Clinical Policy: Ruxolitinib (Jakafi)

Reference Number: PA.CP.PHAR.98 Coding Implications
Effective Date: 01/18 Revision Log
Last Review Date: 01/19

Description
Ruxolitinib (Jakafi®) is a kinase inhibitor.

FDA Approved Indication(s)
Jakafi is indicated:

- For treatment of patients with intermediate or high-risk myelofibrosis (MF), including primary MF, post-polycythemia vera (post-PV MF) and post-essential thrombocythemia (post-ET MF);
- For treatment of patients with polycythemia vera (PCV)who have had an inadequate response to or are intolerant to hydroxyurea.

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness that Jakafi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Myelofibrosis (must meet all):

1. Diagnosis of MF (includes primary MF, post-PV MF, post-ET MF)
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 50 mg per day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

B. Polycythemia Vera (must meet all):

1. Diagnosis of PCV;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 years;
4. Failure of hydroxyurea, peginterferon, or interferon *(see Appendix B)* unless contraindicated or clinically significant adverse effects are experienced;*
   **Prior authorization may be required.*
5. Request meets one of the following (a or b):
   a. Dose does not exceed 50 mg per day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 25 mg twice daily.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:
Ruxolitinib, a kinase inhibitor, inhibits Janus Associated Kinases (JAKs) JAK1 and JAK2 which mediate the signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. JAK signaling involves recruitment of STATs (signal transducers and activators of transcription) to cytokine receptors, activation and subsequent localization of STATs to the nucleus leading to modulation of gene expression. Myelofibrosis (MF) and polycythemia vera (PV) are myeloproliferative neoplasms (MPN) known to be associated with dysregulated JAK1 and JAK2 signaling. In a mouse model of JAK2V617F-positive MPN, oral administration of ruxolitinib prevented splenomegaly, preferentially decreased JAK2V617F mutant cells in the spleen and decreased circulating inflammatory cytokines (e.g., TNF-α, IL-6).

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MF: myelofibrosis
PCV: polycythemia vera
Post-ET MF: post-essential thrombocythemia myelofibrosis
Post-PV MF: post-polycythemia vera myelofibrosis

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
hydroxyurea (Droxia®, Hydrea®)	PCV Adults: 1000 to 2000 mg PO per day divided into 1 to 3 doses initially. The dose is adjusted as needed to normalize	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	the blood counts of red cells, neutrophils, and platelets.	
Intron A® (interferon alfa-2b)	PCV: Varies (off-label use)	Varies
Pegasys®, Pegasys ProClick® (peginterferon alfa-2a)	PCV: Varies (off-label use)	Varies
PegIntron®, Sylatron® (peginterferon alfa-2b)	PCV: Varies (off-label use)	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
Examples of positive response to therapy include:

- Myelofibrosis: reduction in spleen size or improvement in symptoms such as pruritus, fatigue, night sweats, bone pain since initiation of therapy;
- Polycythemia vera: reduction in thromboembolic events, spleen size, or phlebotomy requirement, improvement in platelet or white-cell count, or improvement in symptoms such as pruritus, fatigue, or night sweats since initiation of therapy.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MF	5 mg to 25 mg PO BID	50 mg/day
PCV	10 mg to 25 mg PO BID	50 mg/day

V. Product Availability

Tablets: 5 mg, 10 mg, 15 mg, 20 mg, 25 mg

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Removed request for bloodwork. Removed NCCN off-label use for myelofibrosis. References reviewed and updated.	02/18	
1Q 2019 annual review; intermediate or high-risk MF is removed to accommodate additional NCCN recommendations; interferons are added to PCV as a failed trial choice per NCCN; references reviewed and updated.	01/19	

References

1. Jakafi Prescribing Information. Wilmington, DE: Incyte Corporation; December 2017. Available at http://www.jakafi.com. Accessed October 18, 2018.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 18, 2018.
3. Hydroxyurea. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed October 19, 2018.
5. Myeloproliferative neoplasms (Version 1.2019). National Comprehensive Cancer Network Guidelines. Available at nccn.org. Accessed October 18, 2018.