Swiss Summary of the Risk Management Plan (RMP)

Version 5 (04 March 2025)

Skyrizi® (Risankizumab)

150 mg solution for injection in pre-filled pen

75 mg and 150 mg solution for injection in pre-filled syringe

600 mg concentrate for solution for infusion

180 mg and 360 mg solution for injection in a cartridge for a dose dispenser

Based on Core/EU RMP version 5.3 (23 May 2024)

MA holder: AbbVie AG

Alte Steinhauserstrasse 14, 6330 Cham, Switzerland

Disclaimer

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 minimise them.
The RMP summary of SKYRIZI® 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 SKYRIZI® in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. AbbVie AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of SKYRIZI®.

Part VI: Summary of the Risk Management Plan

Summary of risk management plan for Skyrizi® (risankizumab)

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

Skyrizi's summary of product characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals and patients on how Skyrizi should be used.

This summary of the RMP for Skyrizi 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 are part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Skyrizi's RMP.

I The Medicine and What it Is Used For

Skyrizi is authorized for treatment of

- Moderate to severe plaque psoriasis in adults
- Psoriatic arthritis alone or in combination with methotrexate in adults
- Moderately to severely active Crohn's disease in adults
- Moderately to severely active ulcerative colitis (UC) in adults

See the SmPC for the full indication statements. Skyrizi contains risankizumab as the active substance and is given by subcutaneous (SC) injection and IV infusion.

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

II Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of Skyrizi, together with measures to minimize such risks and the proposed studies for learning more about Skyrizi's risks, are outlined below.

Measures to minimize 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 authorized pack size – the amount of medicine in a pack is chosen so 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 minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed so that immediate action can be taken, as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Skyrizi is not yet available, it is listed under "missing information" below.

II.A List of Important Risks and Missing Information

Important risks of Skyrizi are risks that need special risk management activities to further investigate or minimize 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 Skyrizi. 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 been established yet 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., on the long-term use of the medicine).

List of Important Risks and Missing Information	
Important identified risks	None
Important potential risks	• Major adverse cardiac events (MACE) • Serious infections • Malignancies • Serious hypersensitivity reactions
Missing information	• Use during pregnancy and lactation • Long-term safety

II.B Summary of Important Risks

Important identified risk: None	
Important potential risk 1: MACE	
Evidence for linking the risk to the medicine	Adjudicated MACE in the integrated risankizumab clinical trial was used to assess the risk with risankizumab therapy.
Risk factors and risk groups	Patients with traditional cardiac risk factors, i.e., age, sex, family history of premature coronary artery disease (CAD), current smoking, hypertension (HTN), low high-density lipoprotein, are at higher risk of CAD. Other risk factors include DM (insulin resistance, hyperinsulinemia, and elevated blood glucose are associated with atherosclerotic cardiovascular disease [CVD]) (Almdal 2004, Gerstein 1999, Kannel 1979a, Kannel 1979b, Zavaroni 1989), chronic kidney disease (increased coronary heart disease [CHD] risk in patients with end-stage renal disease has been well described, but there is now clear evidence that mild to moderate renal dysfunction is also associated with a substantial increase in CHD risk) (Gansevoort 2013), other lifestyle factors (lack of exercise, psychosocial factors), and metabolic syndrome.
Risk minimization measures	Routine risk minimization measures: No specific measures are required for patients receiving risankizumab; standard of care is adequate.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Long-Term Prospective Cohort Study in Patients with Psoriasis in Real World Setting • Risankizumab Psoriasis Long-Term Extension Study LIMMITLESS • Risankizumab Psoriatic Arthritis Studies KEEPsAKE 1 and KEEPsAKE 2 • Long-Term Comparative Cohort Study in Patients with Crohn's Disease in a Real World Setting See Section II.C of this summary for an overview of the post-authorization development plan.

Important potential risk 2: Serious infections	
Evidence for linking the risk to the medicine	As with many immune-modulating agents, risankizumab may impair immune function, resulting in a risk of serious infection. In patients with psoriasis not treated with biologics, the incidence rates of serious infections ranged from approximately 0.3 to 2.1 per 100 PY (Gottlieb 2014, Reich 2015). In patients with psoriatic arthritis, the incidence rate of serious infections was (3.98 events per 100 PY) (Shah 2017). Among patients with inflammatory bowel disease (IBD), including CD and UC, the incidence rate (per 100 PY) was 0.94 for serious infections (Kirchgesner 2018). Integrated risankizumab clinical trial data were used to assess the risk with risankizumab therapy, and epidemiologic data were used to contextualize the risankizumab data.
Risk factors and risk groups	The elderly and patients with other risk factors compromising immunity such as diabetes or chronic renal insufficiency are at increased risk.
Risk minimization measures	Routine risk minimization measures: Product labeling
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Long-Term Prospective Cohort Study in Patients with Psoriasis in Real World Setting • Risankizumab Psoriasis Long-Term Extension Study LIMMITLESS • Risankizumab Psoriatic Arthritis Studies KEEPsAKE 1 and KEEPsAKE 2 • Long-Term Comparative Cohort Study in Patients with Crohn's Disease in a Real World Setting See Section II.C of this summary for an overview of the post-authorization development plan.
Important potential risk 3: Malignancies	
Evidence for linking the risk to the medicine	Integrated risankizumab clinical trial data were used to assess the risk with risankizumab therapy.
Risk factors and risk groups	Multiple factors may contribute to an increased rate of malignancy in patients with psoriasis, Crohn's Disease, and/or UC, including the effects of immunosuppressive or immunomodulatory therapies. Psoralen and ultraviolet A, when given long-term, is associated with increased risks of cutaneous squamous cell carcinoma and malignant melanoma. Reviews of studies on ultraviolet B, both narrowband and broadband, do not indicate any increased risk of non-melanoma skin cancer or melanoma (Patel 2009). The traditional systemic therapies, methotrexate, cyclosporine A, and mycophenolate mofetil, may be associated with an increased risk of lymphoproliferative disorders during treatment, demonstrated in clinical trials in patients with rheumatoid arthritis and Crohn's disease documented in case reports concerning psoriasis patients The risk of malignancy with biologic therapy is still unclear. However, the majority of the studies examining this carcinogenic risk suggest that tumor necrosis factor alpha inhibitors may cause a slightly increased risk of cancer, including non-melanoma skin cancer and hematologic malignancies.

Risk minimization measures	Routine risk minimization measures: No specific measures are required for patients receiving risankizumab; standard of care is adequate.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Long-Term Prospective Cohort Study in Patients with Psoriasis in Real World Setting • Risankizumab Psoriasis Long-Term Extension Study LIMMITLESS • Risankizumab Psoriatic Arthritis Studies KEEPsAKE 1 and KEEPsAKE 2 • Long-Term Comparative Cohort Study in Patients with Crohn's Disease in a Real World Setting See Section II.C of this summary for an overview of the post-authorization development plan.
Important potential risk 4: Serious hypersensitivity reactions	
Evidence for linking the risk to the medicine	The risk varies depending on the biologic used and is reflected in the individual biologic labels. Integrated risankizumab clinical trial data were used to assess the risk with risankizumab therapy.
Risk factors and risk groups	Several factors influence the propensity towards development of hypersensitivity reactions including degree of humanization of the antibody, cell line from which the drug is obtained (Chinese hamster ovary [CHO] cells produce virtually no 1,3-galactosyltransferase, resulting in a glycosylation pattern much different from that of other drugs such as cetuximab [derived from the murine cell line SP2/O], thereby reducing the risk of hypersensitivity reactions) and the excipients used (Corominas 2014). Host factors include the indication for the treatment (e.g., atopic tendencies in patients with asthma), patient's immune status, concomitant medications.
Risk minimization measures	Routine risk minimization measures: Product labeling
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Long-Term Prospective Cohort Study in Patients with Psoriasis in Real World Setting • Risankizumab Psoriasis Long-Term Extension Study LIMMITLESS • Risankizumab Psoriatic Arthritis Studies KEEPsAKE 1 and KEEPsAKE 2 • Long-Term Comparative Cohort Study in Patients with Crohn's Disease in a Real World Setting See Section II.C of this summary for an overview of the post-authorization development plan.

Missing information 1: Use during pregnancy and lactation	
Risk minimization measures	Routine risk minimization measures: Product labeling
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Pregnancy Exposure and Outcomes for Women with Psoriasis Treated with Risankizumab • Pregnancy Exposure and Outcomes for Women with Crohn's Disease Treated with Risankizumab See Section II.C of this summary for an overview of the post-authorization development plan.

Missing information 2: Long-term safety	
Risk minimization measures	Routine risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Risankizumab Psoriasis Long-Term Extension Study LIMMITLESS • Long-Term Prospective Cohort Study in Patients with Psoriasis in Real World Setting • Risankizumab Psoriatic Arthritis Studies KEEPsAKE 1 and KEEPsAKE 2 • Long-Term Comparative Cohort Study in Patients with Crohn's Disease in a Real World Setting See Section II.C of this summary for an overview of the post-authorization development plan.

II.C Post-Authorization Development Plan

II.C.1 Studies Which are Conditions of the Marketing Authorization

There are no studies which are conditions of the marketing authorization or specific obligation of Skyrizi.

II.C.2 Other Studies in Post-Authorization Development Plan

Long-Term Prospective Cohort Study in Patients with Psoriasis in Real World Setting

A prospective cohort study of population-based patients in the real-world is being conducted to monitor the incidence of safety outcomes coincident with exposure to risankizumab in patients with psoriasis (which includes patients with arthropathic psoriasis [ICD-10-CM L40.5x]) in two European national registers with linkage data from national quality registers. The aim of Study P19-633 is to estimate the risks of overall malignancy excluding NMSC, NMSC, MACE, serious infections, and serious hypersensitivity reactions among individuals who were exposed to risankizumab for the treatment of psoriasis, relative to similar patients on other systemic treatments (biologics and non-biologics). In addition, a separate cohort study will be conducted (synopsis below) to assess pregnancy exposures and outcomes utilizing large electronic healthcare databases with mother-baby linkage in the United States.

Pregnancy Exposure and Outcomes in Women with Psoriasis Treated with Risankizumab

A population-based, non-interventional, cohort study of women with moderate-to-severe psoriasis (which includes patients with arthropathic psoriasis [ICD-10-CM L40.5x]) who are exposed to risankizumab or comparator biologic during pregnancy is ongoing. The specific objectives of Study P16-751 are (1) to evaluate the rate of major congenital malformations in infants born to women exposed to risankizumab during pregnancy compared to those exposed to comparator treatments (primary outcome for sample size estimation); (2) to evaluate and compare pregnancy outcomes (i.e., live birth, spontaneous abortion, elective abortion, stillbirth) among women exposed to risankizumab versus comparators during pregnancy; and (3) to assess and compare additional infant outcomes (premature birth, small for gestational age, neonatal deaths, serious infections up to 6 months of age) among infants born to women exposed to risankizumab during pregnancy compared to those exposed to other biologic treatments. Adult women of child-bearing years with moderate-to-severe psoriasis will serve as the study population. There will be 3 specific cohorts of women included in this study: 1) women exposed to risankizumab but not exposed to other biologic therapies at any time during pregnancy (risankizumab-exposed cohort); 2) women exposed to an anti-TNF, IL-17 biologics or their biosimilars for moderate-to-severe psoriasis at any time during pregnancy (comparator biologic-exposed cohort); and, 3) women with psoriasis who received no psoriasis therapy, or treatment for psoriasis other than risankizumab or comparator biologics (e.g., phototherapy or nonbiologic therapy).

This untreated psoriasis group was chosen to serve as a frame of reference and provide context to the rates of outcomes observed in the risankizumab-exposed and comparator biologic-exposed groups. This study will be conducted using administrative claims data in the Innovation in Medical Evidence Development and Surveillance System (IMEDS) Distributed Databases (IMEDS-DD).

Risankizumab Long-Term Extension Study (Psoriasis)

A multicenter, open-label study assessing the long-term safety and efficacy of risankizumab in subjects with moderate to severe plaque psoriasis is ongoing. The primary objective of Study M15-997 is to investigate long-term safety (including the safety concerns e.g., MACE, malignancies, serious infections and serious hypersensitivity reactions) and tolerability of risankizumab in subjects with psoriasis who have completed one of the preceding Phase 2/3 studies. The secondary objective of Study M15-997 is to investigate the long-term efficacy of risankizumab in the treatment of psoriasis.

Risankizumab Psoriatic Arthritis Studies

Study M15-998 is a 2-part, multicenter study assessing the long-term safety and efficacy of risankizumab in subjects with moderately to severely active psoriatic arthritis who have a history of inadequate response or intolerance to at least 1 disease-modifying anti-rheumatic drug or to biologic therapy(ies). The primary objective of the open-label period of the study is to evaluate the long-term safety, tolerability, and efficacy of risankizumab 150 mg in subjects who have completed the double-blind period of the study.

Study M16-011 is a 2-part, multicenter study assessing the long-term safety and efficacy of risankizumab with moderately to severely active psoriatic arthritis who have a history of inadequate response to or intolerance to at least 1 disease-modifying antirheumatic drug therapy. The primary objective of the open-label period of the study is to evaluate the long-term safety, tolerability, and efficacy of risankizumab 150 mg in subjects who have completed the double-blind period of the study.

Pregnancy Exposure and Outcomes for Women with Crohn's Disease Treated with Risankizumab

AbbVie proposes to add the UC study population to planned Study P23-653 once the study protocol has been approved for CD and procedure MEA009 has concluded.

Study Short Name and Title: Pregnancy exposures and outcomes in women with Crohn's disease treated with risankizumab: A Cohort Study Utilizing Large Electronic Healthcare Databases with Mother-Baby Linkage in the United States (Study P23-653)

Rationale and Study Objectives: The clinical trial programs did not assess the safety of risankizumab use during pregnancy. In addition to the study of risankizumab exposure in psoriasis patients, a study of pregnancy outcomes in patients with Crohn's disease who are exposed to risankizumab, compared to alternative biologic treatments, will be conducted.

Study Design: A comparative cohort study will be conducted to describe risankizumab exposure in pregnant patients with Crohn's disease, and compare pregnancy and infant outcomes to pregnant patients with Crohn's disease who were treated with alternative therapies. In addition, descriptive analyses of pregnancy outcomes in Crohn's disease patients without exposure to any treatments under investigation will also be conducted.

Study Population: Women of child-bearing age with Crohn's disease will comprise the study population. Patients (with age per labeled indication) who have filled at least one prescription for risankizumab or comparator treatment and are considered to be exposed to treatment during pregnancy will be included in the study. The study will be conducted within the network of administrative claims data with mother-baby linkage within the FDA Sentinel Distributed Database.

Long-Term Comparative Cohort Study in Patients with Crohn's Disease in a Real World Setting

AbbVie proposes to add the UC study population to planned Study P23-654 once the study protocol has been approved for CD and procedure EMEA/H/C/004759/MEA/010 has concluded.

Study Short Name and Title: A comparative cohort study of long-term safety of risankizumab in patients with Crohn's disease (Study P23-654)

Rationale and Study Objectives: The clinical trial program was not able to fully characterize the safety profile of risankizumab in the Crohn's disease population. Additional long-term data are needed from the real-world experience of patients with Crohn's disease treated with risankizumab to assess product potential risks.

Study Design: A comparative cohort study will be conducted to estimate rates of malignancy (malignancy excluding NMSC, NMSC), serious infections, serious hypersensitivity reactions, and MACE in risankizumab treated patients with Crohn's disease, relative to alternative systemic therapies (e.g., biologics). The study will be conducted within the Swedish Inflammatory Bowel Disease Register (SWIBREG) in Sweden and the National Registers within Sweden and Denmark. Validated disease and outcome definitions, and appropriate methods for confounding control will be utilized.

Study Population: All patients with Crohn's disease (with age per labeled indication) who have filled at least one prescription for risankizumab or comparator treatment will be identified in the data source after a specified start date and included in the study.