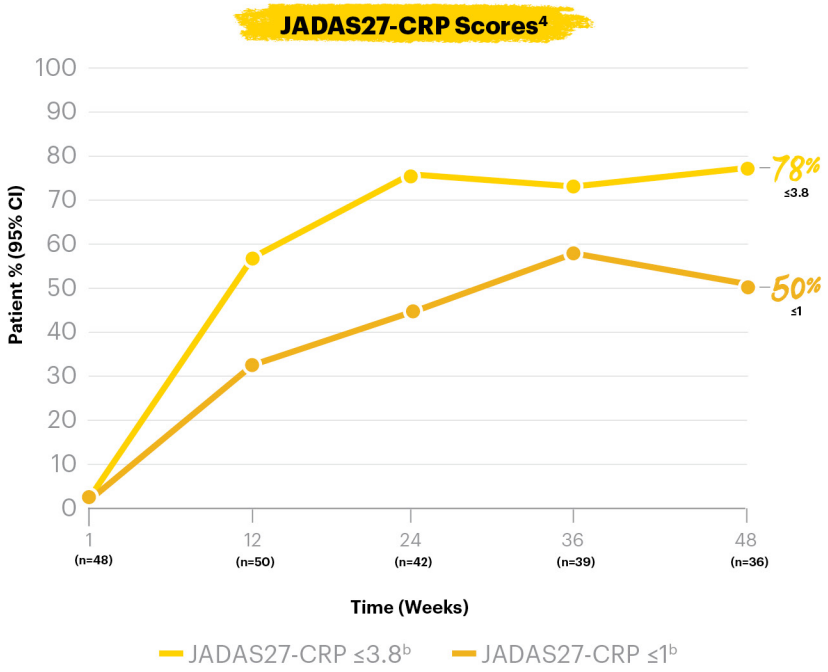
IMPROVEMENTS WERE OBSERVED IN MEASURES OF ACR AND JADAS27-CRP IN pJIA AGES 2+

Results shown were measured out to Week 48[4,a]

Measures of ACR[4]



JADAS27-CRP Scores[4]



DATA LIMITATIONS: Phase 1 open-label study that only evaluated RINVOQ and did not include a placebo or another active comparator arm.

RINVOQ IS ALSO APPROVED TO TREAT PEDIATRIC PATIENTS WITH JPsA[1,c]

[a]ACR30/50/70/100=improvement of at least 30%, 50%, 70%, 100% from baseline in 3 of 6 ACR core criteria for pJIA.[3]
[b]JADAS27-CRP ≤3.8 and ≤1 are proposed definitions for minimal disease activity and remission, respectively.
[c]JPsA=juvenile psoriatic arthritis in pediatric patients aged 2 to less than 18 years.

IMPORTANT SAFETY INFORMATION (cont'd)[1]

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)

In a large, randomized, postmarketing study comparing another JAK inhibitor with TNF blockers in RA patients ≥50 years old with at least one CV risk factor, a higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) was observed with the JAK inhibitor. Patients who are current or past smokers are at additional increased risk. Discontinue RINVOQ in patients that have experienced a myocardial infarction or stroke.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with RINVOQ, particularly in patients who are current or past smokers and patients with other CV risk factors. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

Please see accompanying full Prescribing Information, including Boxed Warning.

RINVOQ/RINVOQ LQ ADVERSE EVENTS ACROSS ALL pJIA AGE GROUPS

Overview of RINVOQ/RINVOQ LQ Safety (All Patients Treated in Parts 1, 2, and 3 as of June 2023)[5]

	Age Cohort (years)							
	2 to <6 (n=22; PY=25.7)		6 to <12 (n=36; PY=47.6)		12 to <18 (n=25; PY=50.4)		Overall (n=83; PY=123.7)	
Adverse Event	**n (%)**	**E/100 PY**	**n (%)**	**E/100 PY**	**n (%)**	**E/100 PY**	**n (%)**	**E/100 PY**
Any TEAE	20 (90.9)	590.9	33 (91.7)	595.1	23 (92.0)	349.3	76 (91.6)	494.1
Any serious TEAE	2 (9.1)	11.7	3 (8.3)	6.3	6 (24.0)	23.8	11 (13.3)	14.6
Serious Infections	0	0	1 (2.8)	2.1	1 (4.0)	2.0	2 (2.4)	1.6
Active TB	0	0	0	0	0	0	0	0
Opportunistic Infection (excluding TB and HZ)	0	0	1 (2.8)	2.1	1 (4.0)	2.0	2 (2.4)	1.6
Herpes Zoster	0	0	0	0	0	0	0	0
Malignancy (excluding NMSC)	0	0	0	0	0	0	0	0
Lymphoma	0	0	0	0	0	0	0	0
NMSC	0	0	0	0	0	0	0	0
Adjudicated VTE	0	0	0	0	0	0	0	0
Adjudicated MACE	0	0	0	0	0	0	0	0
Adjudicated GI perforations	0	0	0	0	0	0	0	0
TEAE leading to discontinuation	0	0	2 (5.6)	6.3	2 (8.0)	4.0	4 (4.8)	4.0

Data as of June 2023

Overall, the safety profile observed in pediatric patients with JIA with active polyarthritis treated with RINVOQ/RINVOQ LQ was consistent with the known safety profile of RINVOQ.

ONCE-DAILY ORAL TABLET OR WEIGHT-BASED TWICE-DAILY ORAL SOLUTION FOR pJIA AND JPsA[1,a]

[a]Tablet (once daily) or oral solution (twice daily).

IMPORTANT SAFETY INFORMATION (cont'd)[1]

THROMBOSIS

Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis have occurred in patients treated with JAK inhibitors used to treat inflammatory conditions. Many of these adverse events were serious and some resulted in death.

In a large, randomized, postmarketing study comparing another JAK inhibitor to TNF blockers in RA patients ≥50 years old with at least one CV risk factor, a higher rate of thrombosis was observed with the JAK inhibitor. Avoid RINVOQ in patients at risk. Patients with symptoms of thrombosis should discontinue RINVOQ and be promptly evaluated.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

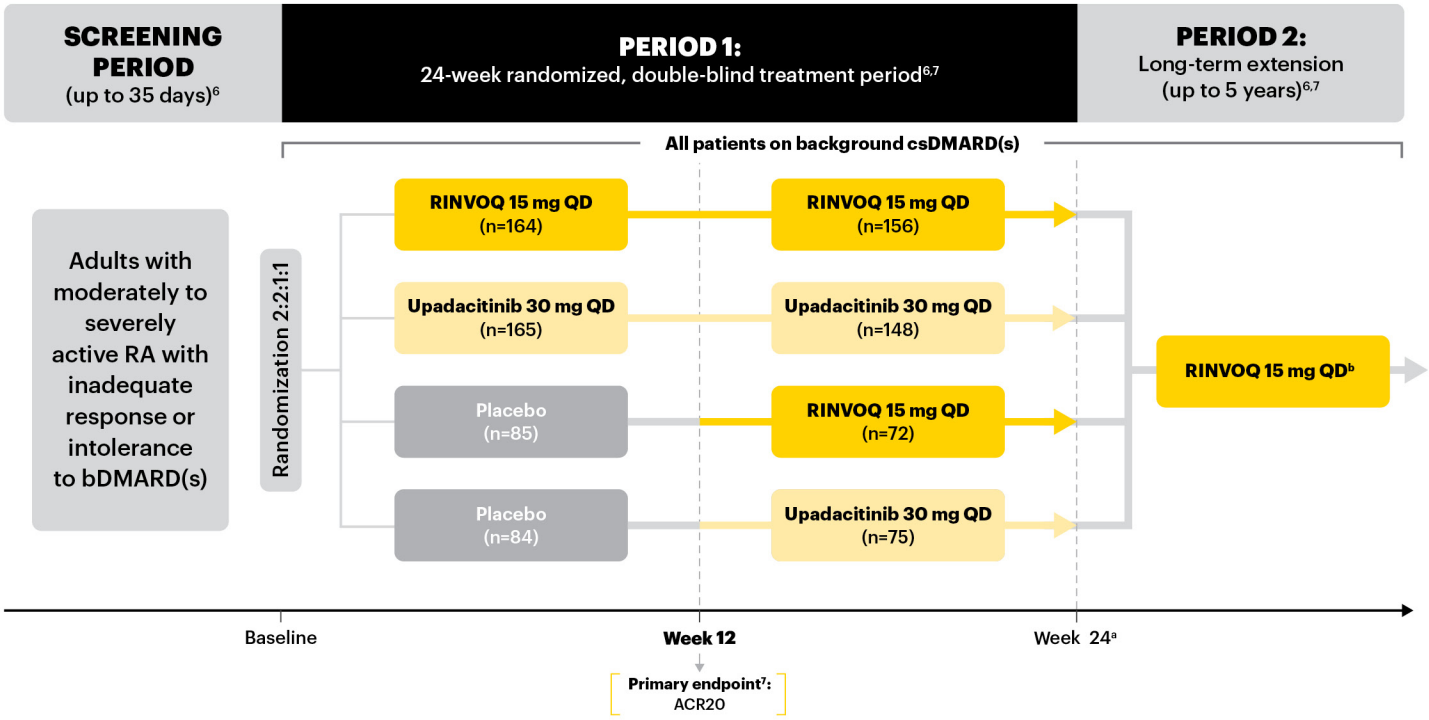
Please see accompanying full Prescribing Information, including Boxed Warning.

E/100 PYs=events per 100 patient-years; GI=gastrointestinal; HZ=herpes zoster; MACE=major adverse cardiovascular event; NMSC=non-melanoma skin cancer; PY=patient-years; VTE=venous thromboembolism.

SINCE 2019, RINVOQ HAS BEEN APPROVED FOR THE TREATMENT OF RA[1]

SELECT-BEYOND Study Design

Adults with moderately to severely active RA who had an inadequate response to bDMARDs[1]



Upadacitinib 30 mg is not an approved dose for RA.[1]

[a]Starting at Week 24, initiation of or change in corticosteroids, NSAIDs, acetaminophen, and csDMARDs was permitted. Patients not achieving response criteria ≥20% improvement in SJC and TJC at 2 consecutive visits were removed from the study.[6]

[b]Following a protocol amendment, all patients in the LTE received RINVOQ 15 mg QD, including those previously on upadacitinib 30 mg.[8]

IMPORTANT SAFETY INFORMATION (cont'd)[1]

HYPERSENSITIVITY

RINVOQ is **contraindicated** in patients with known hypersensitivity to upadacitinib or any of its excipients. Serious hypersensitivity reactions, such as anaphylaxis and angioedema, were reported in patients receiving RINVOQ in clinical trials. If a clinically significant hypersensitivity reaction occurs, discontinue RINVOQ and institute appropriate therapy.

GASTROINTESTINAL PERFORATIONS

Gastrointestinal (GI) perforations have been reported in clinical trials with RINVOQ. Monitor RINVOQ-treated patients who may be at risk for GI perforation (e.g., patients with a history of diverticulitis and patients taking NSAIDs or corticosteroids). Promptly evaluate patients presenting with new onset abdominal pain for early identification of GI perforation.

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Please see accompanying full Prescribing Information, including Boxed Warning.

LTE=long-term extension; NSAID=nonsteroidal anti-inflammatory drug; QD=once daily; SJC=swollen joint count; TJC=tender joint count.

SELECT-BEYOND TRIAL

Baseline Characteristics[7]

Mean (SD) or n (%)	Placebo + csDMARDs (n=169)	RINVOQ 15 mg + csDMARDs (n=164)
Female, n (%)	143 (85)	**137 (84)**
Age (years), mean (SD)	57.6 (11.4)	**56.3 (11.3)**
Duration of RA diagnosis (years), mean (SD)	14.5 (9.2)	**12.4 (9.4)**
RF+ and/or anti-CCP, n (%)	128 (76)	**131 (80)**
csDMARD use at baseline[a]		
– MTX alone,[b] n (%)	122 (73)	**118 (73)**
– MTX plus other csDMARD,[c] n (%)	17 (10)	**19 (12)**
– MTX dose (mg),[d] mean (SD)	16.6 (4.7)	**17.3 (4.6)**
– csDMARD other than MTX, n (%)	29 (17)	**24 (15)**
– Missing, n	1	**3**
Prior bDMARD exposure, n (%)		
1, n (%)	83 (49)	**86 (52)**
2, n (%)	46 (27)	**40 (24)**
≥3, n (%)	40 (24)	**38 (23)**
– Inadequate response or intolerance to ≥1 anti-TNF drug	152 (90)	**146 (89)**
– Lack of efficacy with ≥1 bDMARD	159 (94)	**146 (89)**
– Lack of efficacy with ≥1 anti-IL-6	30 (18)	**27 (16)**
Oral glucocorticoid use, n (%)	74 (44)	**83 (51)**
– Oral glucocorticoid dose (mg),[e] mean (SD)	6.3 (2.4)	**5.7 (2.4)**
TJC68, mean (SD)	28.5 (15.3)	**27.8 (16.3)**
SJC66, mean (SD)	16.3 (9.6)	**17.0 (10.8)**
PtGA (0-100 mm VAS), mean (SD)	66.3 (22.7)	**67.2 (19.6)**
PhGA (0-100 mm VAS), mean (SD)	66.9 (16.9)	**68.7 (16.6)**
Pain (0-100 mm VAS), mean (SD)	68.9 (21.0)	**68.2 (19.8)**
hs-CRP (mg/L), mean (SD)	16.3 (21.1)	**16.2 (18.6)**
DAS28-CRP, mean (SD)	5.8 (1.0)	**5.9 (1.0)**
HAQ-DI, mean (SD)	1.6 (0.6)	**1.7 (0.6)**
CDAI, mean (SD)	41.0 (13.3)	**41.7 (13.3)**
SDAI, mean (SD)	42.6 (13.9)	**43.3 (13.8)**

In this difficult-to-treat patient population, *89%* failed treatment with **at least 1 previous TNFi.**[7]

[a]Oral or parenteral MTX 7.5-25 mg per week.[7]
[b]Data is available for 168 patients who received placebo and 161 patients who received RINVOQ 15 mg.[7]
[c]All combinations were allowed except MTX and leflunomide.[7]
[d]The mean MTX dose was calculated only for patients receiving MTX.[7]
[e]Based on prednisone equivalent.[7]

All patients were on stable background csDMARD therapy.

IMPORTANT SAFETY INFORMATION (cont'd)[1]

LABORATORY ABNORMALITIES

Neutropenia
Treatment with RINVOQ was associated with an increased incidence of neutropenia (absolute neutrophil count [ANC] <1000 cells/mm^3). Treatment with RINVOQ is not recommended in patients with an ANC <1000 cells/mm^3. Evaluate neutrophil counts at baseline and thereafter according to routine patient management.

Lymphopenia
Absolute lymphocyte counts (ALC) <500 cells/mm^3 were reported in RINVOQ-treated patients. Treatment with RINVOQ is not recommended in patients with an ALC <500 cells/mm^3. Evaluate at baseline and thereafter according to routine patient management.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

Please see accompanying full Prescribing Information, including Boxed Warning.

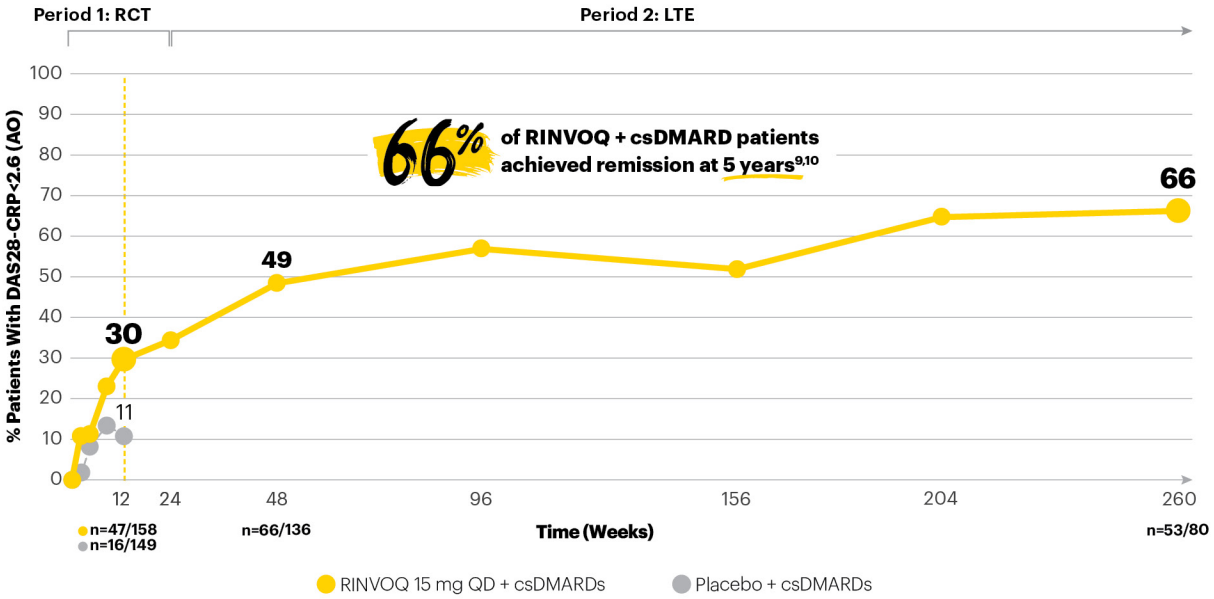
anti-CCP=anti-cyclic citrullinated peptide; CDAI=Clinical Disease Activity Index; HAQ-DI=Health Assessment Questionnaire Disability Index; MTX=methotrexate; hs-CRP=high sensitivity C-reactive protein; PhGA=physician global assessment; PtGA=patient global assessment; SDAI=Simplified Disease Activity Index; SJC68=swollen joint count of 68 joints; TJC68=tender joint count of 68 joints.

EXPLORE THE EFFICACY AND SAFETY DATA IN ADULT PATIENTS

RINVOQ MET ITS PRIMARY ENDPOINT IN SELECT-BEYOND[1,7]
ACR20 at Week 12 (NRI): 65% RINVOQ + csDMARDs (n=164) vs 28% placebo + csDMARDs (n=169), *P*<0.0001

Durable Remission Rates Out to 5 Years[9,10]

ALL DATA ARE OBSERVED CASES
DAS28-CRP<2.6



REMISSION (DAS28-CRP <2.6)* at Week 12 (NRI)[1]:

29% of patients on RINVOQ + csDMARDs vs 9% placebo + csDMARDs

***Does not mean drug-free remission or absence of disease activity.**

Starting at Week 24, initiation of or change in corticosteroids, NSAIDs, acetaminophen, and csDMARDs was permitted. Patients who did not achieve response criteria ≥20% improvement in SJC and TJC at 2 consecutive visits were removed from the study.[6,11]

In an **As Observed (AO)** analysis, patients with missing data at a specific time are not included, which may enrich the population and increase the response rates.[7]

LTE LIMITATIONS: There is potential for enrichment of LTE data; unblinding patients may cause bias related to overall treatment effect.

DATA LIMITATIONS: Prespecified nonranked endpoints were not controlled for multiplicity; therefore, treatment differences could represent chance findings. No conclusions regarding these comparisons can be made.

IMPORTANT SAFETY INFORMATION (cont'd)[1]

LABORATORY ABNORMALITIES (cont'd)

Anemia
Decreases in hemoglobin levels to <8 g/dL were reported in RINVOQ-treated patients. Treatment should not be initiated or should be interrupted in patients with hemoglobin levels <8 g/dL. Evaluate at baseline and thereafter according to routine patient management.

Lipids
Treatment with RINVOQ was associated with increases in lipid parameters, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Manage patients according to clinical guidelines for the management of hyperlipidemia. Evaluate patients 12 weeks after initiation of treatment and thereafter according to the clinical guidelines for hyperlipidemia.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

Please see accompanying full Prescribing Information, including Boxed Warning.

NRI=nonresponder imputation; RCT=randomized controlled trial.

CONSISTENT SAFETY PROFILE OF AEs OBSERVED IN LONG-TERM ANALYSIS FOR RINVOQ

Data as of August 15, 2023[14]

TEAEs of Special Interest*	PLACEBO-CONTROLLED TRIALS[1,12,13] NEXT, COMPARE, and BEYOND: Week 12/14 n/100 PYs (n/PYs) unless otherwise stated		LONG-TERM SAFETY ANALYSIS[14-16] Phase 3 Programs†: Any RINVOQ 15 mg QD‡ E/100 PYs unless otherwise stated	
	PLACEBO + csDMARDs n=1042	RINVOQ 15 mg QD + csDMARDs n=1035	2.8 yrs max exposure 1.4 yrs median n=2630, PYs=3446.2	~7.5 yrs max exposure ~4.2 yrs median n=3209, PYs=11,661.5
INFECTIONS				
Serious infections	2.3 (6/256.6)	4.6 (12/258.3)	3.5	3.6
Active TB	0	0	0.1	<0.1
Opportunistic infection[a] (excluding TB, HZ, and oral candidiasis)	1.2 (3/256.8)	1.9 (5/258.5)	0.3	0.3
HZ	1.2 (3/256.4)	2.7 (7/258.7)	3.5	3.2
MALIGNANCY[b]				
Malignancy (excluding NMSC)	0.4 (1/256.8)	0.4 (1/259.3)	0.8	0.7
Lymphoma	0	0	<0.1	<0.1
NMSC	0.4 (1/256.8)	0	0.3	0.4
CARDIOVASCULAR EVENTS[b]				
Adjudicated VTE[c]	0.4 (1/256.8)	0.8 (2/259.2)	0.6	0.4
Adjudicated MACE[d]	1.2 (3/256.8)	0.4 (1/259.3)	0.6	0.3
GASTROENTEROLOGICAL EVENTS[b]				
Adjudicated GI perforations	0	0	0.1	<0.1

*A TEAE is defined as any adverse event with an onset date on or after the first dose of the study drug and no more than 30 days after the last dose of the study drug if subject discontinued the study drug prematurely.[13]

†**In RA studies, patients could advance or switch to RINVOQ from placebo, or be rescued to RINVOQ from active comparator or placebo, as early as Week 12, depending on the study design.[1]**

‡Included RINVOQ monotherapy and combination therapy with csDMARDs across 6 trials.[1,17]

Adverse reaction rates observed in clinical trials and LTE studies may not predict the rates observed in clinical practice.[1]

The most common adverse reactions reported in ≥1% of patients with moderate to severe RA treated with RINVOQ 15 mg in placebo-controlled studies[e] included upper respiratory tract infection (URTI),[f] nausea, cough, and pyrexia.[1]

SELECT-EARLY: Adults with moderately to severely active RA who were MTX-naïve[1]

SELECT-NEXT: Adults with moderately to severely active RA who had an inadequate response to csDMARD[1]

SELECT-MONOTHERAPY: Adults with moderately to severely active RA who had an inadequate response to MTX[1]

SELECT-COMPARE: Adults with moderately to severely active RA who had an inadequate response to MTX[1]

SELECT-CHOICE: Adults with moderately to severely active RA and inadequate response or intolerance to bDMARDs[17]

[a]Placebo-controlled trial rates exclude TB only.
[b]Rates shown are n/100 PYs=number of subjects with at least one event per 100 PYs.
[c]Includes deep vein thrombosis (DVT) and pulmonary embolism (PE).[16]
[d]MACE is defined as cardiovascular death, myocardial infarction, and stroke.[16]
[e]Patients were on background MTX or csDMARDs.[1]
[f]URTI includes: acute sinusitis, laryngitis, nasopharyngitis, oropharyngeal pain, pharyngitis, pharyngotonsillitis, rhinitis, sinusitis, tonsillitis, and viral upper respiratory tract infection.[1]

IMPORTANT SAFETY INFORMATION (cont'd)[1]

LABORATORY ABNORMALITIES (cont'd)

Liver enzyme elevations

Treatment with RINVOQ was associated with increased incidence of liver enzyme elevation compared to placebo. Evaluate at baseline and thereafter according to routine patient management. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury.

If increases in aspartate aminotransferase (AST) or alanine aminotransferase (ALT) are observed during routine patient management and drug-induced liver injury is suspected, RINVOQ should be interrupted until this diagnosis is excluded.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

Please see accompanying full Prescribing Information, including Boxed Warning.

AE=adverse event.

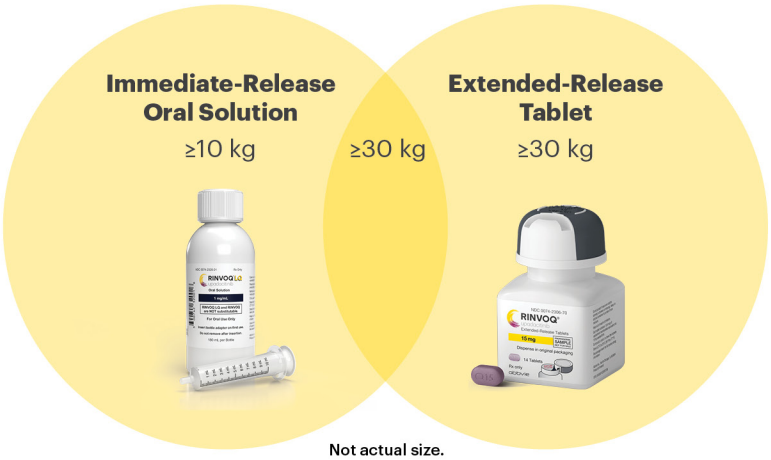
RINVOQ® upadacitinib | RINVOQ® LQ upadacitinib 1 mg/mL oral solution

ONCE-DAILY ORAL TABLET OR A WEIGHT-BASED TWICE-DAILY ORAL SOLUTION FOR pJIA AND JPsA[1,a,b]

RINVOQ/RINVOQ LQ dosage for pediatric patients aged 2 to less than 18 years of age with pJIA and JPsA

Body Weight	RINVOQ LQ	RINVOQ
10 to <20 kg	3 mg (3 mL oral solution) twice daily	Not recommended
20 to <30 kg	4 mg (4 mL oral solution) twice daily	Not recommended
≥30 kg	6 mg (6 mL oral solution) twice daily	15 mg (one 15-mg tablet) once daily

RINVOQ LQ oral solution is not substitutable with RINVOQ extended-release tablets. Changes between RINVOQ LQ oral solution and RINVOQ extended-release tablets should be made by the healthcare provider.[1]



Not actual size.

[a]Tablet (once daily) or oral solution (twice daily).
[b]JPsA=juvenile psoriatic arthritis in pediatric patients aged 2 to less than 18 years.

IMPORTANT SAFETY INFORMATION (cont'd)[1]

EMBRYO-FETAL TOXICITY
Based on findings in animal studies, RINVOQ may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with RINVOQ and for 4 weeks after the final dose. Verify pregnancy status of females of reproductive potential prior to starting treatment with RINVOQ.

VACCINATION
Avoid use of live vaccines during, or immediately prior to, RINVOQ therapy. Prior to initiating RINVOQ, patients should be brought up to date on all immunizations, including prophylactic varicella zoster or herpes zoster vaccinations, in agreement with current immunization guidelines.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

Please see accompanying full Prescribing Information, including Boxed Warning.

RINVOQ/RINVOQ LQ is indicated for pediatric TNFi-IR patients 2 years of age and older with active pJIA or active PsA[1]

ABBVIE'S COMMITMENT TO EXCEPTIONAL ACCESS AND PATIENT SUPPORT

RINVOQ HAS 99% PREFERRED COMBINED COMMERCIAL AND MEDICARE PART D COVERAGE[18,a,b]

National commercial and Medicare Part D formulary coverage under the pharmacy benefit as of January 2025.

Encourage your patient's caregiver to enroll in RINVOQ® COMPLETE

Affordability: Eligible commercially insured patients may pay as little as $0 per month[c]

Access: No charge for eligible patients experiencing initial insurance delay or denial for up to 24 months or until insurance approval, whichever occurs earlier[d]

Support: Exceptional 1:1 patient support when your patients enroll in RINVOQ Complete

[a]RINVOQ is on a preferred tier or otherwise has preferred status on the plan's formulary.

[b]Coverage requirements and benefit designs vary by payer and may change over time. Please consult with payers directly for the most current reimbursement policies.

[c]Eligibility terms and conditions apply. See terms and conditions at https://www.rinvoq.com/resources/rinvoq-complete

[d]Eligibility criteria: Available to patients aged 63 or younger with commercial insurance coverage. Patients must have a valid prescription for RINVOQ for an FDA approved indication and a denial of insurance coverage based on a prior authorization request on file along with a confirmation of appeal. Continued eligibility for the program requires the submission of an appeal of the coverage denial every 180 days. Program provides for RINVOQ at no charge to patients for up to two years or until they receive insurance coverage approval, whichever occurs earlier, and is not contingent on purchase requirements of any kind. Program is not available to patients whose medications are reimbursed in whole or in part by Medicare, Medicaid, TRICARE, or any other federal or state program. Offer subject to change or discontinuance without notice. This is not health insurance and program does not guarantee insurance coverage. No claims for payment may be submitted to any third party for product dispensed by program. Limitations may apply.

References: 1. RINVOQ [package insert]. North Chicago, IL: AbbVie Inc; 2024. **2.** Data on file, AbbVie Inc. REF-124357. **3.** Brunner HI, Horneff G, Foeldvari I, et al. Safety and efficacy of upadacitinib for pediatric patients with polyarticular course juvenile idiopathic arthritis: an interim analysis of the open-label, phase 1 trial. Oral presentation at: the EULAR European Congress of Rheumatology; May 31-June 3, 2023; Milan, Italy. **4.** Data on file, AbbVie Inc. ABVRRTI78086. **5.** Data on file, AbbVie Inc. ABVRRTI78413. **6.** Data on file, AbbVie Inc. ABVRRTI68670. **7.** Genovese MC, Fleischmann R, Combe B, et al. Safety and efficacy of upadacitinib in patients with active rheumatoid arthritis refractory to biologic disease-modifying anti-rheumatic drugs (SELECT-BEYOND): a double-blind, randomised controlled phase 3 trial. *Lancet*. 2018;391(10139):2513-2524. **8.** A study to compare upadacitinib (ABT-494) to placebo in adults with rheumatoid arthritis on stable dose of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) with an inadequate response or intolerance to biologic DMARDs (SELECT-BEYOND). ClinicalTrials.gov identifier: NCT02706847. Updated August 2, 2023. Accessed April 15, 2024. https://clinicaltrials.gov/ct2/show/NCT02706847 **9.** Fleischmann R, Meerwein S, Charles-Schoeman C, et al. Safety and efficacy of upadacitinib in patients with rheumatoid arthritis and inadequate response or intolerance to biologic treatments: results through 5 years from the SELECT-BEYOND study. *RMD Open*. 2024;10:e003918. doi:10.1136/rmdopen-2023-003918 **10.** Data on file, AbbVie Inc. ABVRRTI74946. **11.** Data on file, AbbVie Inc. ABVRRTI68669. **12.** Data on file, AbbVie Inc. ABVRRTI69047. **13.** Data on file, AbbVie Inc. ABVRRTI71258. **14.** Data on file, AbbVie Inc. ABVRRTI77110. **15.** Data on file, AbbVie Inc. ABVRRTI70518. **16.** Data on file, AbbVie Inc. ABVRRTI74963. **17.** Rubbert-Roth A, Enejosa J, Pangan AL, et al. Trial of upadacitinib or abatacept in rheumatoid arthritis. *N Engl J Med*. 2020;383(16):1511-1521. **18.** Data on file, AbbVie Inc. Source: AbbVie internal analytics and Managed Markets Insight and Technology™, LLC, a trademark of MMIT. Data as of January 2025.

IMPORTANT SAFETY INFORMATION (cont'd)[1]

MEDICATION RESIDUE IN STOOL

Reports of medication residue in stool or ostomy output have occurred in patients taking RINVOQ. Most reports described anatomic or functional GI conditions with shortened GI transit times. Instruct patients to contact their healthcare provider if medication residue is observed repeatedly.

Monitor patients clinically and consider alternative treatment if there is an inadequate therapeutic response.

Please see additional Important Safety Information, including BOXED WARNING on Serious Infections, Mortality, Malignancies, Major Adverse Cardiovascular Events, and Thrombosis, throughout and on page 12.

Please see accompanying full Prescribing Information, including Boxed Warning.

FDA=US Food and Drug Administration.

IMPORTANT SAFETY INFORMATION FOR RINVOQ/RINVOQ LQ® (upadacitinib)[1]

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. Test patients for latent TB before RINVOQ use and during therapy. Consider treatment for latent TB infection prior to RINVOQ use.**
- **Invasive fungal infections, including cryptococcosis and pneumocystosis.**
- **Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.**

Carefully consider the risks and benefits of treatment with RINVOQ prior to initiating therapy in patients with chronic or recurrent infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with RINVOQ, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

MORTALITY
In a large, randomized, postmarketing safety study comparing another Janus kinase (JAK) inhibitor with tumor necrosis factor (TNF) blockers in rheumatoid arthritis (RA) patients ≥50 years old with at least one cardiovascular (CV) risk factor, a higher rate of all-cause mortality, including sudden CV death, was observed with the JAK inhibitor. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with RINVOQ.

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

In a large, randomized, postmarketing safety study comparing another JAK inhibitor with TNF blockers in RA patients, a higher rate of malignancies (excluding non-melanoma skin cancer [NMSC]), lymphomas, and lung cancer (in current or past smokers) was observed with the JAK inhibitor. Patients who are current or past smokers are at additional increased risk.

With RINVOQ, consider the benefits and risks for the individual patient prior to initiating or continuing therapy, particularly in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy when on treatment, and patients who are current or past smokers. NMSCs have been reported in patients treated with RINVOQ. Periodic skin examination is recommended for patients who are at increased risk for skin cancer. Advise patients to limit sunlight exposure by wearing protective clothing and using sunscreen.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)
In a large, randomized, postmarketing study comparing another JAK inhibitor with TNF blockers in RA patients ≥50 years old with at least one CV risk factor, a higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) was observed with the JAK inhibitor. Patients who are current or past smokers are at additional increased risk. Discontinue RINVOQ in patients that have experienced a myocardial infarction or stroke.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with RINVOQ, particularly in patients who are current or past smokers and patients with other CV risk factors. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur.

THROMBOSIS
Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis have occurred in patients treated with JAK inhibitors used to treat inflammatory conditions. Many of these adverse events were serious and some resulted in death.

In a large, randomized, postmarketing study comparing another JAK inhibitor to TNF blockers in RA patients ≥50 years old with at least one CV risk factor, a higher rate of thrombosis was observed with the JAK inhibitor. Avoid RINVOQ in patients at risk. Patients with symptoms of thrombosis should discontinue RINVOQ and be promptly evaluated.

HYPERSENSITIVITY
RINVOQ is **contraindicated** in patients with known hypersensitivity to upadacitinib or any of its excipients. Serious hypersensitivity reactions, such as anaphylaxis and angioedema, were reported in patients receiving RINVOQ in clinical trials. If a clinically significant hypersensitivity reaction occurs, discontinue RINVOQ and institute appropriate therapy.

GASTROINTESTINAL PERFORATIONS
Gastrointestinal (GI) perforations have been reported in clinical trials with RINVOQ. Monitor RINVOQ-treated patients who may be at risk for GI perforation (e.g., patients with a history of diverticulitis and patients taking NSAIDs or corticosteroids). Promptly evaluate patients presenting with new onset abdominal pain for early identification of GI perforation.

LABORATORY ABNORMALITIES
Neutropenia
Treatment with RINVOQ was associated with an increased incidence of neutropenia (absolute neutrophil count [ANC] <1000 cells/mm^3). Treatment with RINVOQ is not recommended in patients with an ANC <1000 cells/mm^3. Evaluate neutrophil counts at baseline and thereafter according to routine patient management.

Lymphopenia
Absolute lymphocyte counts (ALC) <500 cells/mm^3 were reported in RINVOQ-treated patients. Treatment with RINVOQ is not recommended in patients with an ALC <500 cells/mm^3. Evaluate at baseline and thereafter according to routine patient management.

Anemia
Decreases in hemoglobin levels to <8 g/dL were reported in RINVOQ-treated patients. Treatment should not be initiated or should be interrupted in patients with hemoglobin levels <8 g/dL. Evaluate at baseline and thereafter according to routine patient management.

Lipids
Treatment with RINVOQ was associated with increases in lipid parameters, including total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. Manage patients according to clinical guidelines for the management of hyperlipidemia. Evaluate patients 12 weeks after initiation of treatment and thereafter according to the clinical guidelines for hyperlipidemia.

Liver enzyme elevations
Treatment with RINVOQ was associated with increased incidence of liver enzyme elevation compared to placebo. Evaluate at baseline and thereafter according to routine patient management. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. If increases in aspartate aminotransferase (AST) or alanine aminotransferase (ALT) are observed during routine patient management and drug-induced liver injury is suspected, RINVOQ should be interrupted until this diagnosis is excluded.

EMBRYO-FETAL TOXICITY
Based on findings in animal studies, RINVOQ may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with RINVOQ and for 4 weeks after the final dose. Verify pregnancy status of females of reproductive potential prior to starting treatment with RINVOQ.

VACCINATION
Avoid use of live vaccines during, or immediately prior to, RINVOQ therapy. Prior to initiating RINVOQ, patients should be brought up to date on all immunizations, including prophylactic varicella zoster or herpes zoster vaccinations, in agreement with current immunization guidelines.

MEDICATION RESIDUE IN STOOL
Reports of medication residue in stool or ostomy output have occurred in patients taking RINVOQ. Most reports described anatomic or functional GI conditions with shortened GI transit times. Instruct patients to contact their healthcare provider if medication residue is observed repeatedly. Monitor patients clinically and consider alternative treatment if there is an inadequate therapeutic response.

LACTATION
There are no data on the presence of RINVOQ in human milk, the effects on the breastfed infant, or the effects on milk production. Available data in animals have shown the excretion of RINVOQ in milk. Advise patients that breastfeeding is not recommended during treatment with RINVOQ and for 6 days after the last dose.

HEPATIC IMPAIRMENT
RINVOQ is not recommended for use in patients with severe hepatic impairment.

ADVERSE REACTIONS
The most common adverse reactions in RINVOQ clinical trials were upper respiratory tract infections, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, acne, headache, increased blood creatine phosphokinase, hypersensitivity, folliculitis, abdominal pain, increased weight, influenza, fatigue, neutropenia, myalgia, influenza-like illness, elevated liver enzymes, rash, and anemia.

Inform patients that retinal detachment has been reported in clinical trials with RINVOQ. Advise patients to immediately inform their healthcare provider if they develop any sudden changes in vision while receiving RINVOQ.

Dosage Forms and Strengths: RINVOQ is available in 15 mg, 30 mg, and 45 mg extended-release tablets. RINVOQ LQ is available in a 1 mg/mL oral solution.

*Unless otherwise stated, "RINVOQ" in the IMPORTANT SAFETY INFORMATION refers to RINVOQ and RINVOQ LQ.

Please see accompanying full Prescribing Information, including Boxed Warning.

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