swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Omjjara

International non-proprietary name:	momelotinib
Pharmaceutical form:	film-coated tablet
Dosage strength(s):	100 mg, 150 mg, 200 mg
Route(s) of administration:	oral use
Marketing authorisation holder:	GlaxoSmithKline AG
Marketing authorisation no.:	69428
Decision and decision date:	approved on 25 September 2024

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

ACVR1	Activin A receptor type 1
AE	Adverse event
AUC	Area under the plasma concentration-time curve
BID	Twice daily
C_{max}	Maximum observed plasma/serum concentration of drug
DAN	Danazol
EMA	European Medicines Agency
ERA	Environmental risk assessment
ET	Essential thrombocythaemia
FDA	Food and Drug Administration (USA)
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
INN	International non-proprietary name
JAK	Janus kinase
JAKi	Janus kinase inhibitor
LoQ	List of Questions
MAH	Marketing Authorisation Holder
Max	Maximum
MF	Myelofibrosis
Min	Minimum
MMB	Momelotinib
NO(A)EL	No observed (adverse) effect level
OS	Overall survival
PMF	Primary myelofibrosis
PV	Polycythaemia vera
QD	Once daily
QSAR	Quantitative structure-activity relationship
RMP	Risk management plan
SMF	Secondary myelofibrosis
STAT	Signal transducer and activator of transcription
SwissPAR	Swiss Public Assessment Report
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
TSS	Total symptom score
UPLC	Ultra-performance liquid chromatography

2 Background information on the procedure

2.1 Applicant's request(s)

New active substance status
The applicant requested new active substance status for momelotinib in the above-mentioned medicinal product.

Orphan drug status
The applicant requested orphan drug status in accordance with Article 4 paragraph 1 letter a^{decies} no. 2 TPA.
Orphan drug status was granted on 7 December 2023.

2.2 Indication and dosage

2.2.1 Requested indication

Omjjara is indicated for the treatment of primary myelofibrosis, post-polycythaemia vera myelofibrosis, and post-essential thrombocythaemia myelofibrosis in adults with anaemia.

2.2.2 Approved indication

Omjjara as monotherapy is indicated for the treatment of intermediate or high-risk primary myelofibrosis, myelofibrosis secondary to polycythaemia vera, or myelofibrosis secondary to essential thrombocythaemia in adults with moderate or severe anaemia, who have been treated previously with ruxolitinib or are not eligible for treatment with ruxolitinib, and who are not eligible for allogeneic stem cell transplantation (see "*Clinical efficacy*").

2.2.3 Requested dosage

Summary of the requested standard dosage:
The recommended dosage is 200 mg orally once daily. Omjjara may be taken with or without food.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	16 May 2023
Formal objection	5 June 2023
Response to formal objection	13 June 2023
Formal control completed	20 June 2023
List of Questions (LoQ)	17 October 2023
Response to LoQ	15 January 2024

Preliminary decision	12 April 2024
Response to preliminary decision	11 June 2024
Labelling corrections and/or other aspects	11 September 2024
Response to labelling corrections and/or other aspects	20 September 2024
Final decision	25 September 2024
Decision	approval

3 Medical context

Myelofibrosis (MF) is a rare Philadelphia chromosome-negative myeloproliferative neoplasm, which can present as a *de novo,* primary myelofibrosis (PMF) or as secondary MF (SMF) following the progression of polycythaemia vera (PV) and essential thrombocythaemia (ET) [post-PV MF or post-ET MF]. At a biological level, MF is characterised by clonal expansion of malignant haematopoietic stem and progenitor cells, with aberrant trafficking to extramedullary sites of haematopoiesis and secretion of inflammatory cytokines. The histopathological consequences are bone marrow hypercellularity, and reticulin and collagen fibrosis. The clinical picture is heterogeneous but in general includes progressive cytopenia, organomegaly, debilitating systemic symptoms, and the potential for evolution to acute myeloid leukaemia. Myelocytosis and systemic proinflammatory conditions significantly increase the risk of arterial and venous vascular events.

Therapy of MF is risk-adapted. While observation alone is advised for asymptomatic low-risk disease, allogeneic haematopoietic cell transplant is currently the only known cure for MF and the preferred treatment of choice for high-risk and selected intermediate-risk disease. Drug therapy for MF is palliative and aims at improving the key clinical features anaemia, splenomegaly, and MF-related symptoms. Because hyperactivity of the JAK-STAT signalling pathway is the central biological hallmark of MF, with somatic mutations involving the 3 genes *JAK2*, *CALR,* and *MPL* comprising 90% of driver mutations, JAK inhibitors (JAKi), such as ruxolitinib, are a standard treatment for MF. However, there is currently no convincing evidence regarding disease-modifying effects and impact on long-term efficacy outcomes such as overall survival (OS), and objective responses such as complete or partial responses are hardly ever achieved. In addition, while the currently approved JAKi might be able to address splenomegaly and MF-related symptoms, disease-related cytopenias, remain a therapeutic challenge, and might be even exacerbated or induced by JAKi therapy.

Despite its debilitating character, the management of anaemia is particularly challenging as neither hydroxyurea nor approved JAKi show satisfactory effectiveness against MF-associated anaemia. Other drugs used to treat MF-associated anaemia include danazol, androgens, prednisone, and thalidomide or lenalidomide ± prednisone. Erythropoiesis-stimulating agents are often ineffective in transfusion-dependent patients and could exacerbate splenomegaly. Response rates to the aforementioned drugs are approximately 15 to 25%, and response durations average about 1 to 2 years. In summary, there is still a medical need for the management of MF-associated anaemia, especially when associated with symptomatic splenomegaly or MF-related symptoms.

Hyperactivity of the JAK-STAT signalling pathway leads to hyperactivation of activin A receptor type 1 (ACVR1) and consequently elevated hepcidin levels. Besides JAK 1 and 2, momelotinib (MMB) and its major human circulating metabolite inhibit ACVR1, which produces subsequent inhibition of liver hepcidin expression and increased iron availability, resulting in increased red blood cell production.

4 Quality aspects

4.1 Drug substance

Momelotinib
INN: Momelotinib dihydrochloride monohydrate

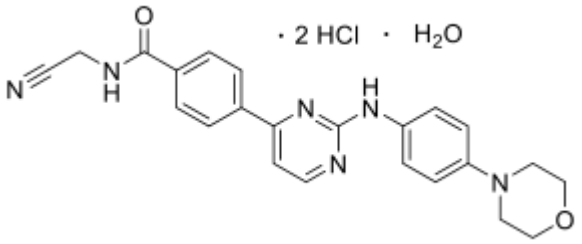
Chemical name:
IUPAC:
N-(cyanomethyl)-4-(2-{[4-(morpholin-4-yl)phenyl] amino}pyrimidin-4-yl)benzamide dihydrochloride hydrate

Other chemical names:
Benzamide, N-(cyanomethyl)-4-[2-[[4-(4-morpholinyl)phenyl]amino]-4-pyrimidinyl]
N-(cyanomethyl)-4-[2-(4-morpholin-4-ylanilino)pyrimidin-4-yl]benzamide dihydrochloride monohydrate

Molecular formula:
$C_{23}H_{22}N_6O_2 \cdot 2HCl \cdot H_2O$
$C_{23}H_{22}N_6O_2$ (free base)

Molecular mass:
Momelotinib dihydrochloride monohydrate = 505.40
Momelotinib free base = 414.47

Molecular structure:



Physicochemical properties:
BCS Class 2.
One polymorphic form for momelotinib dihydrochloride monohydrate (GS-0387-01, Form II) has been observed.

Synthesis:
The manufacturing process of momelotinib dihydrochloride monohydrate drug substance (DS) is composed of 5 steps.

Specification:
Visual appearance, identification (IR and UPLC retention time), identification of crystalline form II, water content, residual solvents by GC, assay by UPLC, related substances by UPLC, hydrochloride content by titration, particle size by laser light scattering, residue on ignition/sulphated ash, microbial limits.

Stability:
The proposed retest period is justified based on the available results of stability studies performed according to ICH requirements.

4.2 Drug product

Description and composition:
Momelotinib tablets are manufactured in strengths of 100 mg, 150 mg, and 200 mg.
Momelotinib tablets, 100 mg, are brown, round, film-coated tablets, debossed with an underscored M on one side and 100 on the other side.

Momelotinib tablets, 150 mg, are brown, triangle-shaped, film-coated tablets, debossed with an underscored M on one side and 150 on the other side.

Momelotinib tablets, 200 mg, are brown, capsule-shaped, film-coated tablets, debossed with an underscored M on one side and 200 on the other side.

Excipients: microcrystalline cellulose, lactose monohydrate, sodium starch glycolate, magnesium stearate, silica colloidal anhydrous, propyl gallate. Film coating: polyvinyl alcohol, macrogol 3350, titanium dioxide, talc, yellow iron oxide, red iron oxide.

Pharmaceutical development:
An overview of the formulations employed in clinical trials throughout the development of momelotinib is provided.
There were no process changes between Phase 3 and commercial process.

Manufacture:
The manufacturing process utilises conventional steps to produce a powder blend by dry granulation. Tablet production involves tablet compression and tablet coating.

Specification:
Appearance, identification (UV and UPLC retention time), water content by Karl Fischer, assay by UPLC, degradation products by UPLC, uniformity of dosage units, dissolution, propyl gallate content, microbial limits.

Container closure system:
High-density polyethylene (HDPE) bottle with silica gel desiccant and polyester coil. Capped with a white, continuous thread, child resistant polypropylene cap fitted with an induction-sealed, aluminium-faced liner.

Stability:
The proposed shelf life of 36 months is supported by sufficient data.

4.3 Quality conclusions

Satisfactory and consistent quality of the drug substance and drug product has been demonstrated.

5 Nonclinical aspects

5.1 Pharmacology

Momelotinib is a potent inhibitor of Janus kinase 1 and 2 (JAK 1 and JAK 2) with IC_{50} values in a low nanomolar range. In comparison with JAK2, its affinity for JAK3 and tyrosine kinase 2 (TYK2) was at least 4.5 and 1.3 times lower. In the ATP-independent competitive binding assay, M21 (the major human metabolite) exhibited similar activities for members of JAK family as momelotinib. The applicant did not clearly clarify the selectivity of momelotinib and M21 for other JAK family members.

In vitro, momelotinib and M21 inhibited intracellular Janus kinase/signal transducer and activator of transcription (JAK/STAT) signalling in activated primary human peripheral blood mononuclear cells, mediated by JAK homo- or heterodimers with EC_{50} values of 59.6 to 725 nM. Momelotinib treatment inhibited hepcidin RNA transcription stimulated by bone morphogenetic protein 6 (BMP6) in a concentration-dependent manner, with an EC50 value of 652 nM. M21 was 2.2 times less potent. These data indicate that momelotinib and M21 may restore iron homeostasis via regulation of activin A receptor type 1 (ACVR1)-mediated hepcidin expression. Momelotinib inhibited the nuclear factor-κB reporter activity with an IC_{50} of 600 nM *in vitro*. M21 was 5-fold less potent. These data suggest that momelotinib may have a beneficial role in myelofibrosis (MF) inflammation, via a JAK-independent mechanism.
In a mouse model of myeloproliferative neoplasm, oral administration of momelotinib at 50 mg/kg (i.e. 240 mg human equivalent dose for an adult of 60 kg) normalised white cell counts, haematocrit, spleen size, and restored physiologic levels of inflammatory cytokines in addition to significantly reducing the concentration of inflammatory cytokines IL-17, IL-3, and IP-10 relative to control animals.
In a rat model of anaemia, oral momelotinib treatment (5 to 25 mg/day for 21 days) normalised haemoglobin and red blood cell numbers, reduced STAT3 levels in the liver and serum hepcidin, and increased serum iron as well as mature red blood cells in the bone marrow.
Secondary pharmacodynamics studies revealed a significant inhibition of UDP glucuronosyltransferase 1 family polypeptide A1 (UGT1A1) at clinically relevant concentration. The clinical consequence of this interaction seems to be minimal.
In safety pharmacology studies, momelotinib did not show any cardiovascular, respiratory, or central nervous system (CNS) effects up to exposure levels corresponding to 3.3-fold (cardiac function) and 6-fold (respiratory and CNS function), when compared to human exposure at therapeutic dosing. In the 26-week study in rats, a reversible, mild slowing of caudal and digital nerve conduction velocity was observed at exposure levels corresponding to 11-fold human exposure based on AUC. No adverse effects, however, were observed in the observational test battery in this study. In clinical trials, peripheral neuropathy was frequently observed and is mentioned in the Information for healthcare professionals and RMP.

5.2 Pharmacokinetics

The pharmacokinetics of momelotinib and its metabolites was investigated in *in vitro* studies and after single intravenous and oral administration in mice, rats, and dogs. Momelotinib dihydrochloride salt was selected for nonclinical and clinical development.
In dogs, rats, and mice, momelotinib salt was rapidly absorbed following oral administration, with T_{max} ≤3 hours post-dose. $T_{1/2}$ was normally ≤ 1.8 hours (similar to humans: T_{max}: 1.8 hours and $T_{1/2}$: 5.1h). The oral bioavailability was approx. 20% in dogs and 50-70% in rats. The volume of distribution was higher in rats than in dogs (6.8 L/kg vs 2.4 L/kg). Momelotinib, M19, M20, and M21 exposure normally increased in a greater than dose-proportional manner. No sex-dependency in pharmacokinetics was observed.
Momelotinib plasma binding was 97.5% in rats, 88.2% in mice, and 80.8% in dogs and humans *in vitro*. In clinical studies, the fraction of bound momelotinib was 91%. The applicant calculated the

safety margins based on the comparison of animal momelotinib exposure to human momelotinib plus M21 exposure.
Wide tissue distribution of ^{14}C-momelotinib was observed with C_{max} at 4 h post-dose, and the highest concentrations of radioactivity were found in the alimentary canals in non-pigmented (Sprague Dawley) and pigmented (Long Evans) rats. No radioactivity was found in bone, brain, spinal cord, and testes. Radioactivity was cleared from tissues by 72 hours post-dose except for pigmented skin and the uveal tract in Long Evans rats, where radioactivity was still quantifiable at 168 hours post-dose.
Placental and milk transfer of momelotinib and its metabolites were not studied. In the PPND study, momelotinib and its metabolites were found in the plasma of the pups, suggesting that momelotinib is secreted in milk.
Momelotinib was moderately metabolised in liver microsomes and in hepatocytes from humans, mice, rats, and dogs. The primary metabolism pathways were oxidation and hydrolysis following a single oral administration of ^{14}C-momelotinib in all three nonclinical species. There were no unique human metabolites. Thiocyanate is generated in rats and dogs as a consequence of hydrolysis of momelotinib to M19. M19 is a major metabolite in animals, but a minor metabolite in humans. Clinically relevant thiocyanate plasma levels were not detected in humans. The pharmacological activity of M21 is similar to momelotinib and its toxicity is adequately assessed in nonclinical species.
In mice, rats, and dogs, ^{14}C-momelotinib-related radioactivity was excreted predominantly in faeces (≥70% of dose), similarly to humans (69.3% via faeces).

5.3 Toxicology

The applicant conducted the toxicological evaluation of momelotinib dihydrochloride salt by single-dose and repeat-dose administration in mice, rats, rabbits, and dogs. Repeat-dose oral administration studies were conducted in mice (up to 56 days with 14-day recovery period), once daily or twice daily (BID) for up to 26 weeks in Sprague Dawley rats (with10-week recovery), once daily for 7 days in New Zealand White (NZW) nonpregnant rabbits, and once daily or BID for up to 39 weeks in beagle dogs (with a 6-week recovery period). The oral route of administration and the duration of the studies in rodents and non-rodents support the clinical use. Mortality was observed in all species or animals had to be prematurely terminated, mostly because of weakness and debilitation and/or clinical signs of continued inappetence, thin appearance, reduced activity, and weight loss.
Momelotinib treatment resulted in a dose-dependent reduction of body weight gain in all species. The main target organs for toxicity were the haematopoietic system and the reproductive organs. In all species, momelotinib treatment was associated with a reduction in red blood cell count, haemoglobin, and haematocrit, as well as a lower white blood cell count, which correlated with dose-related cellular depletion in the bone marrow and lymphoid depletion in the spleen, lymph nodes, thymus, and/or gut-associated lymphoid tissue. There was a trend to recovery from the cellular and lymphoid depletion in the off-dose period. These findings are consistent with the pharmacological activity of momelotinib on Janus kinases involved in haematopoiesis and immune response. No infections were identified in the nonclinical species, although in the clinical trials with momelotinib, infection was a very common adverse reaction, in line with the class effect reported with other JAK inhibitors.
Cataracts were observed in the 39-week study in dogs at 50 mg/kg/day (approx. 1-fold human unbound AUC) and were still present after the recovery period. The clinical relevance of this finding is unknown. In the 26-week study in rats, minimal renal tubular degeneration/regeneration was observed with NOAEL at doses corresponding to 4.5-fold human exposure based on free AUC.

Momelotinib (dihydrochloride salt) was not genotoxic. There were no momelotinib-related neoplasms in animals administered up to 100 mg/kg/day in the 26-week transgenic mouse carcinogenicity study. In the 104-week rat carcinogenicity study, in which rats were treated with either momelotinib (up to 15 mg/kg/day) or with momelotinib (5 mg/kg/day) and M21 (25 mg/kg/day), a momelotinib-related increased incidence of testicular interstitial (Leydig) cell adenoma was observed. This effect is related to the JAK2-mediated inhibition of prolactin signalling pathways in rats and therefore irrelevant for

humans. However, JAK inhibitors carry a risk of carcinogenicity, which is followed by the pharmacovigilance department.

In the fertility and early embryonic development study in rats, momelotinib irreversibly affected male and female reproductive system at ≥ 25 mg/kg/day in a dose-dependent manner. The NOAEL for males and the NOEL for early embryonic development was 5 mg/kg/day, which corresponds to a safety margin of 1-fold based on free AUC in humans at the therapeutic dose.
Momelotinib exerted embryo-fetal toxicity in embryo-fetal growth and development studies in rats and rabbits (no safety margin). JAK2 is involved in embryonal development. Given the known class effects of other marketed JAK inhibitors, momelotinib is to be contra-indicated in pregnancy.
In a pre- and post-natal development study momelotinib maternal toxicity and embryotoxicity was observed at ≥6 mg/kg/day. Pup survival was reduced from birth to weaning by 15% and 11% in pups from the dams administered 6 and 12 mg/kg/day, respectively. This finding was considered a direct effect on the offspring via exposure through the milk. In the post-weaning F1 generation, there were no momelotinib-related clinical findings or effects on any of the developmental landmarks or neurobehavioral parameters. The exposure at NOAEL was lower than the AUC observed at the recommended dose of 200 mg daily. Considering that exposure to momelotinib through the milk was observed at clinically relevant exposure levels and the proven toxic profile of approved JAK inhibitors, momelotinib is contraindicated during breast-feeding.
In a study with juvenile rats treated orally from post-natal day 7 to 21 with up to 30 mg/kg/day, no additional clinical signs were observed in juvenile animals except for a reversible deficit in learning in males. The NOAEL for juvenile toxicity was 3 mg/kg/day (no safety margin).

No immunotoxicology or immunophenotyping studies were conducted with momelotinib as immune suppression is an expected pharmacological effect of JAK inhibitors. This is acceptable.
Impurities are controlled by the toxicity studies, QSAR analysis, and literature. There are no concerns with regard to the excipients.

The submitted ERA is incomplete; an updated assessment is requested as a post-approval requirement.

The Nonclinical Safety Specifications in the RMP adequately address the nonclinical findings and their relevance for clinical use.

5.4 Nonclinical conclusions

The pharmaco-toxicological profile of momelotinib is considered sufficiently characterised. The submitted nonclinical data support the approval of Omjjara in the proposed indication. The identified safety concerns in pharmacologically relevant animal species relate to the haematopoietic system and to reproduction. The relevant information has been included in the Information for healthcare professionals.

6 Clinical aspects

6.1 Clinical pharmacology

The evaluation of the clinical pharmacology data of this application has been carried out in reliance on a previous regulatory decision by the US FDA. The available assessment reports and the Information for healthcare professionals from the US FDA were used as a basis for the clinical pharmacology evaluation. For further details concerning clinical pharmacology, please see section 8 of this report.

6.2 Dose finding and dose recommendation

Overall, 4 clinical studies conducted in patients with PMF or post PV/ET MF and healthy subjects contributed to the selection of the dose for the pivotal study. In addition, supportive exposure-response analyses were submitted. However, these were based on studies which had used no other dosage than 200 mg once daily (QD). Despite this limitation, the dose finding based on 4 Phase 1 and 2 studies and leading to the proposed dosage of 200 mg QD momelotinib (MMB), which was subsequently used in 3 Phase 3 studies, including the pivotal MOMENTUM study, was considered acceptable.

6.3 Efficacy

The pivotal double-blind, randomised Phase 3 MOMENTUM study was conducted in symptomatic and anaemic (haemoglobin <10 g/dl) patients with MF, who had received prior JAK inhibitor (JAKi) therapy. While all patients had received prior therapy with ruxolitinib, 3.6% of patients had also been treated with fedratinib. In total 195 patients were randomly assigned 2:1 to either 200 mg QD MMB or 300 mg twice daily (BID) danazol (DAN). Following the 24-week double-blind treatment phase, all patients received open-label MMB.

The median age of patients was 71 years (range 38 to 86 years); 79% were 65 years or older, and 63% were male. Sixty-four percent had PMF, 19% had post-PV MF, and 17 % had post-ET MF. While 5% of patients had intermediate-1 risk MF, 57% had intermediate-2 risk, and 35% high-risk MF. All patients had a symptomatic MF at screening, with a total symptom score (TSS) ≥10 based on Myelofibrosis Symptom Assessment Form (MFSAF) v4.0; the average TSS at baseline was 27. Median haemoglobin at baseline was 8 g/dl; 79% of patients had received red blood cell transfusions within 8 weeks prior to entering the study. Median platelet count at baseline was 96 × 10^9/l.

The MOMENTUM study met its first primary endpoint, demonstrating a statistically significant improvement in the TSS response rate at Week 24, i.e. the proportion of patients whose TSS decreased (improved) by at least 50% compared to baseline: 25% (95% CI: 17, 33) in the MMB arm vs 9% (95% CI: 3, 19) in the DAN arm; the treatment difference was 16% (95% CI: 6, 26).

Noninferiority could be demonstrated for the second primary endpoint of transfusion independency rate at Week 24, defined as the absence of any red blood cell transfusions along with a haemoglobin level of at least 8 g/dl during the 12-week interval prior to Week 24. The delta for noninferiority was 14% (95% CI: 2, 25); the transfusion independency rate increased from 13% at baseline to 30% at Week 24 in the MMB treatment arm, and from 15% at baseline to 20% at Week 24 in the DAN treatment arm.

In addition, a statistically significant higher proportion of patients in the MMB group vs DAN treatment had no need to receive any transfusion units during treatment and up to Week 24 (35% vs 17%, respectively), which was a secondary efficacy endpoint.

6.4 Safety

The safety pool is comprised of 725 patients who were treated with MMB monotherapy for MF. The most common adverse events were infections (55.4%), haemorrhages (29%), diarrhoea (26.8%), thrombocytopenia (25%), nausea (19.4%), fatigue (17.5%), cough (17.4%), dizziness (15.4%), peripheral neuropathy (14.6%), abdominal pain (14.1%), headache (13.9%), and asthenia (13.2%). Thrombocytopenia was the most common adverse event of ≥ Grade 3 (16.4%), and is an AE related to the mechanism of action of JAKi. It was also the most frequent AE leading to discontinuation of treatment.

Infections included serious and fatal bacterial and viral infections, mainly due to COVID-19. Haemorrhages included 5 serious gastro-intestinal haemorrhages in patients treated with MMB. Peripheral neuropathy included a significant proportion of cases that were irreversible/unresolved by the time of study cut-off. Peripheral neuropathy is considered an adverse reaction of MMB, which is supported by pertinent findings in preclinical (slowing of nerve conduction velocity in rats) and exposure-response analyses (trend for higher incidence of any grade peripheral neuropathy at higher MMB exposure).

Notably, MMB carries a significant risk of hepatocellular drug-induced liver injury (DILI) in MF patients, and increased transaminases have been commonly reported in patients treated with MMB.

6.5 Final clinical benefit-risk assessment

MF-associated anaemia can be debilitating, represents a significant burden to patients, and is frequently associated with a need for red blood cell transfusions and transfusion dependency. Therefore, improving MF-associated anaemia and related symptoms is of clinical relevance.

Non-haematologic toxicities reported on MMB treatment were mainly known JAKi class effects. Haematological toxicities on MMB treatment included thrombocytopenia, which could result in early treatment discontinuations. However, patients with low platelet counts were also treated in the MOMENTUM study, and few serious bleeding adverse events were reported. One of the notable toxicities is peripheral neuropathy, which was generally of low grade but irreversible or reported as ongoing in a substantial proportion of patients. Overall, the observed safety profile is considered manageable and acceptable for the indication, and is adequately labelled in the Information for healthcare professionals.

Considering the unmet medical need for the management of MF-associated anaemia, and based on the consistent anti-anaemic effects of MMB and the manageable safety profile, the benefit-risk balance was considered positive for the approved indication (*in German*):

Omjjara als Monotherapie ist indiziert zur Behandlung der primären Myelofibrose, der Myelofibrose nach Polycythaemia vera oder der Myelofibrose nach essentieller Thrombozythämie mit intermediärem oder hohem Risiko bei Erwachsenen mit moderater oder schwerer Anämie, die vorgängig mit Ruxolitinib behandelt wurden oder für eine Behandlung mit Ruxolitinib nicht in Frage kommen, und die nicht für eine allogene Stammzelltransplantation vorgesehen sind (siehe "Klinische Wirksamkeit").

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Omjjara was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.