Swiss Summary of the Risk Management Plan (RMP)
for

Omjjara

(Momelotinib)

RMP Summary:	Version 1
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The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.

The RMP summary of Omjjara is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the “Arzneimittelinformation / Information sur le médicament” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Omjjara in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic.

GlaxoSmithKline AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Omjjara.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for Omjjara (momelotinib)

This is a summary of the risk management plan (RMP) for momelotinib. The RMP details important risks of Omjjara, how these risks can be minimised, and how more information will be obtained about risks and uncertainties (missing information).

The Omjjara Summary of Product Characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals and patients on how the product should be used.

This summary of the RMP for momelotinib should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current risks will be included in updates of the RMP for momelotinib.

1. The medicine and what it is used for

Omjjara is indicated for the treatment of disease-related splenomegaly or symptoms, and moderate to severe anaemia in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis, who are Janus Associated Kinase (JAK) inhibitor naïve or have been treated with a JAK inhibitor (see SmPC for the full indication). Omjjara contains momelotinib dihydrochloride monohydrate as the active substance and it is given by the oral route.

Further information about the evaluation of the benefits can be found in Omjjara EPAR, including in its plain language summary, available on the EMA website, under medicine's webpage.

2. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of momelotinib, together with measures to minimise such risks are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions and advice on correct use, in the PL and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size - the amount of medicine in a pack is chosen to ensure

that the medicine is used correctly;

- The medicine's legal status - the way a medicine is supplied to the patient (e.g., with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation measures*.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including periodic safety update report assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A. List of important risks and missing information

Important risks of Omjjara are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Omjjara. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not yet been established and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., use of the medicine in children or adolescents).

List of Important Risks and Missing Information	
Important Identified Risk:	Serious Infections
Important Potential Risks:	Major Adverse Cardiovascular Events (MACE)
	Thromboembolism
	Secondary Malignancies
Missing Information:	None

II.B. Summary of important risks

Important Identified Risk: Serious Infections	
Evidence for linking the risk to the medicine	In animal studies, haematologic findings at all dose levels included dose-dependent decreases in white blood cell counts. In the integrated analysis, during RT, serious infections were higher in the momelotinib group compared to the ruxolitinib group. The danazol group had the highest rate of serious infections (9.8% momelotinib, 4.6% ruxolitinib, 16.9% danazol), but had no fatal infections (2.2% momelotinib, 1.1% ruxolitinib, 0 danazol). The most reported serious infection across groups was pneumonia (2.2% momelotinib, 1.1% ruxolitinib, 9.2% danazol). Grade 3, grade ≥ 3, and serious infections were all ≥ 5 percentage points higher for momelotinib over ruxolitinib and for danazol over momelotinib. Further, an imbalance in COVID-19 events in the momelotinib group was noted. Therefore, the risk of serious infections is considered an important identified risk for momelotinib.
Risk factors and risk groups	Immunocompromised individuals, including MF patients as well as the elderly population are at risk for infections including COVID-19 infections (Barbui, 2021).
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 4.8 SmPC section 4.4 – recommendations on patient selection, patient observation, and initiating treatment promptly. PL sections 2 and 4 Legal status: Prescription only medicine Additional risk minimisation measures**:** None

Important Potential Risk: MACE	
Evidence for linking the risk to the medicine	In a large randomised active-controlled study of tofacitinib (another JAK inhibitor) in rheumatoid arthritis patients 50 years and older with at least one additional cardiovascular risk factor, a higher rate of MACE, defined as cardiovascular death, non-fatal myocardial infarction (MI) and non-fatal stroke, was observed with tofacitinib compared to TNF inhibitors. Events of MACE have been reported in patients receiving JAK inhibitors, however, a causal relationship has not been established for momelotinib. In momelotinib clinical trials with MF, event rates for MACE decreased from momelotinib RT to open-label treatment (from 9.2 to 5.8 events per 100 person-years), suggesting no cumulative toxicity of treatment.
Risk factors and risk groups	Patients with MF are at an increased risk of other comorbidities such as cardiovascular disease.
Risk minimisation measures	Routine risk minimisation measures: Prior to initiating or continuing therapy with momelotinib, the benefits and risks for the individual patient should be considered, particularly in patients 65 years of age and older, patients who are current or past long-time smokers, and patients with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors. SmPC section 4.4 - recommendation on patient selection Legal status: Prescription only medicine Additional risk minimisation measures**:** None

Important Potential Risk: Thromboembolism	
Evidence for linking the risk to the medicine	In a large randomised active-controlled study of tofacitinib (another JAK inhibitor) in rheumatoid arthritis patients 50 years and older with at least one additional cardiovascular risk factor, a dose dependent higher rate of venous thromboembolic events (VTE) including deep venous thrombosis (DVT) and pulmonary embolism (PE) was observed with tofacitinib compared to TNF inhibitors. Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving JAK inhibitors, however, a causal relationship has not been established for momelotinib. In momelotinib clinical trials with MF, event rates for thromboembolism decreased from momelotinib RT to open-label treatment (from 11.9 to 6.7 events per 100 person years), suggesting no cumulative toxicity of treatment.
Risk factors and risk groups	Given the median age of MF diagnosis as well as the pathophysiology of the underlying disease, patients with MF are at an increased risk of other comorbidities such as thromboembolic disease.

Risk minimisation measures	Routine risk minimisation measures: Prior to initiating or continuing therapy with momelotinib, the benefits and risks for the individual patient should be considered, particularly in patients with cardiovascular factors. In patients with known VTE risk factors other than cardiovascular or malignancy risk factors, momelotinib should be used with caution. VTE risk factors other than cardiovascular or malignancy risk factors include previous VTE, patients undergoing major surgery, immobilisation, use of combined hormonal contraceptives or hormone replacement therapy, and inherited coagulation disorder. Patients should be re-evaluated periodically during momelotinib treatment to assess for changes in VTE risk. Promptly evaluate patients with signs and symptoms of VTE and discontinue momelotinib in patients with suspected VTE, regardless of dose. SmPC section 4.4 - recommendation on patient selection Legal status: Prescription only medicine Additional risk minimisation measures**:** None

Important Potential Risk: Secondary Malignancies	
Evidence for linking the risk to the medicine	In a large randomised active controlled study of tofacitinib (another JAK inhibitor) in rheumatoid arthritis patients 50 years and older with at least one additional cardiovascular risk factor, a higher rate of malignancies, particularly lung cancer, lymphoma and non-melanoma skin cancer (NMSC) was observed with tofacitinib compared to TNF inhibitors. Lymphoma and other malignancies have been reported in patients receiving JAK inhibitors, however, a causal relationship has not been established for momelotinib.
Risk factors and risk groups	Given the median age of MF diagnosis, patients with MF are at an increased risk of secondary malignancies.
Risk minimisation measures	Routine risk minimisation measures: Prior to initiating or continuing therapy with momelotinib, the benefits and risks for the individual patient should be considered, particularly in patients 65 years of age and older, and patients who are current or past long-term smokers. SmPC section 4.4 - recommendation on patient selection Legal status: Prescription only medicine Additional risk minimisation measures**:** None

II.C. Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Omjjara.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Omjjara.