

<b>CLINICAL POLICY</b>	
<b>DEPARTMENT:</b> Medical Management	<b>DOCUMENT NAME:</b> Jakafi™
<b>PAGE:</b> 1 of 6	<b>REFERENCE NUMBER:</b> NH.PHAR.98
<b>EFFECTIVE DATE:</b> 03/12	<b>REPLACES DOCUMENT:</b>
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<b>SPECIALIST REVIEW:</b>	<b>REVISED:</b> 05/14, 07/16
<b>PRODUCT TYPE:</b> All	<b>COMMITTEE APPROVAL:</b> 03/12, 05/13, 05/14

### **IMPORTANT REMINDER**

This Clinical Policy has been developed by appropriately experienced and licensed health care professionals based on a thorough review and consideration of generally accepted standards of medical practice, peer-reviewed medical literature, government agency/program approval status, and other indicia of medical necessity.

The purpose of this Clinical Policy is to provide a guide to medical necessity. Benefit determinations should be based in all cases on the applicable contract provisions governing plan benefits (“Benefit Plan Contract”) and applicable state and federal requirements, as well as applicable plan-level administrative policies and procedures. To the extent there are any conflicts between this Clinical Policy and the Benefit Plan Contract provisions, the Benefit Plan Contract provisions will control.

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

### **Subject:**

Medical necessity criteria for Jakafi™ (ruxolitinib)

### **Description:**

The intent of the criteria is to ensure that patients follow selection elements established by Centene®.

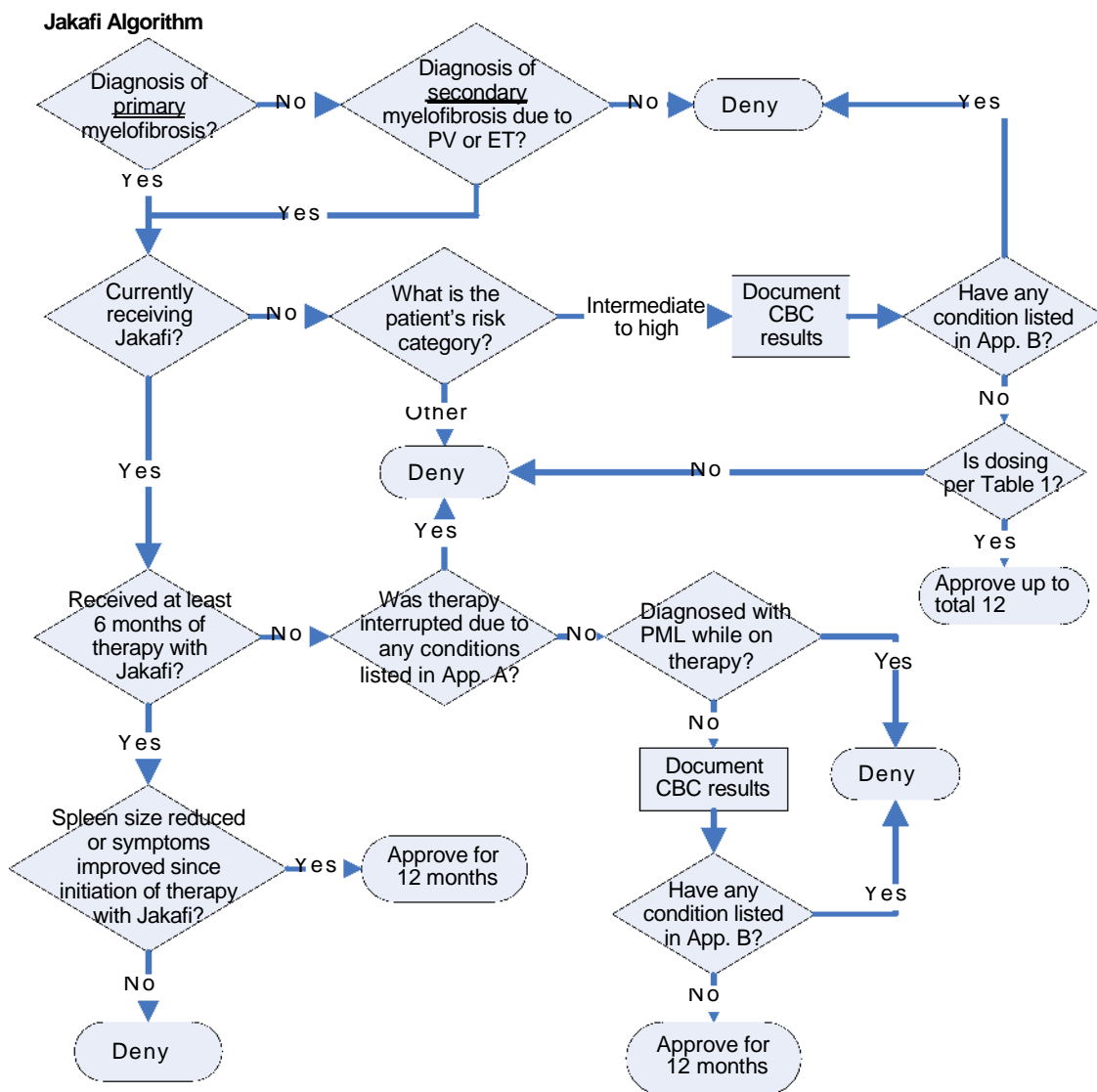
### **FDA-Approved Indications**

Jakafi is indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis.<sup>1</sup> Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of the standard reference compendia.

### **Policy/Criteria and Authorization Protocols:**

It is the policy of Health Plans affiliated with Centene Corporation® that Jakafi is **medically necessary** for members who meet the criteria in the following Jakafi clinical algorithm:

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ABBREVIATION KEY: ET = essential thrombocythemia; PV = polycythemia vera

**Background:**

Myelofibrosis (MF) is part of a related group of conditions referred to as myeloproliferative neoplasms (MPNs) of hematopoietic stem cells which lead to an inappropriate release of

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cytokines, fibrosis of the bone marrow and extramedullary hematopoiesis.<sup>2</sup> MF may present as a primary condition or may develop late in the course of essential thrombocythemia (ET) or polycythemia vera (PV), the two most common and benign MPNs.<sup>2,3</sup> Other classic MPNs include chronic myeloid leukemia (CML), chronic neutrophilic leukemia, chronic eosinophilic leukemia, and mast cell disease.<sup>4</sup> Among these MPNs, PV, ET, and primary MF (PMF) are BCR-ABL1-negative and screening for the BCR-ABL gene to rule out other secondary causes of myelofibrosis such as CML may be recommended.<sup>4,5</sup> PMF is uncommon, affecting about 2 out of 1,000,000 people annually.<sup>6</sup> About 10 to 15% of patients with PV or ET transform into MF.<sup>6</sup>

MF is characterized by progressive anemia, bone marrow fibrosis, splenomegaly and a constellation of debilitating symptoms such as fatigue, abdominal discomfort, bone and muscle pain, night sweats, and weight loss which significantly impact quality of life.<sup>7,8</sup> MF can also transform into acute myeloid leukemia (AML) leading to premature death.<sup>7,8</sup> The median survival time after a diagnosis of MF is about 5 years or less, though some people live much longer.<sup>2,9</sup> Survival in MF is related to the number of prognostic risk factors and ranges from 2 to 4 years among patients with two or more risk factors (intermediate-2 or high risk) to 8 to 11 years among patients with no risk or one risk factor (intermediate-1 or low risk).<sup>7</sup>

Currently, there is no curative therapy for MF except for allogeneic stem cell transplantation (ASCT).<sup>8,10</sup> However, ASCT is not an option for most patients.<sup>8</sup> Also, ASCT is complicated by relatively high treatment-related mortality and morbidity.<sup>10</sup> Thus, the main treatment goal of MF has been focused on relieving symptoms related to massive splenomegaly and anemia.<sup>2,3</sup> To date, there were no FDA-approved therapies for MF.<sup>8</sup> Therapies that are currently available such as hydroxyurea, erythropoietin, androgens, decitabine, and thalidomide are being used in an off-label setting.<sup>7,8,10</sup>

It has been found that MF is associated with mutations in the Janus Associated Kinase 2 (JAK2) gene, most commonly JAK2-V617F.<sup>2,3</sup> The JAK2 V617F mutation is present in more than 90% of patients with PV and approximately 60% of patients with primary MF or ET.<sup>3,10</sup> Some clinical signs of the disease, such as anemia and splenomegaly, and the risk of transformation to AML have been related to JAK2 V617F mutational status or the JAK2 V617F allele burden.<sup>7</sup> On November 16, 2011, the Food and Drug Administration approved Jakafi (ruxolitinib), the first drug approved to specifically treat patients with intermediate or high risk MF. Jakafi inhibits both JAK1 and JAK2 which mediate the signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function.<sup>1</sup>

The safety and efficacy of Jakafi was evaluated in two randomized Phase 3 studies (Studies 1 and 2).<sup>1</sup> All patients had an enlarged spleen and risk category of intermediate 2 or high risk. Study 1 was a double-blind, randomized, placebo-controlled study with 309 patients who were refractory

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to or were not candidates for available therapy. Patients were randomized to receive either Jakafi or placebo. The primary efficacy endpoint was the proportion of patients achieving at least 35% reduction in spleen volume from baseline to week 24. The secondary endpoints were duration of a 35% or more reduction in spleen volume and proportion of patients with at least 50% reduction in myelofibrosis-related symptoms from baseline to week 24. Study 2 was an open-label, randomized study with 219 patients who were randomized to receive either Jakafi or best available therapy (e.g., hydroxyurea, a chemotherapy agent, or glucocorticoids). The primary and secondary endpoints were the proportion of patients achieving at least 35% reduction in spleen volume from baseline to week 48 and to week 24, respectively. In both studies, a significantly higher portion of patients in the Jakafi group achieved a 35% or more reduction in spleen volume from baseline. Also, a higher proportion of patients in the Jakafi group had a 50% or more reduction in their myelofibrosis-related symptoms as compared to placebo.

### **Safety**

Treatment with Jakafi can cause hematologic adverse reactions, including thrombocytopenia, anemia and neutropenia.<sup>1</sup> Complete blood counts must be performed before starting Jakafi therapy and should be monitored as clinically indicated and as dosing is adjusted.

Thrombocytopenia and neutropenia are generally reversible and may be managed by temporarily withholding Jakafi doses. Thrombocytopenia and anemia may also be managed by blood transfusions if indicated. Patients should be assessed for signs and symptoms of infection and any active serious infections should be resolved prior to starting therapy with Jakafi. Progressive multifocal leukoencephalopathy (PML) has been reported with Jakafi treatment. If PML is suspected, stop Jakafi therapy and evaluate. Advise patients about the early signs and symptoms of herpes zoster and latent or active tuberculosis as these conditions has also been reported while on Jakafi therapy.<sup>1</sup>

### **Appendices**

**Appendix A:** Avoid Jakafi treatment based on the following conditions

1. ANC < 0.5 x 10<sup>9</sup>/L
2. Platelet Count < 25 x 10<sup>9</sup>/L
3. End-stage renal disease (CrCL < 15 mL/min) not requiring dialysis and in patients with moderate or severe renal impairment with platelet counts < 100 x 10<sup>9</sup>/L
4. Hepatic impairment with platelet counts < 100 x 10<sup>9</sup>/L

**Appendix B:** Interruption to Jakafi treatment based on the following conditions

1. Platelet Count falls below 50 x 10<sup>9</sup>/L (if starting PLT Count ≥ 100 x 10<sup>9</sup>/L)
2. Platelet Count falls below 25 x 10<sup>9</sup>/L (if starting PLT Count ≥ 50 x 10<sup>9</sup>/L to < 100 x 10<sup>9</sup>/L)
3. ANC falls < 0.5 x 10<sup>9</sup>/L
4. Bleeding occurs while on therapy

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5. Active serious infection; discontinue therapy if patient diagnosed with PML

**Table 1.** Recommended Starting Dose Based on Platelet Count

<b>Platelet Count*</b>	<b>Starting Dose</b>
Greater than 200 x 10 <sup>9</sup> /L	20 mg orally twice daily
100 x 10 <sup>9</sup> /L to 200 x 10 <sup>9</sup> /L	15 mg orally twice daily
50 x 10 <sup>9</sup> /L to less than 100 x 10 <sup>9</sup> /L	5 mg orally twice daily

**References:**

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<b>Revision Log</b>	<b>Date</b>
No criteria changes	04/13
Converted to Centene policy template	04/13
Added requirement to document CBC results	05/14
Added Appendix A, B and Table 1 and associated questions in algorithm	

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Added Coverage for other cancer diagnoses may be authorized provided effective treatment with such drug is recognized for treatment of such indication in one of <u>the standard reference compendia</u>	07/15
Annual Review, No changes	08/16
Extended duration of approval from 6 to 12 months	07/17

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