DRUG DETERMINATION POLICY

Title: DDP-41 Janus Kinase Inhibitors: Xeljanz and Rinvoq

Effective Date: 08/31/2021

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) and Rinvoq (upadacitinmib) are specialty drugs indicated for a number of 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. 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 Rheumatoid Arthritis [must meet all listed below]:

A. Age: at least 18 years.

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

C. Other therapies: contraindicated, inadequate response after four months with each agent or significant adverse effects with two agents below:

1. Methotrexate: one must be methotrexate unless contraindicated.

2. Other: leflunomide, sulfasalazine, cyclosporine, azathioprine.

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

1. Xeljanz oral tofacitinib).

a. Immediate release - 5mg two times daily; or

b. Extended release - 11mg daily.

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

E. Approval.

1. Initial: six months.

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

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

A. Age: at least 18 years.

B. Diagnosis and severity: active psoriatic arthritis with at least five swollen and tender joints.

C. Other therapies: contraindicated, inadequate response after four months or significant adverse effects from one category below:

1. Peripheral disease: disease modifying rheumatoid drugs (methotrexate, leflunomide, sulfasalazine).

2. Axial disease, enthesitis, dactylitis and uveitis: non-steroidal anti-inflammatory drugs.

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

1. Xeljanz IR oral (tofacitinib): 5mg two times daily; or

2. Xeljanz XR oral (tofacitinib XR): 11mg daily.

E. Approval.

a. Initial: six months.

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

IV. Inflammatory bowel disease: ulcerative colitis [must meet all listed below]:

A. Age: at least 18 years.

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

C. Other therapies: contraindicated, inadequate response after four months with each agents or significant adverse effects to one conventional and one disease modifying rheumatoid agent.

1. Conventional therapies: mesalamine.

2. Disease modifying rheumatoid agent: sulfasalazine.

D. Dosage regimen (refer to Appendix I for adjustments).

1. Xeljanz immediate release (tofacitinib IR): 10mg once daily for eight to sixteen weeks, then 5mg to 10mg twice daily depending on response.

2. Xeljanz extended release (tofacitinib ER): 22mg once daily for eight to 16 weeks, then 11mg to 22mg once daily depending on response.

E. Approval.

1. Initial: six months.

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

4.0 Coding:

None.

5.0 References, Citations & Resources:

1. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Xeljanz, Rinvoq, accessed July. 2021.

6.0 Appendices:

See pages 5 and 6.

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 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,

Revision Date	Reason for Revision
	added appropriate use section

Appendix I: Dosage Adjustment

State	Value	Recommendation
Xeljanz and Rinvoq		
Anemia	Hemoglobin (Hgb) at least 9g/dL and decreased less than 2gm/dL	Maintain dose
	Hgb less than 8g/dL or decreased more than 2gm/dL	Stop dosing until Hgb normalizes
Lymphopenia	Lymphocytes at least 500 cells/mm^3	Maintain dose
	Lymphocytes less than 500 cells/mm^3	Discontinue
Neutropenia	Absolute Neutrophil Count (ANC) more than 1,000 cells/mm^3	Maintain dose
	ANC 500 to 1,000 cells/mm^3	Persistent decrease: stop dosing until ANC more than 1,000 cells/mm^3 when ANC more than 1,000 cells/mm^3 resume normal dose
	ANC less than 500 cells/mm^3*	Discontinue
Concurrent CYP450	Potent P450 3A4 Inducer (rifampin)	Not recommended
	Potent Inhibitor (ketoconazole) or more than one moderate CYP3A inhibitor positive Potent CYP2C19 inhibitor (fluconazole)	Reduce dose
Xeljanz		
Renal function	Mild impairment	No adjustment
	Moderate to severe impairment	Decrease 5mg once daily
	Dialysis	Not recommended
Hepatic function	Mild impairment	No adjustment
	Moderate impairment	Decrease 5mg once daily
	Severe Impairment	Not recommended

Appendix II: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring & Contraindications	REMS
Xeljanz tofacitinib	• Respiratory: nasopharyangitis (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	• None needed
Rinvoq	• 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	• None needed