

OJJAARA- momelotinib tablet

GlaxoSmithKline LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OJJAARA safely and effectively. See full prescribing information for OJJAARA.

OJJAARA (momelotinib) tablets, for oral use
Initial U.S. Approval: 2023

INDICATIONS AND USAGE

OJJAARA is a kinase inhibitor 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. (1)

DOSAGE AND ADMINISTRATION

- Recommended dosage: 200 mg orally once daily with or without food. (2.1)
- Severe hepatic impairment (Child-Pugh Class C): Reduce the starting dose to 150 mg orally once daily. (2.3)

DOSAGE FORMS AND STRENGTHS

Tablets: 100 mg, 150 mg, 200 mg. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Risk of Infections: Do not initiate OJJAARA in patients with an active infection. Monitor for signs and symptoms of infection, including reactivation of hepatitis B, and initiate appropriate treatment promptly. (5.1)
- Thrombocytopenia and Neutropenia: Manage by dose reduction or interruption. (5.2)
- Hepatotoxicity: Obtain liver tests before initiation of and periodically throughout treatment with OJJAARA. (5.3)
- Major Adverse Cardiovascular Events (MACE): Monitor for symptoms, evaluate and treat promptly. (5.4)
- Thrombosis: Evaluate and treat symptoms of thrombosis promptly. (5.5)
- Malignancies: Monitor for development of secondary malignancies, particularly in current or past smokers. (5.6)

ADVERSE REACTIONS

The most common adverse reactions ($\geq 20\%$ in either study) are thrombocytopenia, hemorrhage, bacterial infection, fatigue, dizziness, diarrhea, and nausea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Organic Anion Transporting Polypeptide (OATP)1B1/B3 inhibitors: Monitor for adverse reactions. (7.1)
- Breast Cancer Resistance Protein (BCRP) substrates: Reduce rosuvastatin (BCRP substrate) dosage. Follow approved product information recommendations for other BCRP substrates. (7.2)

USE IN SPECIFIC POPULATIONS

- Pregnancy: May cause fetal harm. (8.1)
- Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 9/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Recommended Dosage
- 2.2 Laboratory Monitoring for Safety
- 2.3 Dosage Modification for Hepatic Impairment
- 2.4 Dosage Modification for Adverse Reactions

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Risk of Infections
- 5.2 Thrombocytopenia and Neutropenia
- 5.3 Hepatotoxicity
- 5.4 Major Adverse Cardiovascular Events (MACE)
- 5.5 Thrombosis
- 5.6 Malignancies

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience

7 DRUG INTERACTIONS

- 7.1 Effect of Other Drugs on OJJAARA
- 7.2 Effect of OJJAARA on Other Drugs

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation
- 8.3 Females and Males of Reproductive Potential
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Hepatic Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

OJJAARA 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.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of OJJAARA is 200 mg orally once daily. OJJAARA may be taken with or without food.

Swallow OJJAARA tablets whole. Do not cut, crush, or chew tablets.

If a dose of OJJAARA is missed, the next scheduled dose should be taken the following day.

2.2 Laboratory Monitoring for Safety

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

- Complete blood count (CBC) with platelets [see *Warnings and Precautions (5.2)*]
- Hepatic panel [see *Warnings and Precautions (5.3)*]

2.3 Dosage Modification for Hepatic Impairment

The recommended starting dosage in patients with severe hepatic impairment (Child-Pugh Class C) is 150 mg orally once daily [see *Use in Specific Populations (8.6)*]. No dose adjustment is recommended for patients with mild or moderate hepatic impairment.

2.4 Dosage Modification for Adverse Reactions

Manage hematologic and non-hematologic adverse reactions as described in Table 1.

Table 1: Dose Modifications for OJJAARA-Related Adverse Reactions

Thrombocytopenia		Dose Modification ^a
Baseline Platelet Count	Platelet Count	
≥100 × 10 ⁹ /L	20 × 10 ⁹ /L to <50 × 10 ⁹ /L	Reduce daily dose by 50 mg from the last given dose
	<20 × 10 ⁹ /L	Interrupt treatment until platelets recover to 50 × 10 ⁹ /L Restart OJJAARA at a daily dose of 50 mg below the last given dose ^b
≥50 × 10 ⁹ /L to <100 × 10 ⁹ /L	<20 × 10 ⁹ /L	Interrupt treatment until platelets recover to 50 × 10 ⁹ /L Restart OJJAARA at a daily dose of 50 mg below the last given dose ^b
<50 × 10 ⁹ /L	<20 × 10 ⁹ /L	Interrupt treatment until platelets recover to baseline Restart OJJAARA at a daily dose of 50 mg below the last given dose ^b

Neutropenia	Dose Modification^a
Absolute neutrophil count (ANC) $<0.5 \times 10^9/L$	Interrupt treatment until $ANC \geq 0.75 \times 10^9/L$ Restart OJJAARA at a daily dose of 50 mg below the last given dose ^b
Hepatotoxicity (unless other apparent causes)	Dose Modification^a
ALT and/or AST $>5 \times ULN$ (or $>5 \times$ baseline, if baseline is abnormal) and/or total bilirubin $>2 \times ULN$ (or $>2 \times$ baseline, if baseline is abnormal)	Interrupt treatment until AST and ALT $\leq 2 \times ULN$ or baseline ^c and total bilirubin $\leq 1.5 \times ULN$ or baseline ^d Restart OJJAARA at a daily dose of 50 mg below the last given dose ^b If reoccurrence of ALT or AST elevations $>5 \times ULN$, permanently discontinue OJJAARA
Other Non-Hematologic	Dose Modification^a
Grade 3 or higher ^e	Interrupt treatment until the toxicity resolves to Grade 1 or lower (or baseline) Restart OJJAARA at a daily dose of 50 mg below the last given dose ^b

ALT = alanine transaminase; AST = aspartate transaminase; ULN = upper limit of normal.

^a Reinitiate or escalate treatment up to starting dosage as clinically appropriate.

^b May reinitiate treatment at 100 mg if previously dosed at 100 mg.

^c If baseline $>2 \times ULN$.

^d If baseline $>1.5 \times ULN$.

^e Graded using the National Cancer Institute Common Terminology Criteria for Adverse Events per (CTCAE).

Discontinue OJJAARA in patients unable to tolerate 100 mg once daily.

3 DOSAGE FORMS AND STRENGTHS

100 mg round tablet – brown with an underlined “M” debossed on one side and “100” on the other side.

150 mg triangular tablet – brown with an underlined “M” debossed on one side and “150” on the other side.

200 mg capsule-shaped tablet – brown with an underlined “M” debossed on one side and “200” on the other side.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Infections

Serious (including fatal) infections (e.g., bacterial and viral, including COVID-19) occurred

in 13% of patients treated with OJJAARA. Infections regardless of grade occurred in 38% of patients treated with OJJAARA [see *Adverse Reactions (6.1)*]. Delay starting therapy with OJJAARA until active infections have resolved. Monitor patients receiving OJJAARA for signs and symptoms of infection and initiate appropriate treatment promptly.

Hepatitis B Reactivation

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine transaminase (ALT) or aspartate transaminase (AST), have been reported in patients with chronic hepatitis B virus (HBV) infection taking Janus Kinase (JAK) inhibitors, including OJJAARA. The effect of OJJAARA on viral replication in patients with chronic HBV infection is unknown. In patients with HBV infections, check hepatitis B serologies prior to starting OJJAARA. If HBsAg and/or anti-HBc antibody is positive, consider consultation with a hepatologist regarding monitoring for reactivation versus prophylactic hepatitis B therapy. Patients with chronic HBV infection who receive OJJAARA should have their chronic HBV infection treated and monitored according to clinical HBV guidelines.

5.2 Thrombocytopenia and Neutropenia

OJJAARA can cause thrombocytopenia and neutropenia [see *Adverse Reactions (6.1)*].

New or worsening thrombocytopenia, with platelet count less than $50 \times 10^9/L$, was observed in 20% of patients treated with OJJAARA. Eight percent of patients treated with OJJAARA had baseline platelet counts less than $50 \times 10^9/L$.

Severe neutropenia, absolute neutrophil count (ANC) less than $0.5 \times 10^9/L$, was observed in 2% of patients treated with OJJAARA.

Assess complete blood counts (CBC), including platelet and neutrophil counts, before initiating treatment and periodically during treatment as clinically indicated. Interrupt dosing or reduce the dose for thrombocytopenia or neutropenia [see *Dosage and Administration (2.4)*].

5.3 Hepatotoxicity

Two of the 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 (all grades) occurred in 23% and 24%, respectively, of patients treated with OJJAARA; Grade 3 and 4 transaminase elevations occurred in 1% and 0.5% of patients, respectively. New or worsening elevations of total bilirubin occurred in 16% of patients treated with OJJAARA. All total bilirubin elevations were Grades 1-2. The median time to onset of any grade transaminase elevation was 2 months, with 75% of cases occurring within 4 months.

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 initiating OJJAARA, refer to dosing in patients with hepatic impairment [see *Dosage and Administration (2.3)*].

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 upon Table 1 [see *Dosage and Administration (2.4)*].

5.4 Major Adverse Cardiovascular Events (MACE)

Another JAK inhibitor increased the risk of MACE, including cardiovascular death, myocardial infarction, and stroke [compared with those treated with tumor necrosis factor (TNF) blockers] in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OJJAARA, particularly 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.

5.5 Thrombosis

Another JAK inhibitor increased the risk of thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis (compared with those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated.

Evaluate patients with symptoms of thrombosis and treat appropriately.

5.6 Malignancies

Another JAK inhibitor increased the risk of lymphoma and other malignancies excluding nonmelanoma skin cancer (NMSC) (compared with those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated. Current or past smokers were at increased risk.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OJJAARA, particularly 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.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Risk of Infections and Hepatitis B Reactivation [see *Warnings and Precautions (5.1)*]
- Thrombocytopenia and Neutropenia [see *Warnings and Precautions (5.2)*]
- Hepatotoxicity [see *Warnings and Precautions (5.3)*]
- Major Adverse Cardiovascular Events [see *Warnings and Precautions (5.4)*]
- Thrombosis [see *Warnings and Precautions (5.5)*]
- Malignancies [see *Warnings and Precautions (5.6)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of OJJAARA was evaluated in 215 patients in 2 clinical trials (MOMENTUM and SIMPLIFY-1 anemic subgroup [hemoglobin (Hb) <10 g/dL]) [see *Clinical Studies (14)*].

MOMENTUM

Patients in the MOMENTUM trial had been previously treated with a JAK inhibitor and were randomly assigned 2:1 to receive double-blind OJJAARA 200 mg orally once daily (n = 130) or danazol 300 mg orally twice daily (n = 65) for 24 weeks, after which they were eligible to receive open-label OJJAARA in an extended treatment phase. Among patients who received OJJAARA, 72% were exposed for 24 weeks or longer and 52% were exposed for 48 weeks or longer [see *Clinical Studies (14)*].

Serious adverse reactions occurred in 35% of patients who received OJJAARA during the randomized treatment period of the MOMENTUM trial; the most common serious adverse reactions ($\geq 2\%$) included bacterial infection (8%), viral infection (5%), hemorrhage (4%), acute kidney injury (3%), pneumonia (3%), pyrexia (3%), thrombosis (3%), syncope (2%), thrombocytopenia (2%), and renal and urinary tract infection (2%). Fatal adverse reactions occurred in 12% of patients who received OJJAARA; the most common ($\geq 2\%$) fatal adverse reaction was viral infection (5%).

Permanent discontinuation of OJJAARA due to an adverse reaction occurred in 18% of patients during the randomized treatment period of the MOMENTUM trial. Adverse reactions that resulted in permanent discontinuation ($\geq 2\%$) included viral infection (2%) and thrombocytopenia (2%). Dosage reduction or treatment interruption due to an adverse reaction occurred in 34% of patients. Adverse reactions requiring dosage reduction and/or treatment interruption ($\geq 2\%$) included thrombocytopenia (13%), bacterial infection (2%), diarrhea (2%), and neutropenia (2%).

Among the 130 patients treated with OJJAARA during the randomized treatment period of MOMENTUM, the most common adverse reactions ($\geq 20\%$) were thrombocytopenia, diarrhea, hemorrhage, and fatigue (Table 2).

Table 2: Adverse Reactions Occurring in $\geq 5\%$ of Patients Receiving OJJAARA during Randomized Treatment in MOMENTUM

Adverse Reaction	OJJAARA n = 130		Danazol ^a n = 65	
	All Grades ^b %	Grade ≥ 3 %	All Grades %	Grade ≥ 3 %
Thrombocytopenia ^c	28	22	17	12
Diarrhea ^c	22	0	9	2
Hemorrhage ^c	22	2	18	8
Fatigue ^c	21	2	20	5
Nausea ^c	16	2	9	3
Bacterial infection ^{c,d}	15	8	18	8
Abdominal pain ^c	13	1	18	3
Viral infection ^{c,d}	12	5	3	0
Pruritus ^c	11	2	11	0
Elevated liver enzymes ^c	10	2	9	3
Pyrexia ^c	10	2	8	0
Cough ^c	8	0	5	0
Paresthesia ^c	8	1	2	0
Dizziness ^c	8	2	2	0

Vomiting ^c	8	1	0	0
Rash ^c	6	0	11	0
Renal and urinary tract infection ^{c,d}	6	2	11	5
Arrhythmia ^c	5	1	6	2
Neutropenia	5	5	3	3

^a Study was not designed to evaluate meaningful comparisons of the incidence of adverse reactions across treatment groups.

^b Adverse reactions graded using CTCAE v.5.

^c Grouped term includes other related terms.

^d Excludes opportunistic infections.

SIMPLIFY-1

Patients in the SIMPLIFY-1 trial were JAK inhibitor naïve and randomly assigned 1:1 to receive double-blind OJJAARA 200 mg orally once daily (n = 215) or ruxolitinib 5 to 20 mg orally twice daily (n = 217). Upon completion of the double-blind treatment phase, all patients were eligible to receive OJJAARA during the open-label phase. The safety of OJJAARA was evaluated in the population of patients with MF who were anemic at study entry. SIMPLIFY-1 enrolled 180 anemic patients who received OJJAARA (n = 85) or ruxolitinib (n = 95). Among these anemic patients who received OJJAARA, 78% were exposed for 24 weeks or longer and 61% were exposed for 48 weeks or longer [see *Clinical Studies (14)*].

Serious adverse reactions occurred in 28% of the anemic patients who received OJJAARA during the randomized treatment period of the SIMPLIFY-1 trial; the most common serious adverse reactions ($\geq 2\%$) included bacterial infection (7%), pneumonia (6%), heart failure (4%) arrhythmia (2%), and respiratory failure (2%). A fatal adverse reaction (bacterial infection) occurred in 1 patient who received OJJAARA.

Permanent discontinuation of OJJAARA due to an adverse reaction occurred in 19% of the anemic patients during the randomized treatment period of the SIMPLIFY-1 trial. Adverse reactions that resulted in permanent discontinuation of OJJAARA ($\geq 2\%$) included bacterial infection (2%), dizziness (2%), fatigue (2%), hypotension (2%), and thrombocytopenia (2%). Dosage reductions or treatment interruptions of OJJAARA due to an adverse reaction occurred in 21% of patients. Adverse reactions requiring dosage reduction and/or treatment interruption ($\geq 2\%$) were thrombocytopenia (8%), pneumonia (4%), bacterial infection (2%), abdominal pain (2%), elevated liver enzymes (2%), and hypotension (2%).

Among the 85 anemic patients treated with OJJAARA during the randomized treatment period of SIMPLIFY-1, the most common adverse reactions ($\geq 20\%$) were dizziness, fatigue, bacterial infection, hemorrhage, thrombocytopenia, diarrhea, and nausea (Table 3).

Table 3: Adverse Reactions Occurring in $\geq 5\%$ of Anemic Patients Receiving OJJAARA during Randomized Treatment in SIMPLIFY-1

	OJJAARA n = 85	Ruxolitinib^a n = 95 Baseline Hb
--	--------------------------	--

Adverse Reactions	Baseline Hb <10 g/dL		<10 g/dL	
	All Grades ^b %	Grade ≥3 %	All Grades %	Grade ≥3 %
Dizziness ^c	24	1	15	2
Fatigue ^c	22	0	25	1
Bacterial infection ^{c,d}	21	8	12	2
Hemorrhage ^c	21	1	18	2
Thrombocytopenia ^c	21	11	34	6
Diarrhea ^c	20	1	20	1
Nausea ^c	20	0	3	1
Abdominal pain ^c	18	1	14	1
Cough ^c	14	0	11	0
Hypotension ^c	14	2	0	0
Pain in extremity	12	0	5	0
Pyrexia ^c	12	1	11	0
Rash ^c	12	0	3	0
Renal and urinary tract infection ^{c,d}	12	1	4	0
Elevated liver enzymes ^c	11	4	9	0
Headache ^c	11	0	16	0
Peripheral edema	11	0	8	0
Arrhythmia ^c	8	2	2	1
Paresthesia ^c	8	0	3	0
Pneumonia ^c	8	8	5	3
Vomiting ^c	8	0	5	0
Back pain	7	1	2	0
Viral infection ^{c,d}	6	0	13	2
Vitamin B1 deficiency	6	0	7	0

^a Study was not designed to evaluate meaningful comparisons of the incidence of adverse reactions across treatment groups.

^b Adverse reactions graded using CTCAE v.4.03.

^c Grouped term includes other related terms.

^d Excludes opportunistic infections.

Other Adverse Reactions

Clinically relevant adverse reactions occurring in <5% of anemic patients in the MOMENTUM and SIMPLIFY-1 studies include:

Eye Disorders: Blurred vision.

Infections and Infestations: Fungal infection (excludes opportunistic infections).

Nervous System Disorders: Neuralgia, peripheral neuropathy, peripheral motor neuropathy, polyneuropathy.

Vascular Disorders: Flushing.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on OJJAARA

Organic Anion Transporting Polypeptide (OATP)1B1/B3 Inhibitors

Momelotinib is an OATP1B1/B3 substrate. Concomitant use with an OATP1B1/B3 inhibitor increases momelotinib maximal concentrations (C_{max}) and area under the concentration-time curve (AUC) [see *Clinical Pharmacology (12.3)*], 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 [see *Dosage and Administration (2.4)*].

7.2 Effect of OJJAARA on Other Drugs

Breast Cancer Resistance Protein (BCRP) Substrates

Momelotinib is a BCRP inhibitor. OJJAARA may increase exposure of BCRP substrates, which may increase the risk of BCRP substrate adverse reactions [see *Clinical Pharmacology (12.3)*]. When administered concomitantly with OJJAARA, initiate rosuvastatin (BCRP substrate) at 5 mg and do not increase to more than 10 mg once daily. Dose adjustment of other BCRP substrates may also be needed. Follow approved product information recommendations for other BCRP substrates.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data on the use of OJJAARA in pregnant women are insufficient to determine whether there is a drug-associated risk for major birth defects or miscarriage. Based on animal reproduction studies conducted in rats and rabbits, momelotinib may cause embryo-fetal toxicity at exposures lower than the expected exposure in patients receiving 200 mg once daily (*see Data*). OJJAARA should only be used during pregnancy if the expected benefits to the mother outweigh the potential risks to the fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data: In an embryofetal development study, pregnant rats received momelotinib 2, 6 or 12 mg/kg/day orally, during the period of organogenesis (Gestation Day 6 to 17). Embryo-fetal toxicity (embryonic death, soft tissue anomalies, skeletal variations, and lower mean fetal body weights) was observed at 12 mg/kg (in the presence of maternal toxicity). Skeletal variations were observed (in the absence of maternal toxicity) at 6 mg/kg/day at exposures 3.5 times the exposure at the recommended human dose of 200 mg daily based on combined momelotinib and M21 (a major human metabolite) AUC. No developmental toxicity was observed at 2 mg/kg/day at exposures equivalent to the recommended dose (based on combined momelotinib and M21 AUC).

In an embryofetal developmental study, pregnant rabbits received momelotinib at 7.5, 30 or 60 mg/kg/day orally during the period of organogenesis (Gestation Day 7 to 20). Momelotinib was associated with maternal toxicity at 60 mg/kg/day, which resulted in reduced mean fetal weight, delayed bone ossification, and an abortion at less than the exposure at the recommended dose (based on combined momelotinib and M21 AUC). No developmental toxicity was observed at lower doses tested in rabbits.

In a pre- and post-natal development study, pregnant rats received momelotinib 2, 6 or 12 mg/kg/day orally from organogenesis through lactation (Gestation Day 6 to lactation Day 20). Decreased pup body weights and embryo-lethality were observed in the dams administered 6 and 12 mg/kg/day. Pup survival was significantly reduced in the 12 mg/kg/day group from birth to Day 4 of lactation. Momelotinib exposure in dams at 12 mg/kg and 6 mg/kg were approximately 2 times the exposure at the recommended dose (based on combined momelotinib and M21 AUC). The exposure in dams at the No Observed Adverse Effect Level (NOAEL) dose of 2 mg/kg was less than the exposure at the recommended dose (based on combined momelotinib and M21 AUC).

8.2 Lactation

Risk Summary

There are no data on the presence of momelotinib or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. It is not known whether OJJAARA is excreted in human milk. Momelotinib was present in rat pups following nursing from treated dams with adverse effects observed in the offspring. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because of the potential for serious adverse reactions in a breastfed child, patients should not breastfeed during treatment with OJJAARA, and for at least 1 week after the last dose of OJJAARA.

Data

Animal Data: In a pre- and postnatal development study, momelotinib was administered orally to rats during the lactation period; the drug was detected in plasma of nursing pups, which adversely affected pup survival.

8.3 Females and Males of Reproductive Potential

Contraception

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.

8.4 Pediatric Use

The safety and effectiveness of OJJAARA in pediatric patients have not been established.

8.5 Geriatric Use

There were 275 patients aged 65 years and older in the clinical studies for MF [see *Clinical Studies (14)*]. Of the total number of OJJAARA-treated patients in these studies, 163/216 (75%) were aged 65 years and older, and 63/216 (29%) were aged 75 years and older. No overall differences in safety or effectiveness of OJJAARA have been observed between patients aged 65 years and older and younger adult patients.

8.6 Hepatic Impairment

The recommended starting dose of OJJAARA in patients with severe hepatic impairment (Child-Pugh C) is 150 mg orally once daily [see *Dosage and Administration (2.3)*]. No dose modification is recommended for patients with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B).

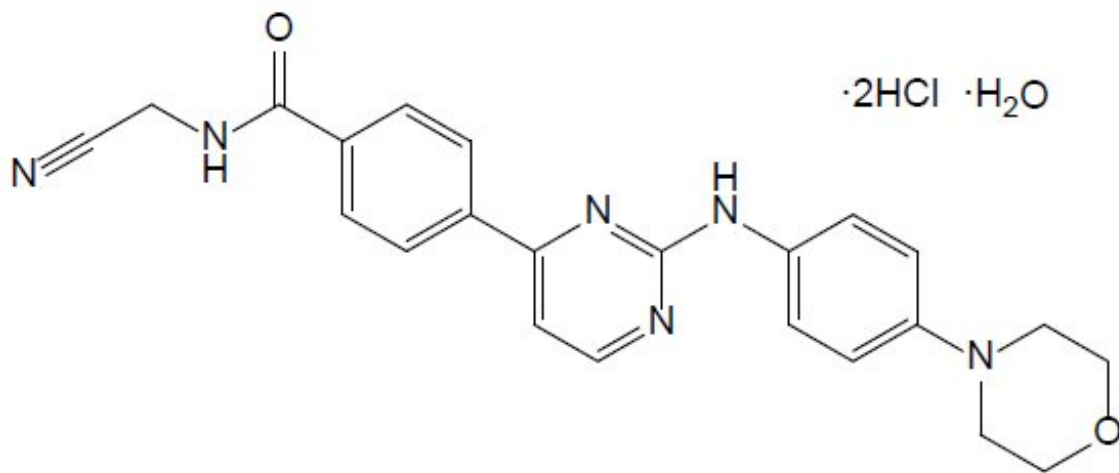
Momelotinib is extensively metabolized [see *Clinical Pharmacology (12.3)*]. Momelotinib exposure increased with severe hepatic impairment (Child-Pugh C). No clinically significant changes in momelotinib exposure were observed in subjects with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B) [see *Clinical Pharmacology (12.3)*].

10 OVERDOSAGE

There is no known antidote for overdose with OJJAARA. If overdose is suspected, the patient should be monitored for signs or symptoms of adverse reactions or effects, and appropriate supportive treatment should be instituted immediately. Further management should be as clinically indicated. Hemodialysis is not expected to enhance the elimination of momelotinib.

11 DESCRIPTION

OJJAARA contains momelotinib dihydrochloride monohydrate, which is a kinase inhibitor with the chemical name N-(Cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl]amino}pyrimidin-4-yl)benzamide dihydrochloride monohydrate. It has a molecular formula of $C_{23}H_{22}N_6O_2 \bullet 2HCl \bullet H_2O$, molecular weight of 505.40 and the following structural formula:



Momelotinib dihydrochloride monohydrate is a light yellow to brown to reddish-brown solid and is slightly soluble in water and insoluble in aqueous buffers across a pH range of 2.1 to 9. Momelotinib free base has a molecular formula of $C_{23}H_{22}N_6O_2$ and a molecular weight of 414.47.

OJJAARA (momelotinib) tablets are for oral administration. Each tablet contains 100 mg, 150 mg, or 200 mg of momelotinib, which is equivalent to 121.94 mg, 182.91 mg, or 243.88 mg, respectively, of momelotinib dihydrochloride monohydrate as the active ingredient. The core of each tablet contains the following inactive ingredients: lactose monohydrate, magnesium stearate, microcrystalline cellulose, propyl gallate, silicon dioxide, and sodium starch glycolate. The film coating of each tablet contains the following inactive ingredients: polyethylene glycol, polyvinyl alcohol, red iron oxide, talc, titanium dioxide, and yellow iron oxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Momelotinib 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 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.

12.2 Pharmacodynamics

Momelotinib inhibited STAT3 phosphorylation in whole blood from patients with MF. Maximal inhibition of STAT3 phosphorylation occurred 2 hours after momelotinib dosing and inhibition persisted for at least 6 hours [see *Clinical Pharmacology (12.1)*]. Iron

availability and erythropoiesis was assessed by analysis of circulating hepcidin concentrations. An acute and sustained reduction of circulating hepcidin was observed for the duration of the 24-week administration of momelotinib to patients with MF [see *Clinical Pharmacology (12.1)*].

Cardiac Electrophysiology

Momelotinib did not prolong the QT interval to any clinically relevant extent at 4 times the highest recommended dosage of 200 mg.

12.3 Pharmacokinetics

Momelotinib pharmacokinetic parameters are presented as mean (%CV) and were derived in patients with MF unless otherwise specified.

The momelotinib steady-state C_{max} is 479 ng/mL (61%) and AUC is 3,288 ng•h/mL (60%) at the maximum recommended dosage. Momelotinib exposure (i.e., C_{max} and AUC) increases dose proportionally from 100 mg to 300 mg (0.5 to 1.5 times the maximum recommended dosage), but less than dose-proportional at doses from 400 mg to 800 mg (2 to 4 times the maximum recommended dosage). There is no clinically significant accumulation.

Absorption

Median time to momelotinib C_{max} (T_{max}) at steady state is 2 hours (Q1: 1 hour; Q3: 3 hours) post dose.

Effect of Food

No clinically significant differences in momelotinib pharmacokinetics were observed following administration of either a high-fat meal (800 kcal; 50% fat) or low-fat meal (400 kcal; 20% fat) in healthy subjects.

Distribution

Momelotinib steady state apparent volume of distribution is 984 L (118%). Momelotinib plasma protein binding is approximately 91% in healthy volunteers.

Elimination

The elimination half-life of momelotinib and the M21 metabolite is 4 to 8 hours. Momelotinib clearance is 103 L/h (87%).

Metabolism: Momelotinib is metabolized by multiple cytochrome P450 (CYP) enzymes including CYP3A4 (36%), CYP2C8 (19%), CYP2C9 (17%), CYP2C19 (19%), and CYP1A2 (9%).

M21 is an active human metabolite that has approximately 40% of the pharmacological activity of the parent. M21 is formed by CYP followed by aldehyde oxidase metabolism of momelotinib. The mean M21 to momelotinib ratio for AUC ranged from 1.4 to 2.1.

Excretion: Following a single oral dose of radiolabeled momelotinib, 69% (13% unchanged) of radioactivity was excreted in feces and 28% (<1% unchanged) in urine. Approximately 12% of the administered dose was excreted in urine as M21.

Specific Populations

No clinically significant differences in momelotinib and M21 pharmacokinetics were

observed based on age (range: 28 to 92 years), race (83% White, 6% Asian, 2% Black), sex (60% male), weight (range: 34 kg to 138 kg), renal impairment (eGFR: 16.4 mL/min/1.73 m² to above 120 mL/min/1.73 m²), or mild or moderate hepatic impairment (Child-Pugh A or B). The effect of end stage renal disease receiving dialysis on momelotinib pharmacokinetics is unknown.

Patients with Hepatic Impairment: Momelotinib C_{max} increased by 13% and AUC increased by 97% in subjects with severe hepatic impairment (Child-Pugh C). The M21 metabolite C_{max} decreased by 76% and AUC decreased by 48% in subjects with severe hepatic impairment (Child-Pugh C).

Drug Interaction Studies

Clinical Studies

OATP1B1/1B3 Inhibitors: Momelotinib C_{max} increased by 40% and AUC increased by 57% following concomitant use with a single dose of a OATP1B1/1B3 inhibitor (rifampin). The M21 metabolite C_{max} increased by 6% and AUC increased by 12%.

BCRP Substrates: A BCRP substrate (rosuvastatin) C_{max} increased by 220% and AUC increased by 170% following concomitant use of a single dose of rosuvastatin at 10 mg with multiple doses of momelotinib (200 mg once daily).

Other Drugs: No clinically significant differences in momelotinib and M21 metabolite pharmacokinetics were observed when used concomitantly with a strong CYP3A4 inducer (tested with multiple-dose rifampin), a strong CYP3A4 inhibitor (ritonavir), or an acid reducing agent (omeprazole, a proton pump inhibitor).

No clinically significant differences in the pharmacokinetics of a CYP3A4 substrate (midazolam) were observed when used concomitantly with momelotinib.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenicity potential of momelotinib was assessed in *rasH2* transgenic mice and Sprague-Dawley rats. There was no evidence of tumorigenicity in male or female mice that received momelotinib doses up to 100 mg/kg/day for 26 weeks. In a 2-year oral carcinogenicity study in Sprague-Dawley rats, momelotinib caused benign Leydig cell tumors at a dose of 15 mg/kg/day (17 times the maximum recommended dose based on combined momelotinib and M21 AUC). The increase in Leydig cell adenomas was considered related to a rat-specific phenomenon (i.e., prolactin-dependent Leydig cell tumorigenesis).

Momelotinib was not mutagenic in a bacterial reverse mutation assay, or clastogenic in an in vitro chromosomal aberration assay with human peripheral blood lymphocytes or in vivo in a rat bone marrow micronucleus assay.

In fertility studies in rats, momelotinib was administered for at least 70 days (males) and 14 days (females) prior to cohabitation and up to the implantation day (gestation Day 7) at doses of 5, 25, and 68 mg/kg/day. Momelotinib reduced sperm concentration and motility and reduced testes and seminal vesicle weights at 25 mg/kg/day or greater (approximately 13 times the recommended dose based on combined momelotinib and M21 AUC) leading to reduced fertility at 68 mg/kg/day. In females, momelotinib reduced

ovarian function (reproductive cycles and ovulation) at 68 mg/kg/day and decreased the number of pregnant females and increased pre- and post-implantation loss with most pregnant rats having total litter loss at 25 mg/kg/day or greater. Exposures at the NOAEL in male and female rats at 5 mg/kg/day are approximately 3-times the recommended dose (based on combined momelotinib and M21 AUC).

14 CLINICAL STUDIES

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 200 mg once daily. Eligible patients had baseline platelet count of $\geq 25 \times 10^9/L$ in MOMENTUM and $\geq 50 \times 10^9/L$ in SIMPLIFY-1.

MOMENTUM

MOMENTUM (NCT04173494) was a double-blind, 2:1 randomized, active-controlled trial in 195 symptomatic and anemic adults with MF who had previously received an approved JAK inhibitor therapy. Patients were treated with OJJAARA 200 mg once daily or danazol 300 mg twice daily for 24 weeks, then switched to open-label treatment with OJJAARA.

The median age was 71 years (range 38 to 86 years) with 79% of patients aged 65 years and older, and 63% of patients were male. Overall, 81% of patients were White, 9% of patients were Asian, 2% of patients were Black, and 6% of patients were Hispanic or Latino. Sixty-four percent of patients had primary MF, 19% had post-PV MF, and 17% had post-ET MF. Five percent of patients 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 (median of 4 RBC units; interquartile range: 1-6). At baseline, 13% and 15% of patients were transfusion independent (defined as no red blood cell transfusions in the 12 weeks before the first dose and Hb ≥ 8 g/dL) in the OJJAARA and danazol groups, respectively. The baseline median Hb count was 8 g/dL and the median platelet count was $96 \times 10^9/L$ (range $24 \times 10^9/L$ to $733 \times 10^9/L$). The baseline median palpable spleen length was 11 cm below the left costal margin; the median central spleen volume measured by magnetic resonance imaging (MRI) or computed tomography (CT) was $2,105 \text{ cm}^3$ (range 609 cm^3 to $9,717 \text{ cm}^3$).

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: fatigue (weariness and tiredness), night sweats (or feeling hot or flushed), itching, abdominal discomfort (feeling pressure or bloating), pain under ribs on left side, feeling of fullness after beginning to eat, and bone pain. For each item, symptom 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 (Table 4). Other endpoints included transfusion independence, spleen volume response, MFSAF v4.0 Total Symptom Score change from baseline, and percentage of patients with no transfusions.

Table 4: Percent of Patients Achieving Symptom Reduction, Transfusion Independence, and Spleen Volume Reduction at Week 24 in MOMENTUM

	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 ^a (95% CI)	16% (6, 26)		
Patients with Transfusion Independence (no transfusion or Hb <8 g/dL between Weeks 12 and 24), n (%)	39 (30%)	13 (20%)	0.023
Non-inferiority treatment difference ^{a, b} (95% CI)	14% (2, 25)		
Patients with Spleen Volume Reduction by 25% or More, n (%)	51 (39%)	4 (6%)	<0.0001
Treatment difference ^a (95% CI)	33% (23, 44)		
MFSAF v4.0 Total Symptom Score Change from Baseline ^b (SE)	-9.4 (1.1)	-3.1 (1.6)	0.001
Treatment difference ^c (95% CI)	-6.2 (-10, -2.4)		
Patients with Spleen Volume Reduction by 35% or More, n (%)	29 (22%)	2 (3%)	0.001
Treatment difference ^a (95% CI)	18% (10, 27)		
Patients with No Transfusions ^{c, d} (during the 24-week treatment period), n (%)	46 (35%)	11 (17%)	0.001
Treatment difference ^a (95% CI)	17% (8, 26)		

^a Analyses stratified by baseline MFSAF v4.0 Total Symptom Score (<22 vs. ≥22), baseline palpable spleen length below the left costal margin (<12 vs. ≥12 cm), and baseline red blood cell or whole blood units transfused in the 8-week period before randomization (0, 1-4, ≥5 units).

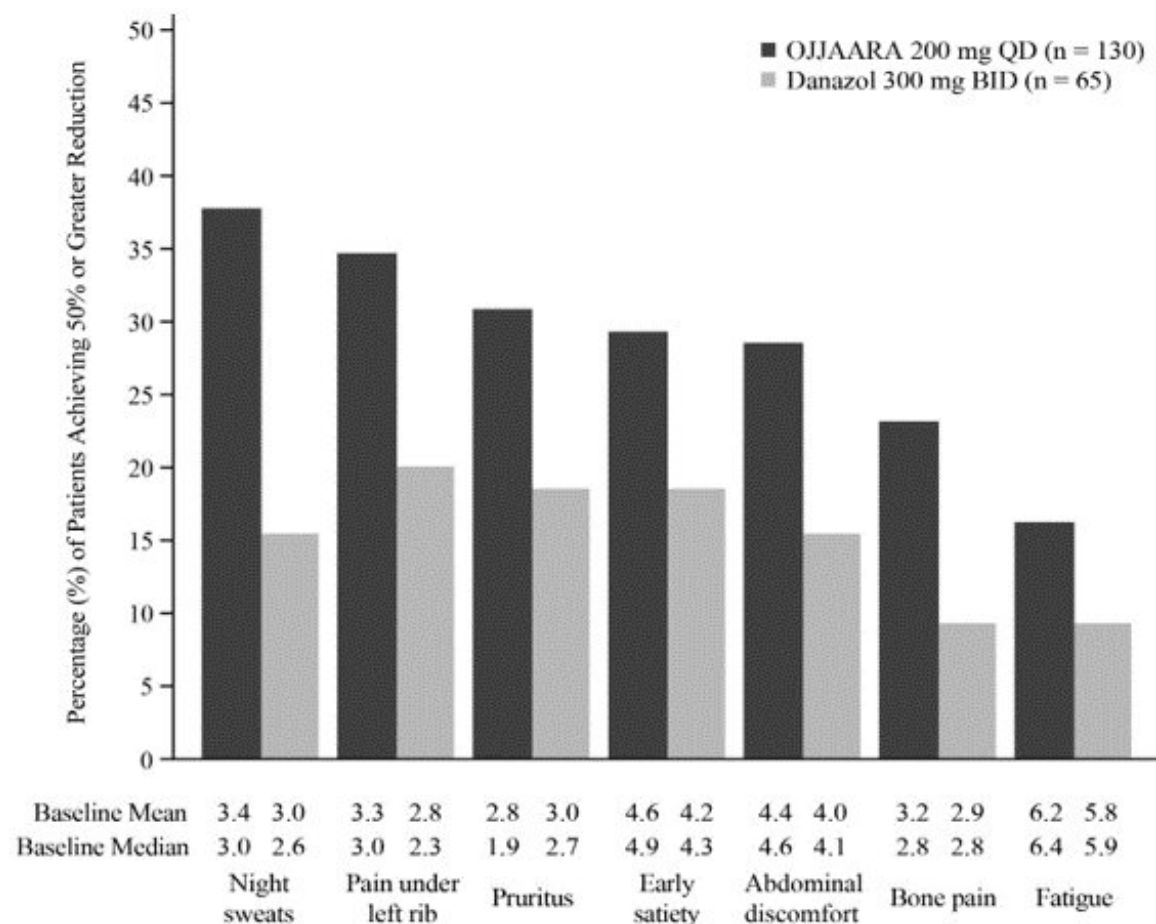
^b Non-inferiority difference between OJJAARA response rate and 80% of danazol response rate.

^c Least squares means and difference are reported.

^d Eight subjects treated with OJJAARA and 3 subjects treated with danazol had no transfusion, but discontinued treatment prior to Week 24.

Figure 1 shows the percentage of patients treated with OJJAARA and danazol who achieved a 50% or greater reduction from baseline for each individual symptom in the MFSAF v4.0.

Figure 1: Percent of Patients Achieving a 50% or Greater Reduction in Individual MFSAF v4.0 Symptom Scores at Week 24^a in MOMENTUM



QD = once daily; BID = twice a day.

^a Thirty-six (27.7%) subjects treated with OJJAARA and 27 (41.5%) subjects treated with danazol discontinued treatment prior to Week 24.

SIMPLIFY-1

SIMPLIFY-1 (NCT01969838) was a double-blind, randomized, active-controlled trial in 432 adults with MF who had not previously received a JAK inhibitor. Patients were treated with OJJAARA 200 mg once daily or ruxolitinib adjusted dose twice daily 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 <10 g/dL) at baseline (n = 181).

The median age was 68 years (range 25 to 86 years) with 67% of patients aged 65 years and older, and 59% of patients were male. Eighty-one percent of patients were White, 8% of patients were Asian, 1% of patients were Black, and 2% of patients were

Hispanic or Latino. Sixty-three percent of patients 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 8.8 g/dL and the median platelet count was $193 \times 10^9/L$ (range $54 \times 10^9/L$ to $2,865 \times 10^9/L$). Median palpable spleen length at baseline was 12 cm below the left costal margin; the median spleen volume at baseline (measured by MRI or CT) was $1,843 \text{ cm}^3$ (range 352 cm^3 to $9,022 \text{ cm}^3$).

The efficacy of OJJAARA in the treatment of patients with MF in SIMPLIFY-1 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 Table 5.

Table 5: Percent of Patients^a Achieving 35% or Greater Reduction from Baseline in Spleen Volume at Week 24 in SIMPLIFY-1

	OJJAARA n = 86	Ruxolitinib n = 95
Patients with Spleen Volume Reduction by 35% or More, n (%) (95% CI)	27 (31.4%) (21.8, 42.3)	31 (32.6%) (23.4, 43.0)

^a Subset of patients with anemia (Hb <10 g/dL) at baseline.

Figure 2 shows the percent change from baseline in spleen volume for each patient at Week 24 in SIMPLIFY-1.

Figure 2: Percent Change from Baseline in Spleen Volume for Each Patient at Week 24 in SIMPLIFY-1^{a, b}

^a Subset of patients with anemia (Hb <10 g/dL) at baseline.

^b Missing data rates for OJJAARA and ruxolitinib were 19% and 8%.

16 HOW SUPPLIED/STORAGE AND HANDLING

OJJAARA (mometotinib) tablets are available as follows:

Table 6: OJJAARA Presentations

NDC Number	Strength	Description	Tablets per Bottle
NDC 81864-103-30	100 mg	Round-shaped brown film-coated tablet with " <u>M</u> " on one side and "100" on the other side.	30
NDC 81864-102-30	150 mg	Triangular-shaped brown film-coated tablet with " <u>M</u> " on one side and "150" on the other side.	30
NDC 81864-101-30	200 mg	Capsule-shaped brown film-coated tablet with " <u>M</u> " on one side and "200" on the other side.	30

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Dispense to patient in original bottle only. Store in original bottle to protect from moisture. Replace cap securely each time after opening. Do not discard desiccant.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA approved patient labeling (Patient Information).

Infections

Inform patients that OJJAARA can increase the risk of infections (including COVID-19) and instruct them to promptly report to their healthcare provider any signs and symptoms of infection [see *Warnings and Precautions (5.1)*].

Thrombocytopenia and Neutropenia

Inform patients that OJJAARA can cause thrombocytopenia and neutropenia, and of the need to monitor complete blood count, including platelet and neutrophil counts, before and during treatment. Advise patients to observe for and report any bleeding to their healthcare provider [see *Warnings and Precautions (5.2)*].

Hepatotoxicity

Inform patients that OJJAARA can cause hepatotoxicity, and of the need to monitor liver blood tests before and during treatment [see *Warnings and Precautions (5.3)*].

Major Adverse Cardiovascular Events (MACE)

Advise patients that events of MACE including myocardial infarction, stroke, and cardiovascular death have been reported in clinical studies with another JAK inhibitor used to treat rheumatoid arthritis, a condition for which OJJAARA is not indicated. Advise patients, especially current or past smokers and patients with other cardiovascular risk factors, to be alert for the development of signs and symptoms of cardiovascular events and to report them to their healthcare provider [see *Warnings and Precautions (5.4)*].

Thrombosis

Advise patients that events of deep vein thrombosis (DVT) and pulmonary embolism (PE) have been reported in clinical studies with another JAK-inhibitor used to treat rheumatoid arthritis, a condition for which OJJAARA is not indicated. Advise patients to tell their healthcare provider if they develop any signs or symptoms of a DVT or PE [see *Warnings and Precautions (5.5)*].

Malignancies

Advise patients, especially current or past smokers, that lymphoma and other malignancies (excluding non-melanoma skin cancers (NMSC) have been reported in clinical studies with another JAK inhibitor used to treat rheumatoid arthritis, a condition for which OJJAARA is not indicated [see *Warnings and Precautions (5.6)*].

Pregnancy

- Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their prescriber of a known or suspected pregnancy [see *Use in Specific Populations (8.1)*].

- Advise females of reproductive potential who are not pregnant to use highly effective contraception during therapy and for 1 week after the last dose of OJJAARA [see *Use in Specific Populations (8.3)*].

Lactation

Advise patients not to breastfeed during treatment with OJJAARA and for at least 1 week after the last dose of OJJAARA [see *Use in Specific Populations (8.2)*].

Trademarks are owned by or licensed to the GSK group of companies.

GlaxoSmithKline
Durham, NC 27701

©2023 GSK group of companies or its licensor.

OJJ:1PI

PATIENT INFORMATION

OJJAARA (oh-JAR-uh) (momelotinib) tablets, for oral use

What is OJJAARA?

OJJAARA is a prescription medicine used to treat adults with certain types of myelofibrosis (MF) who have anemia. It is not known if OJJAARA is safe and effective in children.

Before taking OJJAARA, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection. See **“Risk of Infections”** in the section **“What are the possible side effects of OJJAARA?”**.
- have or have had hepatitis B
- have or have had liver problems
- have had a heart attack, or have or have had other heart problems, or stroke
- have or have had a blood clot
- smoke or were a smoker in the past
- have or have had any other cancers
- are pregnant or plan to become pregnant. OJJAARA may harm your unborn baby.

Females who are able to become pregnant:

1. You should use effective birth control (contraception) during treatment and for 1 week after the last dose of OJJAARA.
 2. Tell your healthcare provider right away if you think you are pregnant or become pregnant during treatment with OJJAARA.
- are breastfeeding or plan to breastfeed. It is not known if OJJAARA passes into your breast milk. You should not breastfeed during treatment and for 1 week after the last dose of OJJAARA. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking OJJAARA with certain other medicines may affect the amount of OJJAARA or the other

medicines in your blood and may increase your risk of side effects. Know the medicines you take. Keep a list of the medicines you take to show your healthcare provider and pharmacist when you get a new medicine.

How should I take OJJAARA?

- Take OJJAARA exactly as your healthcare provider tells you to take it.
- Take OJJAARA by mouth 1 time each day.
- Take OJJAARA with or without food.
- Swallow tablets whole. Do not cut, crush or chew tablets.
- If you miss a dose of OJJAARA, skip the missed dose and take your next dose the following day at your regularly scheduled time. Do not take 2 doses at the same time to make up for the missed dose.
- Your healthcare provider will do blood tests before you start taking OJJAARA and during treatment.
- Do not change your dose or stop taking OJJAARA without first talking to your healthcare provider.
- Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with OJJAARA if you have certain side effects.
- If you take too much OJJAARA, call your healthcare provider or go to the nearest emergency room right away and take your bottle of OJJAARA with you.

What are the possible side effects of OJJAARA?

OJJAARA may cause serious side effects, including:

- **Risk of Infections.** People who take OJJAARA may develop serious infections that can lead to death, such as bacterial and viral infections, including COVID-19. If you have an active infection, your healthcare provider should not start treatment with OJJAARA until your infection is gone. If you have had hepatitis B for a long time (chronic), OJJAARA may cause your hepatitis B to become active again, and your healthcare provider will check your blood for active hepatitis B before starting treatment.

Your healthcare provider will monitor you and treat you for any infections that you get during treatment with OJJAARA.

Tell your healthcare provider right away if you develop any of the following symptoms of infection:

- fever
- chills
- cough
- breathing problems
- diarrhea
- vomiting
- pain or burning feeling when passing urine

- **Low platelet and white blood cell counts.** OJJAARA may cause new or worsening low platelet and white blood cell counts. Low platelet counts may increase your risk for bleeding and low white blood cell counts may increase your risk for infection. Your healthcare provider will do blood tests to check your blood counts before you start taking OJJAARA and during treatment. Tell your healthcare provider right away if you have any signs of bleeding during treatment with OJJAARA, including:

- unusual bleeding
 - black or tarry stools
 - bruising
- **Liver problems.** OJJAARA may cause new or worsening increased liver enzymes and bilirubin in your blood. Your healthcare provider will check your liver enzymes before starting treatment, every month for the first 6 months of treatment, and then as needed during treatment with OJJAARA. Your healthcare provider may stop treatment with OJJAARA if your liver enzymes increase. Tell your healthcare provider if you develop any of the following signs or symptoms of liver problems:
 - tiredness
 - loss of appetite
 - pain in your right upper stomach area (abdomen)
 - dark urine
 - yellowing of your skin or the white part of your eyes
- **Major cardiovascular events such as heart attack, stroke, and death.** Major cardiac events have happened, especially in people with cardiac risk factors and who are current or past smokers, taking another Janus kinase (JAK) inhibitor to treat rheumatoid arthritis. OJJAARA is in the JAK family of medicines.
Get emergency help right away if you have any symptoms of a heart attack or stroke while taking OJJAARA, including:
 1. discomfort in your chest that lasts for more than a few minutes, or that goes away and comes back
 2. severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
 3. pain or discomfort in your arms, back, neck, jaw, or stomach
 4. shortness of breath with or without chest discomfort
 5. breaking out in a cold sweat
 6. nausea or vomiting
 7. feeling lightheaded
 8. weakness in one part or on one side of your body
 9. slurred speech
- **Blood clots.** Blood clots in the veins of the legs (deep vein thrombosis, DVT) or lungs (pulmonary embolism, PE) have happened in some people taking another JAK inhibitor to treat rheumatoid arthritis, and may be life-threatening. Tell your healthcare provider if you have had blood clots in the veins of your legs or lungs in the past.
Tell your healthcare provider right away if you have any signs and symptoms of blood clots during treatment with OJJAARA, including:
 10. swelling, pain, or tenderness in one or both legs
 11. sudden, unexplained chest pain
 12. shortness of breath or difficulty breathing
- **New cancers.** New cancers, including lymphoma and other cancers, except non-melanoma skin cancer, have happened in some people taking another JAK inhibitor

to treat rheumatoid arthritis. The risk of new cancers is further increased in people who smoke or who smoked in the past.

The most common side effects of OJJAARA include:

- low platelet count
- bleeding
- bacterial infection
- tiredness
- dizziness
- diarrhea
- nausea

These are not all of the possible side effects of OJJAARA.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store OJJAARA?

- Store OJJAARA at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep OJJAARA in its original bottle. The OJJAARA bottle contains a desiccant packet to help keep your tablets dry (protect from moisture). Keep the desiccant in the bottle.
- Tightly close the OJJAARA bottle after you take your dose.

Keep OJJAARA and all medicines out of the reach of children.

General information about the safe and effective use of OJJAARA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use OJJAARA for a condition for which it was not prescribed. Do not give OJJAARA to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about OJJAARA that is written for health professionals.

What are the ingredients in OJJAARA?

Active ingredient: momelotinib dihydrochloride monohydrate

Inactive ingredients: lactose monohydrate, magnesium stearate, microcrystalline cellulose, propyl gallate, silicon dioxide, and sodium starch glycolate

Film coating: polyethylene glycol, polyvinyl alcohol, red iron oxide, talc, titanium dioxide, and yellow iron oxide

Trademarks are owned by or licensed to the GSK group of companies.

GlaxoSmithKline, Durham, NC 27701

For more information about OJJAARA, call 1-888-825-5249 or visit our website at www.OJJAARA.com.

©2023 GSK group of companies or its licensor.

OJJ:1PIL

This Patient Information has been approved by the U.S. Food and Drug Administration
Issued: September 2023

PRINCIPAL DISPLAY PANEL

NDC 81864-103-30

Ojjaara

(momelotinib)

tablets

100 mg

Rx Only

GSK

30 Tablets

Each 100 mg tablet is equivalent to 121.94 mg of momelotinib dihydrochloride monohydrate. **Swallow tablets whole.**

Do not cut, crush, or chew tablets.

Store at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). (see USP Controlled Room Temperature). Dispense and store in original bottle with desiccant to protect from moisture.

Do not accept if safety seal under cap is missing or broken.

Recommended dosage: See Prescribing Information

Keep out of reach of children.

Trademarks owned or licensed by GSK.

Mfd for: GSK Durham, NC 27701

Product of Sweden

©2023 GSK or licensor.

Rev. 6/23

2000015377

NDC 81864-103-30
Rx Only

Ojjaara
(momelotinib)
tablets

100 mg

30 tablets

2000015377

Each tablet contains 100 mg of momelotinib equivalent to 121.94 mg of momelotinib dihydrochloride monohydrate. **Swallow tablets whole. Do not cut, crush, or chew tablets.** Store at 20°C to 25°C (68°F to 77°F); Excursions permitted to 15°C to 30°C (59°F to 86°F) (see USP Controlled Room Temperature). Dispense and store in original bottle with desiccant to protect from moisture. **Do not accept if safety seal under cap is missing or broken.** Recommended dosage: See Prescribing Information. **Keep out of reach of children.** Trademarks owned or licensed by GSK. Mfd for: GSK, Durham, NC 27701 Product of Sweden ©2023 GSK or licensor. Rev. 6/23

GTIN (01) XXXXXXXXXXXXXXXX
EXP MMM YYYY
LOT (10) XXXXX
SN (21) XXXXXXXXXXXXX

3 81864-103-30 5

PRINCIPAL DISPLAY PANEL

NDC 81864-102-30

Ojjaara
(momelotinib)

tablets

150 mg

Rx Only

GSK

30 Tablets

Each 150 mg tablet is equivalent to 182.9 mg of momelotinib dihydrochloride monohydrate. **Swallow tablets whole.**

Do not cut, crush, or chew tablets.

Store at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). (see USP Controlled Room Temperature). Dispense and store in original bottle with desiccant to protect from moisture.

Do not accept if safety seal under cap is missing or broken.

Recommended dosage: See Prescribing Information

Keep out of reach of children.

Trademarks owned or licensed by GSK.

Mfd for: GSK Durham, NC 27701

Product of Sweden

©2023 GSK or licensor.

Rev. 6/23

2000015381

NDC 81864-102-30
Rx Only

GSK

Ojjaara
(momelotinib)
tablets

150 mg

30 tablets

Each tablet contains 150 mg of momelotinib equivalent to 182.91 mg of momelotinib dihydrochloride monohydrate. **Swallow tablets whole. Do not cut, crush, or chew tablets.** Store at 20°C to 25°C (68°F to 77°F); Excursions permitted to 15°C to 30°C (59°F to 86°F) (see USP Controlled Room Temperature). Dispense and store in original bottle with desiccant to protect from moisture. **Do not accept if safety seal under cap is missing or broken.** Recommended dosage: See Prescribing Information. **Keep out of reach of children.** Trademarks owned or licensed by GSK. Mfd for: GSK, Durham, NC 27701 Product of Sweden ©2023 GSK or licensor. Rev. 6/23

GTIN (01) XXXXXXXXXXXXXXX
EXP MMM YYYY
LOT (10) XXXXX
SN (21) XXXXXXXXXXXXXXX

2000015381

81864-102-30 8

PRINCIPAL DISPLAY PANEL

NDC 81864-101-30

Ojjaara

(mometinib)

Tablets

200 mg

Rx Only

GSK

30 Tablets

Each 200 mg tablet is equivalent to 243.9 mg of mometinib dihydrochloride monohydrate. **Swallow tablets whole.**

Do not cut, crush, or chew tablets.

Store at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). (see USP Controlled Room Temperature). Dispense and store in original bottle with desiccant to protect from moisture.

Do not accept if safety seal under cap is missing or broken.

Recommended dosage: See Prescribing Information

Keep out of reach of children.

Trademarks owned or licensed by GSK.

Mfd for: GSK Durham, NC 27701

Product of Sweden

©2023 GSK or licensor.

Rev. 6/23

2000015382



GTIN (01) XXXXXXXXXXXXXXXX
 EXP MMM YYYY
 LOT (10) XXXXX
 SN (21) XXXXXXXXXXXXXXXX

NDC 81864-101-30
 Rx Only



Ojjaara
 (momelotinib)
 tablets

2000015382

200 mg

30 tablets

Each tablet contains 200 mg of momelotinib equivalent to 243.88 mg of momelotinib dihydrochloride monohydrate. **Swallow tablets whole. Do not cut, crush, or chew tablets.**

Store at 20°C to 25°C (68°F to 77°F); Excursions permitted to 15°C to 30°C (59°F to 86°F) (see USP Controlled Room Temperature). Dispense and store in original bottle with desiccant to protect from moisture.

Do not accept if safety seal under cap is missing or broken.

Recommended dosage: See Prescribing Information.

Keep out of reach of children.

Trademarks owned or licensed by GSK.

Mfd for: GSK, Durham, NC 27701

Product of Sweden

©2023 GSK or licensor.

Rev. 6/23



N 81864-101-30 1

OJJAARA

momelotinib tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:81864-103
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MOMELOTINIB DIHYDROCHLORIDE MONOHYDRATE (UNII: LDX8893L5D) (MOMELOTINIB - UNII:6O01GMS00P)	MOMELOTINIB	100 mg

Inactive Ingredients

Ingredient Name	Strength
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
SODIUM STARCH GLYCOLATE TYPE A CORN (UNII: AG9B65PV6B)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
PROPYL GALLATE (UNII: 8D4SNN7V92)	
POLYVINYL ALCOHOL, UNSPECIFIED (UNII: 532B59J990)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WJQ0SDW1A)	
TALC (UNII: 7SEV7J4R1U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	

Product Characteristics				
Color	BROWN	Score	no score	
Shape	ROUND	Size	9mm	
Flavor		Imprint Code	M;;100	
Contains				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:81864-103-30	30 in 1 BOTTLE; Type 0: Not a Combination Product	09/15/2023	
Marketing Information				
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date	
NDA	NDA216873	09/15/2023		

OJJAARA			
momelotinib tablet			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:81864-102
Route of Administration	ORAL		
Active Ingredient/Active Moiety			
Ingredient Name		Basis of Strength	Strength
MOMELOTINIB DIHYDROCHLORIDE MONOHYDRATE (UNII: LDX8893L5D) (MOMELOTINIB - UNII:6O01GMS00P)		MOMELOTINIB	150 mg
Inactive Ingredients			
Ingredient Name			Strength
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)			
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)			
SODIUM STARCH GLYCOLATE TYPE A CORN (UNII: AG9B65PV6B)			
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)			
MAGNESIUM STEARATE (UNII: 70097M6I30)			
PROPYL GALLATE (UNII: 8D45NN7V92)			
POLYVINYL ALCOHOL, UNSPECIFIED (UNII: 532B59J990)			
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WJQ0SDW1A)			
TALC (UNII: 7SEV7J4R1U)			
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)			
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)			

FERRIC OXIDE RED (UNII: 1K09F3G675)

Product Characteristics

Color	BROWN	Score	no score
Shape	TRIANGLE	Size	11mm
Flavor		Imprint Code	M;;150
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:81864-102-30	30 in 1 BOTTLE; Type 0: Not a Combination Product	09/15/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA216873	09/15/2023	

OJJAARA

momelotinib tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:81864-101
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
MOMELOTINIB DIHYDROCHLORIDE MONOHYDRATE (UNII: LDX8893L5D) (MOMELOTINIB - UNII:6O01GMS00P)	MOMELOTINIB	200 mg

Inactive Ingredients

Ingredient Name	Strength
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
SODIUM STARCH GLYCOLATE TYPE A CORN (UNII: AG9B65PV6B)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
PROPYL GALLATE (UNII: 8D4SNN7V92)	
POLYVINYL ALCOHOL, UNSPECIFIED (UNII: 532B59J990)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WJQ0SDW1A)	

TALC (UNII: 7SEV7J4R1U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	

Product Characteristics

Color	BROWN	Score	no score
Shape	CAPSULE	Size	15mm
Flavor		Imprint Code	M;;200
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:81864-101-30	30 in 1 BOTTLE; Type 0: Not a Combination Product	09/15/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA216873	09/15/2023	

Labeler - GlaxoSmithKline LLC (167380711)

Revised: 9/2023

GlaxoSmithKline LLC