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Reviewed: 12/13/23

Revised: 01/15/23

Subject: Momelotinib (Ojjaara) Tablets

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Myelofibrosis, a myeloproliferative neoplasm, can present as a primary disease or can evolve from polycythemia vera or essential thrombocytopenia. It is characterized by marrow fibrosis, progressive anemia, and extramedullary hematopoiesis and manifests primarily as splenomegaly. Myelofibrosis debilitating symptoms (e.g., fatigue, weakness, abdominal pain, cachexia, weight loss, pruritus, night sweats, and bone pain) are thought to be the combined effects of massive splenomegaly and elevated levels of proinflammatory cytokines. Traditional therapeutic options, including splenectomy, have demonstrated only limited benefit and although allogeneic stem-cell transplant may cure myelofibrosis, few individuals are eligible for this treatment. It is hypothesized that the pathogenesis of myelofibrosis is related to direct or indirect activation of the intracellular Janus kinase (JAK) signal transducer and activator transcription (STAT) pathway. Additionally, proinflammatory cytokines that play an important role in myelofibrosis signal through JAK 1 (JAK1) AND JAK2.

Momelotinib (Ojjaara) is a kinase inhibitor with activity against Janus associated kinase 2 (JAK2) and other kinases which can be irregular in myelofibrosis. This impacts the signaling cytokines and growth factors for hematopoiesis and immune function in myelofibrosis. Momelotinib and its metabolite increase red blood cell production via inhibition of activin receptor like kinase 2 (ALK2), which results in the inhibition of liver hepcidin expression and increased iron availability. The FDA-approved momelotinib for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis in adults with anemia.

In a randomized trial in 432 patients with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) MF, momelotinib 200 mg once daily was compared to ruxolitinib 20 mg twice a day. The primary efficacy end point was a greater than or equal to 35% reduction in spleen volume at 24 weeks of therapy. Secondary end points were rates of symptom response using the Myeloproliferative Neoplasm-Symptom Assessment Form Total Symptom

Score (MPN-SAF TSS), a 10-item instrument to monitor clinically relevant symptoms (e.g., fatigue, night sweats, itching, abdominal discomfort). Red blood cell transfusion requirements were also assessed. The primary end point of greater than or equal to a 35% reduction in spleen volume was reached by 26.5% of patients in the momelotinib group and 29% in the ruxolitinib group (non-inferior, p=0.011). A greater than 50% reduction in total symptom score was reached in 28.4% of patients in the momelotinib group and 42.2% of patients in the ruxolitinib group (not met for non-inferiority, p=0.98). Numerical improvements in secondary endpoints were observed in patients treated with momelotinib as compared to ruxolitinib: transfusion rate (0 vs 0.4 units/month), transfusion independence (66.5% vs 49.3%), and transfusion dependence (30.2% vs 40.1%). Anemia occurred in 13.6% of patients treated with momelotinib vs 38% with ruxolitinib (grade 3 or 4 anemia, 5.6% vs 23.1%). Thrombocytopenia occurred 18.7% of patients treated with momelotinib vs 29.2% with ruxolitinib (grade 3 or 4 thrombocytopenia, 7% vs 4.6%). The most common adverse reactions with momelotinib treatment included thrombocytopenia, diarrhea, hemorrhage, fatigue, nausea, bacterial infection, and dizziness.

In a separate phase-3 trial, 195 patients with myelofibrosis who were symptomatic, anemic, and had previously received JAK inhibitor therapy were randomized to receive treatment with momelotinib or danazol. Within the 8 weeks prior to treatment, approximately 79% of patients had received RBC transfusions. Significantly more patients achieved a 50% or more reduction in total symptom score (using the Myelofibrosis Symptom Assessment Form) at week 24 with momelotinib as compared to danazol (25% vs 9%, p<0.01). Transfusion independence occurred in 30% of patient treated with momelotinib as compared to 20% treated with danazol (0.023). Significantly more patients had a spleen volume reduction by 25% or more in the momelotinib group as compared to danazol (39% vs 6%, p<0.0001).

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of momelotinib (Ojjaara®) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Primary myelofibrosis (MF) or secondary myelofibrosis [post-polycythemia vera myelofibrosis (Post-PV-MF), or post-essential thrombocythemia myelofibrosis (Post-ET-MF)] and **ALL** of the following:
    a. **ONE** of the following:
        i. The member had an inadequate response, intolerance, or is not a candidate for treatment with ruxolitinib (Jakafi)
        ii. The member has myelofibrosis-associated anemia with a hemoglobin less than 8 g/dL
    b. Disease is classified as intermediate or high-risk
    c. Hemoglobin is less than 10 g/dL

d. Dose does not exceed 200 mg per day using the fewest number of tablets per day

2. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
   a. **ONE** of the following is met:
      i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
      ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
   b. Dose does not exceed the maximum FDA-approved dose

Approval duration: 180 days

Continuation of momelotinib (Ojjaara®) meets the definition of medical necessity for primary MF, secondary MF [Post-PV-MF, Post-ET-MF], and other FDA-approved or NCCN supported diagnosis when **ALL** of the following criteria are met:

1. The member has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of primary MF, secondary MF [Post-PV-MF, Post-ET-MF], or other FDA-approved or NCCN supported diagnosis, OR the member has previously met ALL indication-specific criteria for coverage
2. The member has experienced a beneficial response to therapy (e.g., reduction in spleen size, improvement in clinical symptoms)
3. The dose does not exceed 200 mg per day using the fewest number of tablets per day

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Momelotinib is indicated for the treatment of intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF [post-polycythemia vera (PV) and post-essential thrombocythemia (ET)], in adults with anemia.
- The recommended dosage is 200 mg orally once daily with or without food.
- Obtain a complete blood count (CBC) with platelets and a hepatic panel prior to initiating treatment.

Dose adjustments:

- Severe hepatic impairment (Child-Pugh Class C): Reduce the starting dose to 150 mg orally once daily.
- See prescribing information for dose modifications for platelet count, absolute neutrophil count, hepatic enzymes and other non-hematologic Grade 3 or higher adverse reactions.

PRECAUTIONS:

Boxed Warning - none

Contraindications - none

Precautions/Warnings

- Risk of infections: do not initiate in patients with an active infection. Monitor for signs and symptoms of infection, including reactivation of hepatitis B, and initiate appropriate treatment promptly.
- Thrombocytopenia and Neutropenia: Manage by dose reduction or interruption.

Dosage forms: 100 mg, 150 mg, 200 mg tablets

BILLING/CODING INFORMATION:

HCPCS Coding

C9399	Unclassified drugs or biologicals
J8999	Prescription drug, oral, chemotherapeutic, not otherwise specified

ICD-10 Diagnosis Codes That Support Medical Necessity

D75.81	Myelofibrosis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

Essential thrombocythemia: an increased number of thrombocytes (platelets) in the blood, without a known cause. Also called essential thrombocytosis.

International Prognostic Scoring System for myelofibrosis: mechanism for assessing a member's prognosis at the time of diagnosis; assigns a value of 1 for each prognostic factor (Table 4). A score of 0 is indicative of low risk, 1 is indicative of intermediate-1 risk, 2 intermediate-2 risk, and 3 or more points is indicative of high risk. The risk group corresponds to a median overall survival that ranges from 2.25 years (high risk) to 11.25 years (low risk); Individuals classified as intermediate-1 or intermediate-2 have an estimated median survival of 7.92 and 4 years, respectively.

Table 1

Prognostic factors
IPSS Risk Factors
Age greater than 65
WBC greater than 25,000
Hemoglobin less than 10 g/dL
Peripheral blood blasts 1% or greater
Constitutional symptoms

Myelofibrosis: myeloproliferative disease in which the proliferation of an abnormal type of bone marrow stem cell results in fibrosis, or the replacement of the marrow with collagenous connective tissue fibers.

Polycythemia vera: A disease in which there are too many red blood cells in the bone marrow and blood, causing the blood to thicken. The number of white blood cells and platelets may also increase. The extra blood cells may collect in the spleen and cause it to become enlarged. They may also cause bleeding problems and make clots form in blood vessels.

Primary myelofibrosis: a progressive, chronic disease in which the bone marrow is replaced by fibrous tissue and blood is made in organs such as the liver and the spleen, instead of the bone marrow. This disease is marked by an enlarged spleen and progressive anemia. Also called agnogenic myeloid metaplasia, chronic idiopathic myelofibrosis, idiopathic myelofibrosis, and myelosclerosis with myeloid metaplasia.

Splenomegaly: enlarged spleen.

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/13/23.

GUIDELINE UPDATE INFORMATION:

11/15/23	New Medical Coverage Guideline.
01/15/24	Updated position statement for treatment of myelofibrosis-associated anemia.