DRUG DETERMINATION POLICY

Title: DDP-41 Janus Kinase Inhibitors

Effective Date:10/26/22

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Xeljanz (tofacitinib), Rinvoq (upadacitinmib), and Cibinqo (abrocitinib) are specialty drugs indicated for several diagnoses and is associated with adverse effects. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of adverse effects, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. General use considerations.

A. Appropriate medication use [must meet one listed below]:

1. Food and Drug Administration (FDA) approval status [must meet one listed below]:

a. FDA approved: product, indication and/or dosage regimen.

b. Non-FDA approved: compendium support (Lexi comp™) for use of a drug for a non-FDA approved indication or dosage regimen.

2. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

B. Exclusions.

1. Excluded Drugs: Olumiant (baricitinib)

   a. Contraindication, inadequate response after four months or significant adverse effects to all preferred agents.

2. Concomitant use with biological disease-modifying anti-rheumatic drugs (DMARDs), tumor necrosis factor (TNF) antagonists, IL-1R antagonist, IL-6R antagonist, anti-CD20 monoclonal antibodies or co-stimulant modulators.

II. Rheumatology

A. Rheumatoid Arthritis [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity: moderate to severe active rheumatoid arthritis.

3. Other therapies: contraindicated, inadequate response after four months or significant adverse effects with methotrexate, one other disease modifying anti-rheumatic agents and one Tumor Necrosis Factor (TNF) Inhibitor:

   a. Methotrexate: one must be methotrexate unless contraindicated.

   b. Other disease modifying anti-rheumatic agent: leflunomide, sulfasalazine, cyclosporine, azathioprine.

   c. TNF-Inhibitors: Humira, Enbrel, Simponi Aria, Renflexis.

4. Dosage regimen: refer to Appendix I for adjustments.

   a. Xeljanz oral (tofacitinib): Immediate release - 5mg two times daily; or Extended release - 11mg daily.

   b. Rinvoq oral (upadacitinib): 15mg daily.

B. Psoriatic Arthritis [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity: active psoriatic arthritis

3. Other therapies: contraindicated, inadequate response after four months or significant adverse effects with methotrexate, one other disease modifying anti-rheumatic drug and one Tumor Necrosis Factor (TNF) Inhibitor:

   a. Methotrexate: one must be methotrexate unless contraindicated.

   b. Other disease modifying anti-rheumatic agent: leflunomide, sulfasalazine, azathioprine.

   c. TNF-Inhibitors: Humira, Enbrel, Simponi Aria, Renflexis.

4. Dosage regimen: refer to Appendix I for adjustments.

a. Xeljanz oral (tofacitinib): Immediate release - 5mg two times daily; or Extended release - 11mg daily.

b. Rinvoq oral (upadacitinib): 15mg daily.

C. Axial spondyloarthritis (ankylosing spondylitis and nonradiographic axial spondyloarthritis) [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity: active ankylosing spondylitis or nonradiographic axial spondyloarthritis

3. Other therapies: contraindicated, inadequate response (after four-month trial) or significant adverse effects from two non-steroidal anti-inflammatory drugs, one disease-modifying anti-rheumatic drugs, and one Tumor Necrosis Factor (TNF) Inhibitor:

a. Non-steroidal anti-inflammatory Agents: prescription agents (e.g., meloxicam, celecoxib, nambutone)

b. Peripheral dominant disease only: First line disease modifying anti-rheumatic drugs: methotrexate, sulfasalazine.

c. TNF-Inhibitors: Humira, Enbrel, Simponi Aria, Renflexis.

4. Dosage regimen: refer to Appendix I for adjustments.

a. Xeljanz oral (tofacitinib): Immediate release - 5mg two times daily; or Extended release - 11mg daily.

b. Rinvoq oral (upadacitinib): 15mg daily.

D. Approval.

1. Initial: six months.

2. Re-approval: one year (decrease or sustained decrease in disease activity)

III. Inflammatory bowel disease

A. Ulcerative Colitis [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity: moderate to severe ulcerative colitis.

3. Other therapies: contraindicated, inadequate response after four months or significant adverse effects to one disease modifying rheumatoid agent and one Tumor Necrosis Factor (TNF) Inhibitor.

a. Disease modifying rheumatoid agent: sulfasalazine.

b. TNF-Inhibitors: Humira, Enbrel, Simponi Aria, Renflexis.

4. Dosage regimen (refer to appendix I for adjustments)

    a. Xeljanz oral (tofacitinib)

        i. Immediate release (IR): 10mg once daily for eight to sixteen weeks, then 5mg to 10mg twice daily depending on response.

        ii. Extended release (ER): 22mg once daily for eight to 16 weeks, then 11mg to 22mg once daily depending on response.

    b. Rinvoq oral (upadacitinib)

        i. 45 mg once daily for 8 weeks, then 15 mg once daily (may increase to 30 mg once daily in patients with refractory, severe, or extensive disease)

        ii. Discontinue if an adequate response is not achieved with the 30 mg dose; use the lowest effective dose needed to maintain response.

B. Approval.

1. Initial: six months.

2. Re-approval: one year (decrease or sustained decrease in disease activity)

IV. Dermatology

A. Atopic Dermatitis

1. Age:

    a. Rinvoq (upadacitinib): at least 12 (at least 88 pounds)

    b. Cibinqo (abrocitinib): at least 18 years.

2. Prescriber: dermatologist or allergist.

3. Diagnosis and severity: moderate to severe atopic dermatitis not controlled with topical prescription therapies or if the therapies are not advisable [must meet all listed below]:

    a. Exacerbating factors that could contribute to the member's atopic dermatitis have been evaluated and addressed (e.g., non-compliance, environmental triggers, allergy patch testing etc.).

    b. Body surface area (BSA): at least 10 percent.

    c. Severity [must meet both below]:

        i. Documentation of current pruritus and other symptoms severity (e.g., erythema, edema, xerosis, erosions. excoriations, oozing/crusting and/or lichenification).

        ii. Interfering with routine daily activities (e.g., skin infections, sleep disturbances).

4. Other therapies: contraindicated, inadequate response after two months, or significant adverse effects to two topical therapies and four months of one biologic option. [must meet all listed below].

a. Mid-strength to super-potent corticosteroid: unless the face, neck and/or intertriginous areas are affected.

b. Topical calcineurin Inhibitor: tacrolimus, pimecrolimus.

c. Interleukin antagonist: Dupixent (dupilumab), Adbry (tralokinumab).

5. Dosage regimen

a. Rinvoq oral (upadacitinib): 15mg once daily; may increase to 30mg if inadequate response.

b. Cibinqo oral (abrocitinib): 100 mg once daily. For insufficient response after 12 weeks, may increase dose to 200 mg once daily.

6. Approval:

a. Initial: 6 months

b. Re-approval: one year; reduced affected body surface area

4.0 Coding:

None.

5.0 References, Citations & Resources:

1. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Xeljanz, Rinvoq, Cibinqo accessed October 2022
2. Xeljanx package insert Pfizer Laboratories Div Pfizer https://labeling.pfizer.com/ShowLabeling.aspx?id=959. Accessed February 2022
3. Rinvoq package insert AbbVie Ireland NL B.V., Sligo, Ireland https://www.rxabbvie.com/pdf/rinvoq_pi.pdf accessed February 2022
4. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 1: Diagnosis and medical management. Journal of Crohn's and Colitis. 2017;11:3-25.
5. Clinical Practice Guidelines for the treatment of patients with axial spondyloarthritis and psoriatic arthritis. Madrid, (Spain): Spanish Society of Rheumatology (SER);2015.
6. American Gastroenterological Association Institute Clinical Guidelines Committee. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. *Gastroenterology*. 2021;160(7):2496-2508. doi:10.1053/j.gastro.2021.04.022

6.0 Appendices:

See pages 7-8.

7.0 Revision History:

Original Effective Date: 01/01/2019

Next Review Date: 07/28/2022

Revision Date	Reason for Revision
12/19	New format, replaced abbreviations, clarified dosage adjustments and UC dose
6/20	Annual review: replaced abbreviations, delete prescriber type, changed other therapies language, added Xeljanz XR dosage for UC indication, deleted

Revision Date	Reason for Revision
	REMs program in safety and monitoring table, added Rinvoq, approved by P&T Committee 8/26/20.
6/21	Annual review, formatting, replaced abbreviations, clarified criteria instructions, added appropriate use section
11/21	Off-cycle review, Listed already excluded drug in the policy
01/22	Off cycle review, added TNF inhibitor step due to PI; clarified other therapies and added black box waning, added Rinvoq and Xeljanz dosing to Ankylosing Spondylitis (new indication); added Atopic Dermatitis indication
4/22	Off-cycle review, added Rinvoq for Ulcerative colitis, Atopic dermatitis and Ankylosing Spondylitis (as well as Xeljanz)
7/22	With approval spelled abbrev and added specialty org references
11/22	Added Cibinqo and IL trial requirement for Atopic Derm

Appendix I: Dosage Adjustment

State	Value	Recommendation
Anemia	Hemoglobin (Hgb) at least 9g/dL and decreased less than 2g/dL	Maintain dose
	Hgb less than 8g/dL or decreased more than 2 g/dL	Stop dosing until Hgb normalizes
Lymphopenia	Lymphocyes at least 500 cells/mm^3	Maintain dose
	Lymphocyes less than 500 cells/mm^3	Discontinue
Neutropenia	Absolute neutrophil count (ANC) more than 1000 cells/mm^3	Maintain dose
	ANC 500 to 1000 cells/mm^3	Persistent decrease: stop dosing until ANC is more than 1000 cells/mm^3 then resume normal dose
	ANC less than 500 cells/mm^3	Discontinue
Concurrent CYP450	Potent CYP 3A4 Inducer (rifampin)	Not recommended
	Potent inhibitor (ketoconazole) or more than one moderate CYP 3A4 inhibitor. Potent CYP2C19 inhibitor (fluconazole)	Reduce dose
Renal Function	Mild impairment	No adjustment
	Moderate to severe impairment	Xeljanz: 5mg once daily Rinvoq: 15mg once daily Cibinqo: decrease dose by 50%
	Dialysis	Not recommended
Hepatic Function	Mild impairment	No adjustment
	Moderate impairment	Xeljanz: 5mg once daily Rinvoq: 15mg once daily Cibinqo: no adjustment
	Severe impairment	Not recommended

Appendix II: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS & Special alerts
Xeljanz tofacitinib	• Respiratory: nasopharyngitis (3-14%), upper respiratory infection (URI) • Miscellaneous: infection (20-22%) • Pregnancy: Class C	• Labs: lymphocytes (pretreatment and every 3 months); neutrophil, Hgb/lipids (pretreatment 6 weeks, then every 6 months); liver function tests • Infections: viral hepatitis (pretreatment), signs and symptoms of infection	Increased risk of serious cardiovascular related events (eg, heart attack, stroke), cancer (eg, lymphoma, lung cancer), thrombosis, and death Must Dispense with Medication Guide
Rinvoq upadacitinib	• Respiratory: upper respiratory tract infection (14%)	• Labs: lymphocytes; neutrophil, Hgb and liver function tests (baselines and periodically; lipids (3 months after treatment starts and periodically) • Cardiovascular: signs and symptoms of thrombosis • Dermatology: skin examinations • Infections: viral hepatitis (pretreatment and periodically), tuberculosis, signs and symptoms of infection	
Cibinqo abrocitinib	• Gastrointestinal: Nausea (6% to 15%) • Infection: Infection (35%; serious infection: ≤1%) • Respiratory: Nasopharyngitis (9% to 12%)	• Labs: lymphocytes; neutrophil, Hgb and liver function tests (baselines and periodically; lipids (3 months af ter treatment starts and periodically) • Cardiovascular: signs and symptoms of thrombosis • Dermatology: skin examinations • Infections: viral hepatitis (pretreatment and periodically) tuberculosis, signs and symptoms of infection	