

# DRUG DETERMINATION POLICY

**Title:** DDP-41 Janus Kinase Inhibitors

**Effective Date:** 8/23/23



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 (upadacitinib), 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 (Lexicomp®) 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. Trial of all preferred formulary agents is required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.
  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.
- C. Pharmaceutical sample use: The Plan does not recognize samples as a medication trial or for continuation of therapy.
- D. Adherence to requested medication required for re-approval: consistent fill history (at least 80% of days covered) electronically or verbally from pharmacy.

## 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: Trials of methotrexate, one additional disease modifying anti-rheumatic agent, and one Tumor Necrosis Factor (TNF) Inhibitor listed below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction:
  - a. Methotrexate.
  - b. Other disease-modifying anti-rheumatic agents: 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: Trials of methotrexate, one additional disease-modifying anti-rheumatic agent, and one Tumor Necrosis Factor (TNF) Inhibitor listed below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction:
  - a. Methotrexate.
  - b. Other disease-modifying anti-rheumatic agents: leflunomide, sulfasalazine, and azathioprine.
  - c. TNF-Inhibitors: Humira, Enbrel, Simponi Aria, Renflexis, Inflectra.

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 non-radiographic axial spondyloarthritis) [must meet all listed below]:

1. Age: at least 18 years.
2. Diagnosis and severity: active ankylosing spondylitis or non-radiographic axial spondyloarthritis
3. Other therapies: Trials of two non-steroidal anti-inflammatory drugs, one disease-modifying anti-rheumatic drug, and one Tumor Necrosis Factor (TNF) Inhibitor below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction:
  - 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, Inflectra.
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 [must meet all listed below]:

A. Crohn's Disease

1. Age: at least 18 years.
2. Diagnosis and severity: moderate to severe active Crohn's disease.
3. Other therapies: Trials of one disease-modifying antirheumatic drug and one Tumor Necrosis Factor (TNF) Inhibitor below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.
  - a. Disease-modifying antirheumatic drug: azathioprine, methotrexate.
  - b. TNF-Inhibitors: Humira, Inflectra, Renflexis.
4. Dosage Regimen

- a. Rinvoq oral (upadacitinib)
  - i. 45mg once daily for 12 weeks, then 15mg or 30mg once daily.
  - ii. Discontinue if an adequate response is not achieved with the 30 mg dose; use the lowest effective dose needed to maintain response.

## B. Ulcerative Colitis

1. Age: at least 18 years.
2. Diagnosis and severity: moderate to severe active ulcerative colitis.
3. Other therapies: Trials of one disease-modifying antirheumatic drug and one Tumor Necrosis Factor (TNF) Inhibitor below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or a severe adverse reaction.
  - a. Disease-modifying antirheumatic drug: azathioprine.
  - b. TNF-Inhibitors: Humira, Inflectra, Renflexis, Simponi Aria.
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.

## C. 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: Trials of one topical therapy and one systemic therapy below are required unless all are contraindicated. Trial must result in an inadequate response after two consecutive months of use per topical therapy and four consecutive months of use per systemic therapy or severe adverse reaction.
  - a. Topical therapies: mid-strength to super-potent corticosteroid, topical calcineurin inhibitor
  - b. Systemic therapies: including Dupixent (dupilumab), and 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, increase the 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. Xeljanz 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](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
  7. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis (2020). American Gastroenterological Association. Available at: [https://www.gastrojournal.org/article/S0016-5085\(20\)30018-4/fulltext](https://www.gastrojournal.org/article/S0016-5085(20)30018-4/fulltext) (Accessed: April 5, 2023).

## 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, deleted prescriber type, changed other therapies language, added Xeljanz XR dosage for UC indication, deleted 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 warning, 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
3/23	Off-cycle review; adjusted dermatology and other therapy requirements. IBD – added Crohn's disease section (expected new indication for Rinvoq), ulcerative colitis other therapies: removed Enbrel and replaced sulfasalazine with azathioprine. Added Ulcerative Colitis guideline reference.
6/23	Annual review; updated other therapies language, pharmaceutical samples use not accepted, added adherence requirement for re-approval

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	Lymphocytes at least 500 cells/mm <sup>3</sup>	Maintain dose
	Lymphocytes less than 500 cells/mm <sup>3</sup>	Discontinue
Neutropenia	Absolute neutrophil count (ANC) more than 1000 cells/mm <sup>3</sup>	Maintain dose
	ANC 500 to 1000 cells/mm <sup>3</sup>	Persistent decrease: stop dosing until ANC is more than 1000 cells/mm <sup>3</sup> then resume normal dose
	ANC less than 500 cells/mm <sup>3</sup>	Discontinue
Concurrent CYP450	Potent CYP 3A4 Inducer (rifampin)	Not recommended
	Potent inhibitor (ketoconazole) or more than one moderate CYP 3A4 inhibitor.	Reduce dose
	Potent CYP2C19 inhibitor (fluconazole)	
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	<ul style="list-style-type: none"> <li>• Respiratory: nasopharyngitis (3-14%), upper respiratory infection (URI)</li> <li>• Miscellaneous: infection (20-22%)</li> <li>• Pregnancy: Class C</li> </ul>	<ul style="list-style-type: none"> <li>• Labs: lymphocytes (pretreatment and every 3 months); neutrophil, Hgb/lipids (pretreatment 6 weeks, then every 6 months); liver function tests</li> <li>• Infections: viral hepatitis (pretreatment), signs and symptoms of infection</li> </ul>	<p>Increased risk of serious cardiovascular related events (eg, heart attack, stroke), cancer (eg, lymphoma, lung cancer), thrombosis, and death</p> <p>Must Dispense with Medication Guide</p>
Rinvoq upadacitinib	<ul style="list-style-type: none"> <li>• Respiratory: upper respiratory tract infection (14%)</li> </ul>	<ul style="list-style-type: none"> <li>• Labs: lymphocytes; neutrophil, Hgb and liver function tests (baselines and periodically; lipids (3 months after treatment starts and periodically)</li> <li>• Cardiovascular: signs and symptoms of thrombosis</li> <li>• Dermatology: skin examinations</li> <li>• Infections: viral hepatitis (pretreatment and periodically), tuberculosis, signs and symptoms of infection</li> </ul>	
Cibinqo abrocitinib	<ul style="list-style-type: none"> <li>• Gastrointestinal: Nausea (6% to 15%)</li> <li>• Infection: Infection (35%; serious infection: ≤1%)</li> <li>• Respiratory: Nasopharyngitis (9% to 12%)</li> </ul>	<ul style="list-style-type: none"> <li>• Labs: lymphocytes; neutrophil, Hgb and liver function tests (baselines and periodically; lipids (3 months after treatment starts and periodically)</li> <li>• Cardiovascular: signs and symptoms of thrombosis</li> <li>• Dermatology: skin examinations</li> <li>• Infections: viral hepatitis (pretreatment and periodically) tuberculosis, signs and symptoms of infection</li> </ul>	