Clinical Policy: Ruxolitinib (Jakafi)

Reference Number: CP.PHAR.98
Effective Date: 03/12
Last Review Date: 04/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for ruxolitinib (Jakafi®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Jakafi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Myelofibrosis (must meet all):

1. Prescribed by or in consultation with a hematologist or oncologist;
2. Member meets one of the following (a or b):
   a. FDA approved use (i, ii, and iii):
      i. Diagnosis of one of the following:
         a) Primary myelofibrosis;
         b) Post-polycythemia vera myelofibrosis;
         c) Post-essential thrombocythemia myelofibrosis;
      ii. Intermediate- or high-risk disease as indicated by one or more of the following:
         a) Age > 65 years;
         b) Leukocyte count > 25,000/microL (> 25 x 10^9/L);
         c) Hemoglobin < 10 g/dL (< 100 g/L);
         d) Circulating blast cells ≥ 1%;
         e) Constitutional symptoms (e.g., pruritus, fatigue, night sweats, bone pain);
         f) Platelet count < 100,000/microL (<100 x 10^9/L);
         g) Anemia requiring transfusion;
         h) Unfavorable karyotype (e.g., complex karyotype or one or two abnormalities that include +8, -7/7q-, i(17q), -5/5q-, 12p-, inv(3), or 11q23 rearrangement)
      iii. Prescribed dose of Jakafi does not exceed 25 mg twice daily;
   b. Off-label NCCN recommended use (i or ii):
      i. Symptomatic low-risk myelofibrosis (MF);
      ii. MF-accelerated phase or MF-blast phase/acute myeloid leukemia for the improvement of splenomegaly and other disease-related symptoms.

Approval duration: 6 months

B. Polycythemia Vera (must meet all):

1. Prescribed by or in consultation with a hematologist or oncologist;

2. Diagnosis of polycythemia vera and all of the following (a, b, and c):
   a. Inadequate response, unacceptable side effects, or contraindication to hydroxyurea;
   b. Phlebotomy dependent;
   c. Splenomegaly or splenectomy;
3. Prescribed dose of Jakafi does not exceed 25 mg twice daily.

Approval duration: 6 months

C. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

A. Myelofibrosis (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Demonstrated therapeutic response as indicated by one or more of the following:
   a. Reduction in spleen size;
   b. Symptom improvement (e.g., pruritus, fatigue, night sweats, bone pain);
3. Prescribed dose of Jakafi does not exceed 25 mg twice daily.

Approval duration: 12 months

B. Polycythemia Vera (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Demonstrated therapeutic response as indicated by one or more of the following:
   a. Reduction in thromboembolic events;
   b. Reduction in spleen size;
   c. Improvement in hematocrit control (reduced phlebotomy requirement), platelet count, or white-cell count;
   d. Symptom improvement (e.g., pruritus, fatigue, night sweats);
3. Prescribed dose of Jakafi does not exceed 25 mg twice daily.

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy**.**

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).

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

FDA Approved Indications:
Jakafi is a kinase inhibitor/oral tablet indicated for:

- Treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis;
- Treatment of patients with polycythemia vera who have had an inadequate response to or are intolerant to hydroxyurea.

Appendices
Appendix A: Abbreviation Key
JAK: Janus Associated Kinase
MF: myelofibrosis
MPN: myeloproliferative neoplasms
PV: polycythemia vera
STAT: signal transducer and activator of transcription

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
No criteria changes	04/13	05/13
Converted to Centene policy template	04/13	
Added requirement to document CBC results Added Appendix A, B and Table 1 and associated questions in algorithm	05/14	05/14
Added new indication for polycythemia vera (PV) throughout policy Added interpretation for all abbreviations addressed in the algorithms Modified safety information to read better	03/15	05/15

Reviews, Revisions, and Approvals	Date	Approval Date
Title Jakafi Algorithm was changed to myelofibrosis algorithm Added request for adverse prognostic features Added dosage adjustment questions in Figure 1 For renewal request, added that **current** CBC must be documented; Added the platelet count and TB indications to appendix B Added blood work and infection monitoring to appendix C Added the appendices A, D, E, F,G, H Added tables 2, 3, 4 Added age requirement of ≥ 18 to both algorithms Added dose increase path to Figure 1 (see corresponding new appendix G)		
Policy converted to new template. Myelofibrosis and PV criteria: specialist requirement added; requests for documentation removed; dose titration and drug interaction details removed; max titrated dose added. Myelofibrosis criteria: intermediate- and high-risk diagnostic criteria added per Tefferi and Gangat; symptom improvement/reduction in spleen size informed by PI clinical trials. PV criteria: initial phlebotomy and splenomegaly requirements, and therapeutic response criteria, informed by Vannucchi/PI clinical trials; initial approval period increased to 6 months to allow for response.	03/16	04/16
Initial MF criteria: removed requirements related to age and other safety criteria; clarified unfavorable karyotype; added NCCN compendial indications. Initial PV criteria: removed requirements related to age, and other safety criteria. Re-auth MF and PV: removed reasons to discontinue and other safety criteria, added max dose, extended approval duration from 6 months to 12months.	03/17	04/17

References

1. Jakafi Prescribing Information. Wilmington, DE: Incyte Corporation; March 2016. Available at http://www.jakafi.com. Accessed March 21, 2017.
2. Gangat N, Caramazza D, Vaidya R, et al. DIPSS plus: a refined Dynamic International Prognostic Scoring System for primary myelofibrosis that incorporates prognostic information from karyotype, platelet count, and transfusion status. J Clin Oncol 2011; 29(4): 392-397.
3. Ruxolitinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed May 21, 2017.
4. Vannucchi AM, Kiladjian JJ, Griesshammer M, et al. Ruxolitinib versus standard therapy for the treatment of polycythemia vera. N Engl J Med 2015; 372(5): 426-435.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of

physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.