RINVOQ® (upadacitinib) in Atopic Dermatitis

Medicaid Clinical Summary

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US Medical Affairs

Atopic Dermatitis is a type of eczema that is chronic, highly pruritic and a systemic inflammatory disease of the skin that can have debilitating physical and psychological burden on the patient.[5] It can occur on any area of the body and its clinical presentation is highly varied.[6]

INDICATIONS AND USAGE[1]

Upadacitinib (UPA) is indicated for the treatment of adults and pediatric patients 12 years of age and older with refractory moderate to severe atopic dermatitis (AD) whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable. **Limitations of Use:** Upadacitinib is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants.

DOSAGE AND ADMINISTRATION[1]

Pediatric patients ≥12 years of age weighing ≥40 kg and adults <65 years of age: Initiate treatment with 15 mg once daily. If an adequate response is not achieved, consider increasing the dosage to 30 mg once daily. Discontinue UPA if an adequate response is not achieved with the 30 mg dose. Use the lowest effective dose needed to maintain response. Adults 65 years and older, the recommended dosage is 15 mg once daily.

IMPORTANT SAFETY CONSIDERATIONS:[1]

Serious Infections: Patients treated with RINVOQ are at increased risk for developing serious infections that may lead to hospitalization or death. These infections include tuberculosis (TB), invasive fungal, bacterial, viral, and other infections due to opportunistic pathogens. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids.

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

Malignancies: Lymphoma and other malignancies have been observed in RINVOQ-treated patients. A higher rate of malignancies (excluding non-melanoma skin cancer [NMSC]), lymphomas, and lung cancer (in current or past smokers) was observed with another JAK inhibitor when compared with TNF blockers in RA patients. Patients who are current or past smokers are at additional increased risk.

Major Adverse Cardiovascular Events: A higher rate of CV death, myocardial infarction, and stroke was observed with a JAK inhibitor in a study comparing another JAK inhibitor with TNF blockers in RA patients ≥50 years of age with at least one CV risk factor. Current or past smokers are at additional increased risk.

Thrombosis: Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis have occurred in patients treated with JAK inhibitors used to treat inflammatory conditions. A higher rate of thrombosis was observed with another JAK inhibitor when compared with TNF blockers in RA patients.

Hypersensitivity: RINVOQ is contraindicated in patients with known hypersensitivity to upadacitinib or any of its excipients.

Other Serious Adverse Reactions: Hypersensitivity Reactions (anaphylaxis and angioedema), Gastrointestinal Perforations, Laboratory Abnormalities (neutropenia, lymphopenia, anemia, lipid elevations, liver enzyme elevations), and Embryo-Fetal Toxicity.

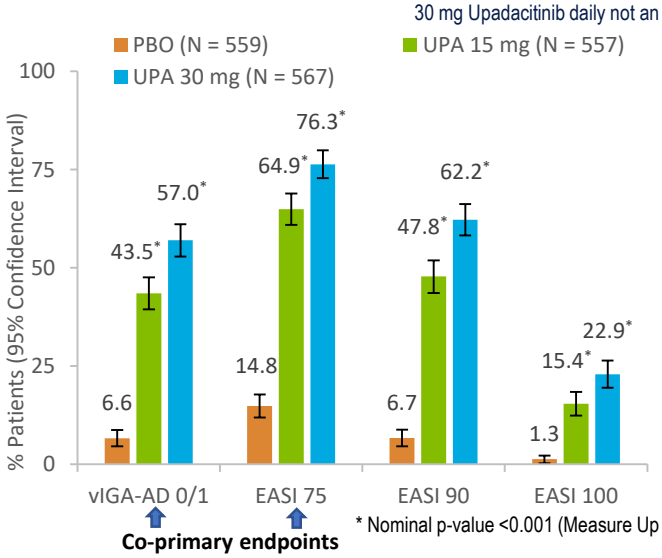
UPADACITINIB ATOPIC DERMATITIS PHASE 3 CLINICAL TRIAL PROGRAM [2,3,4]

Across the phase 3 clinical program for AD, 2,584 patients were treated with upadacitinib (UPA). The co-primary efficacy endpoints were EASI 75 and vIGA-AD 0/1 with at least 2-point improvement, measured at 16 weeks. Long-term blinded extension periods will evaluate upadacitinib for 260 weeks [2,3,4]

	Measure Up 1 [2,4]	Measure Up 2 [2,4]	AD Up [3]
Population	N=847 (adolescents N=124)	N=836 (adolescents N=104)	N=901 (adolescents N=116)
Therapy	Monotherapy	Monotherapy	Combination w/ TCS
Treatment arms (1:1:1)	UPA 15 mg QD	UPA 15 mg QD	UPA 15 mg QD + TCS
	UPA 30 mg QD	UPA 30 mg QD	UPA 30 mg QD + TCS
	Placebo	Placebo	Placebo + TCS
Double-blind period	16 weeks	16 weeks	16 weeks
Key Inclusion criteria	Chronic AD for ≥3 years; moderate to severe AD (vIGA-AD ≥3, EASI ≥16, BSA ≥10%, weekly average of daily worst pruritus NRS ≥4); Inadequate response to TCS/TCI or systemic treatment within 6 months		
Key Exclusion criteria	Use of systemic therapies or phototherapy for AD within 4 weeks of BL or topical treatments within 7 days of BL; Prior exposure to any Janus kinase (JAK) inhibitor or dupilumab		

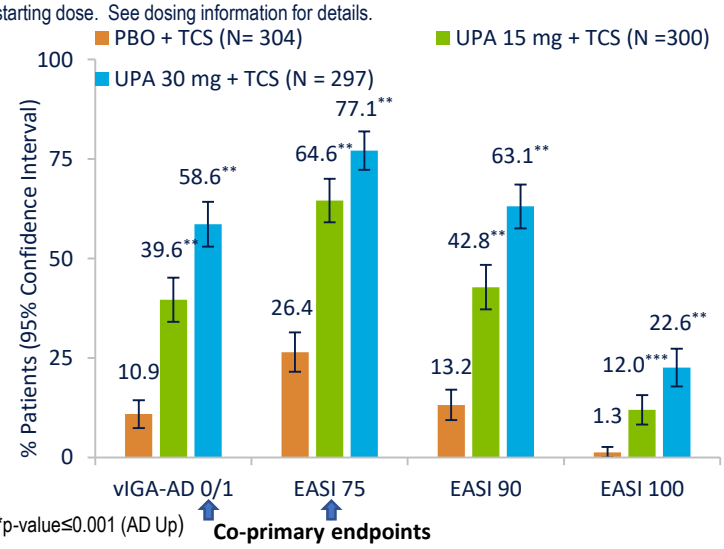
BL, baseline; BSA, body surface area; EASI 75, at least a 75% improvement in the Eczema Area and Severity Index score; NRS, Numeric Rating Scale; TCS, topical corticosteroids; QD, once daily; vIGA-AD, validated Investigator Global Assessment for Atopic Dermatitis

Integrated Measure Up 1[2] and Measure Up 2[2]



AD Up[3]

30 mg Upadacitinib daily not an approved starting dose. See dosing information for details.



* Nominal p-value <0.001 (Measure Up 1 and 2); **p-value≤0.001 (AD Up)

RINVOQ® (upadacitinib) extended-release tablets, for oral use
Safety Supplement

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INDICATIONS

Upadacitinib is a Janus kinase (JAK) inhibitor 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.

Adults with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers.

Limitations of Use for RA and PsA: Use of upadacitinib in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

Adults and pediatric patients 12 years of age and older with refractory moderate to severe atopic dermatitis (AD) whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable.

Limitations of Use for AD: Upadacitinib is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants.

Adults with moderately to severely active ulcerative colitis (UC) who have had an inadequate response or intolerance to one or more TNF blockers.

Limitations of Use for UC: Upadacitinib is not recommended for use in combination with other JAK inhibitors, biological therapies for UC, or with other potent immunosuppressants such as azathioprine and cyclosporine.

IMPORTANT SAFETY CONSIDERATIONS AND BOXED WARNING

Serious Infections: Patients treated with upadacitinib are at increased risk for developing serious infections that may lead to hospitalization or death. These infections include tuberculosis (TB), invasive fungal, bacterial, viral, and other infections due to opportunistic pathogens. Most patients who developed these infections were taking concomitant immunosuppressants, such as methotrexate or corticosteroids. Test for latent TB before and during therapy; treat latent TB prior to use. Consider the risks and benefits prior to initiating therapy in patients with chronic or recurrent infection. If a serious infection develops, interrupt upadacitinib until the infection is controlled.

Mortality: In a postmarketing safety study in RA patients ≥ 50 years of age with at least one cardiovascular (CV) risk factor comparing another JAK inhibitor to TNF blockers, a higher rate of all-cause mortality, including sudden CV death, was observed with the JAK inhibitor.

Malignancies: Malignancies have been observed in upadacitinib treated patients. In RA patients treated with another JAK inhibitor, a higher rate of lymphomas and lung cancers was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with upadacitinib, particularly in patients with a known malignancy (other than a successfully treated non-melanoma skin cancer), patients who develop a malignancy when on treatment, and patients who are current or past smokers.

Major Adverse Cardiovascular Events (MACE): In RA patients who were ≥ 50 years of age with at least one CV risk factor treated with another JAK inhibitor, a higher rate of MACE (CV death, myocardial infarction, and stroke) was observed compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with upadacitinib. Patients should be informed about the symptoms of serious CV events and the steps to take if they occur. **Discontinue upadacitinib in patients that have experienced a myocardial infarction or stroke.**

Thrombosis: Thrombosis, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis, have occurred in patients treated with JAK inhibitors, including upadacitinib. Many of these adverse events were serious and some resulted in death. In RA patients who were ≥ 50 years of age with at least one CV risk factor treated with another JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid upadacitinib in patients at risk. Patients with symptoms of thrombosis should discontinue upadacitinib and be promptly evaluated.

Hypersensitivity Reactions: Upadacitinib 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 upadacitinib in clinical trials. If a clinically significant hypersensitivity reaction occurs, discontinue upadacitinib and institute appropriate therapy.

Other Serious Adverse Reactions: Patients treated with upadacitinib also may be at risk for other serious adverse reactions, including gastrointestinal perforations, neutropenia, lymphopenia, anemia, lipid elevations, liver enzyme elevations, and embryo-fetal toxicity.

Vaccinations: Avoid use of live vaccines during, or immediately prior to, upadacitinib therapy. Prior to initiating upadacitinib, it is recommended that patients be brought up to date with all immunizations, including varicella zoster or prophylactic herpes zoster vaccinations, in agreement with current immunization guidelines.

Common Adverse Reactions in RA and PsA: The most common adverse reactions (≥1%) are upper respiratory tract infections, herpes zoster, herpes simplex, bronchitis, nausea, cough, pyrexia, and acne.

Common Adverse Reactions in AD: The most common adverse reactions (≥1%) are upper respiratory tract infections, acne, herpes simplex, headache, increased blood creatine phosphokinase, cough, hypersensitivity, folliculitis, nausea, abdominal pain, pyrexia, increased weight, herpes zoster, influenza, fatigue, neutropenia, myalgia, and influenza like illness.

Common Adverse Reactions in UC: The most common adverse reactions (≥5%) reported are upper respiratory tract infections, increased blood creatine phosphokinase, acne, neutropenia, elevated liver enzymes, and rash.

Review accompanying upadacitinib full Prescribing Information for additional information, visit www.rxabbvie.com or contact AbbVie Medical Information at 1-800-633-9110.

REFERENCES

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