Iowa Medicaid
IOWA HHS

PDL DRUG REVIEW

Proprietary Name: Ojjaara®
Common Name: momelotinib
PDL Category: Antineoplastics

Comparable Products	Preferred Drug List Status
Inrebic	Non-Recommended with Conditions
Jakafi	Recommended with Conditions
Vonjo	Non-Recommended with Conditions

Pharmacology/Usage: Momelotinib, the active ingredient of Ojjaara®, is a kinase inhibitor. It is an inhibitor of wild type Janus Kinase 1 and 2 (JAK1/JAK2) and mutant $JAK2^{V617F}$, which contribute to signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. Momelotinib and its major human circulating metabolite, M21, have higher inhibitory activity for JAK2 compared to JAK3 and tyrosine kinase 2 (TYK2). Momelotinib and M21 additionally inhibit activin A receptor type 1 (ACVR1), also known as activin receptor like kinase 2 (ALK2), which produces subsequent inhibition of liver hepcidin expression and increased iron availability resulting in increased red blood cell production.

MF (myelofibrosis) is a myeloproliferative neoplasm associated with constitutive activation and dysregulated JAK signaling that contributes to inflammation and hyperactivation of ACVR1. JAK signaling recruits and activates STAT (signal transducers and activation of transcription) proteins resulting in nuclear localization and subsequent regulation of gene transcription.

Indication: 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.

There is no pregnancy category for this medication; however, the risk summary indicates that available data on use in pregnant women are not sufficient to determine whether there is a drug-associated risk for major birth defects or miscarriage. Based on animal reproduction studies, momelotinib may cause embryo-fetal toxicity at exposures lower than the expected exposure in patients receiving 200mg daily. Ojjaara® should only be used during pregnancy if the expected benefits to the mother outweigh the potential risks to the fetus. Advise females of reproductive potential who are not pregnant to use highly effective contraception during therapy and for at least 1 week after the last dose of Ojjaara®. The safety and efficacy of use in the pediatric population have not been established.

Dosage Form: Tablets: 100mg, 150mg, and 200mg. Swallow whole; do not cut, crush, or chew tablets.

Recommended Dosage: Obtain the following blood tests prior to starting treatment, periodically during treatment, and as clinically indicated:

- Complete blood count (CBC) with platelets.
- Hepatic panel.

The recommended dosage is 200mg PO QD, and may be taken with or without food. If a dose is missed, the next scheduled dose should be taken the following day. Refer to the prescribing information regarding information on dosage modifications for adverse reactions, including thrombocytopenia, neutropenia, hepatotoxicity, or other non-hematologic adverse reactions. Discontinue Ojjaara® in patients unable to tolerate 100mg QD.

Dose modifications are not required for patients with mild or moderate hepatic impairment. The recommended starting dose in patients with severe hepatic impairment is 150mg PO QD.

Drug Interactions: Momelotinib is an OATP1B1/B3 substrate. Concomitant use with an OATP1B1/B3 inhibitor increases momelotinib maximal concentrations (Cmax) and area under the concentration-time curve (AUC), which may increase the risk of adverse reactions with Ojjaara®. Monitor patients concomitantly receiving an OATP1B1/B3 inhibitor for adverse reactions and consider Ojjaara® dose modifications.

Momelotinib is a breast cancer resistance protein (BCRP) inhibitor. Ojjaara® may increase exposure of BCRP substrates, which may increase the risk of BCRP substrate adverse reactions. When administered concomitantly with Ojjaara®, initiate rosuvastatin (BCRP substrate) at 5mg and do not increase to more than 10mg once daily. Dose adjustment of other BCRP substrates may also be needed. Follow approved product information recommendations for other BCRP substrates.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Ojjaara®) minus reported % incidence for ruxolitinib for all grades. Please note that an incidence of 0% means the incidence was the same as or less than comparator. Also, note that the study was not designed to evaluate meaningful comparisons of the incidence of adverse reactions across treatment groups.* The most frequently reported adverse events included dizziness (9%), fatigue (0%), bacterial infection (9%), hemorrhage (3%), thrombocytopenia (0%), diarrhea (0%), nausea (17%), abdominal pain (4%), cough (3%), hypotension (14%), pain in extremity (7%), pyrexia (1%), rash (9%), renal and urinary tract infection (8%), elevated liver enzymes (2%), headache (0%), peripheral edema (3%), arrhythmia (6%), paresthesia (5%), pneumonia (3%), vomiting (3%), back pain (5%), viral infection (0%), and vitamin B1 deficiency (0%).

Listed % incidence for adverse drug reactions= reported % incidence for drug (Ojjaara®) minus reported % incidence for danazol for all grades. Please note that an incidence of 0% means the incidence was the same as or less than comparator. Also, note that the study was not designed to evaluate meaningful comparisons of the incidence of adverse reactions across treatment groups. The most frequently reported adverse events included thrombocytopenia (11%), diarrhea (13%), hemorrhage (4%), fatigue (1%), nausea (7%), bacterial infection (0%), abdominal pain (0%), viral infection (9%), pruritus (0%), elevated liver enzymes (1%), pyrexia (2%), cough (3%), paresthesia (6%), dizziness (6%), vomiting (8%), rash (0%), renal and urinary tract infection (0%), arrhythmia (0%), and neutropenia (2%).

Serious, including fatal, infections occurred in 13% of patients treated with Ojjaara®. Infections regardless of grade occurred in 38% of patients treated with Ojjaara®. Delay starting therapy with Ojjaara® until active infections have resolved. Monitor patients receiving Ojjaara® for signs and symptoms of infection and start appropriate treatment promptly. In patients with hepatitis B virus (HBV) infections, check hepatitis B serologies prior to starting Ojjaara®. Patients with chronic HBV infection who receive Ojjaara® should have their chronic HBV infection treated and monitored according to clinical HBV guidelines.

Ojjaara® can cause thrombocytopenia and neutropenia. Assess complete blood counts (CBC), including platelets and neutrophil counts, before starting treatment and periodically during treatment as clinically indicated. Interrupt dosing or reduce the dose for thrombocytopenia or neutropenia.

Two out of 993 patients with MF who received at least one dose of Ojjaara® in clinical trials experienced reversible drug-induced liver injury. Overall, new or worsening elevations of ALT and AST occurred in 23% and 24%, respectively, of patients treated with Ojjaara®. New or worsening elevations of total bilirubin occurred in 16% of patients treated with Ojjaara®. Delay starting therapy in patients presenting with uncontrolled acute and chronic liver disease until apparent causes have been investigated and treated as clinically indicated. When starting Ojjaara®, refer to dosing in patients with hepatic impairment. Monitor liver tests at baseline, every month for 6 months during treatment, then periodically as clinically indicated. If increases in ALT, AST, or bilirubin related to treatment are suspected, modify Ojjaara® dosage (based per information in the prescribing information).

Another JAK inhibitor increased the risk of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, and stroke (compared with those treated with TNF blockers) in patients with

rheumatoid arthritis (RA). Consider the benefits and risks for the individual patient prior to starting or continuing therapy with Ojjaara®, especially in patients who are current or past smokers and patients with other cardiovascular risk factors. Inform patients receiving Ojjaara® of the symptoms of serious cardiovascular events and the steps to take if they occur.

Another JAK inhibitor increased the risk of thrombosis, including deep vein thrombosis, pulmonary embolism, and arterial thrombosis (compared with those treated with TNF blockers) in patients with RA. Evaluate patients with symptoms of thrombosis and treat appropriately.

Another JAK inhibitor increased the risk of lymphoma and other malignancies excluding non-melanoma skin cancer (NMSC, compared with those treated with TNF blockers) in patients with RA. Current or past smokers were at increased risk. Consider the benefits and risks for the individual patient prior to starting or continuing therapy with Ojjaara®, especially in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers.

Contraindications: There are no contraindications listed with this product.

Manufacturer: GlaxoSmithKline LLC.

Analysis: The efficacy of Ojjaara® in the treatment of adults with intermediate 1, intermediate 2, or high-risk MF (including primary MF, post-PV MF, or post-ET MF, as defined by the Dynamic International Prognostic Scoring System (DIPSS) or International Prognostic Scoring System (IPSS) for MF) was established in the MOMENTUM trial and in a subpopulation of adults with anemia in the SIMPLIFY-1 trial. All patients received a starting dosage of Ojjaara® 200mg QD. Eligible patients had baseline platelet count of ≥25 x 10^9/L in MOMENTUM and ≥50 X 10^9/L in SIMPLIFY-1.

The MOMENTUM study was a double-blind, randomized, active-controlled study that included symptomatic and anemic adults with MF (N=195) who had previously received an approved JAK inhibitor therapy. Patients were treated with Ojjaara® 200mg QD or danazol 300mg BID for 24 weeks, then switched to open-label treatment with Ojjaara®. The median age of included patients was 71 years (range 38 to 86), with 79% of patients aged 65 years and older. In addition, 63% were male, 81% were white, 64% had primary MF, 19% had post-PV MF, and 17% had post-ET MF. Five percent had intermediate-1 risk, 57% had intermediate-2 risk, and 35% had high-risk disease. Within the 8 weeks prior to treatment, 79% of patients had received red blood cell (RBC) transfusions. At baseline, 13% and 15% of patients were transfusion independent in the Ojjaara® and danazol groups, respectively. The baseline median Hb count was 8g/dL and the median platelet count was 96 X 10^9/L. The baseline median palpable spleen length was 11cm below the left costal margin; the median central spleen volume measured by MRI or CT was 2,105 cm^3.

Symptoms were measured using the Myelofibrosis Symptom Assessment Form (MFSAF v4.0) diary. The MFSAF v4.0 patient diary, completed throughout the randomized treatment period, captured the core symptoms of MF, including fatigue, night sweats, itching, abdominal discomfort, pain under ribs on left side, feeling of fullness after beginning to eat, and bone pain. For each item, symptoms scores, ranging from 0 (absent) to 10 (worst imaginable) were added to create a daily Total Symptom Score (maximum score of 70). At baseline, the mean MFSAF v4.0 Total Symptom Score was 28 in the Ojjaara® group and 26 in the danazol group.

The efficacy of Ojjaara® in the treatment of patients with primary or secondary MF and anemia was established based on a significantly higher percentage of patients treated with Ojjaara® compared to danazol achieving a MFSAF v4.0 Total Symptom Score reduction of 50% or more at week 24 compared with their own baseline score. Other endpoints included transfusion independence, spleen volume response, MFSAF v4.0 Total Symptom Score change from baseline, and percentage of patients with no transfusions. Results are presented in the table below, which was adapted from the prescribing information.

	Ojjaara® (N=130)	danazol (N=65)	p-value
Patients with MFSAF v4.0 Total Symptom Score Reduction of 50% or more, n (%)	32 (25%)	6 (9%)	<0.01
Treatment difference	16%		
Patients with transfusion independence (no transfusion or Hb <8g/dL between weeks 12 and 24), n (%)	39 (30%)	13 (20%)	0.023
Non-inferiority treatment difference[1]	14%		
Patients with spleen volume reduction by 25% or more, n (%)	51 (39%)	4 (6%)	<0.0001
Treatment difference	33%		
MFSAF v4.0 Total Symptom Score change from baseline[1]	-9.4	-3.1	0.001
Treatment difference	-6.2		
Patients with spleen volume reduction by 35% or more, n (%)	29 (22%)	2 (3%)	0.001
Treatment difference	18%		
Patients with no transfusions (during the 24-week treatment period), n (%)	46 (35%)	11 (17%)	0.001
Treatment difference	17%		

[1] Non-inferiority difference between Ojjaara® response rate and 80% of danazol response rate.

SIMPLIFY-1 was a double-blind, randomized, active-controlled trial that included adults with MF who had not previously received a JAK inhibitor (N=432). Patients were treated with Ojjaara® 200mg QD or ruxolitinib adjusted dose BID for 24 weeks. Patients were eligible to switch to open-label Ojjaara® after 24 weeks (without tapering of the JAK inhibitor received during the randomization period). The baseline characteristics and efficacy results provided are for the subset of patients who had anemia (Hb <10g/dL) at baseline (n=181).

The median age of included patients was 68 years (range 25 to 86), with 67% of patients aged 65 years and older. In addition, 59% were male, 81% were white, 63% had primary MF, 13% had post-PV MF, and 24% had post-ET MF. Four percent of patients had intermediate-1 risk, 25% had intermediate-2 risk, and 71% had high-risk disease. At baseline, 29% and 44% of patients were transfusion independent in the groups treated with Ojjaara® or ruxolitinib, respectively. The baseline median Hb measurement was 8.8g/dL and the median platelet count was 193 X 10^9/L. Median palpable spleen length at baseline was 12cm below the left costal margin; the median spleen volume at baseline was 1,843 cm^3.

The efficacy of Ojjaara® in the treatment of patients with MF in this study was based on spleen volume response (reduction by 35% or greater). A numerically lower percent of patients treated with Ojjaara® (25%) achieved a Total Symptom Score reduction of 50% or more at week 24 compared with ruxolitinib (36%). The spleen volume reduction results are presented in the table below, which was adapted from the prescribing information.

Percent of patients[1] achieving 35% or greater reduction from baseline in spleen volume at week 24	Ojjaara® (N=86)	ruxolitinib (N=95)
Patients with spleen volume reduction by 35% or more, n (%)	27 (31.4%)	31 (32.6%)

[1] Subset of patients with anemia (Hb <10g/dL) at baseline

Place in Therapy: Ojjaara®, an inhibitor of wild type Janus Kinase 1 and 2 (JAK1/JAK2) and mutant $JAK2^{V617F}$, 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 efficacy of Ojjaara® in the treatment of adults with intermediate-1, intermediate-2, or high-risk MF was established in the MOMENTUM trial and in a subpopulation of adults with anemia in the SIMPLIFY-1 trial. In the MOMENTUM trial, a randomized, double-blind, active-controlled study, the efficacy of Ojjaara® was established based on a significantly higher percentage of patients treated with Ojjaara® compared to danazol achieving a MFSAF v4.0 Total Symptom Score reduction of 50% or more at week 24 compared with their own baseline score. Other endpoints, including transfusion independence, spleen volume response, MFSAF v4.0 Total Symptom Score change from baseline, and patients with no transfusions, were significantly in favor of Ojjaara® compared with danazol.

It is recommended that Ojjaara® should be non-recommended in order to confirm the appropriate diagnosis and clinical parameters for use.

PDL Placement: ☐ **Recommended**
☒ **Non-Recommended with Conditions**

References

[1] Ojjaara [package insert]. Durham, NC: GlaxoSmithKline; 2023.