OMVOH®

(mirikizumab)

Omvoh® 300 mg concentrate for solution for infusion

Omvoh® 100 mg solution for injection in prefilled syringe/prefilled pen

Summary of Risk Management Plan (RMP)

Summary of the risk management plan (RMP) for Omvoh (mirikizumab)
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 Omvoh 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 medicament“ 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 Omvoh in Switzerland is the „Arzneimittelinformation/ Information sur le médicament“ (see www.swissmedicinfo.ch) approved and authorized by Swissmedic.
Eli Lilly is fully responsible for the accuracy and correctness of the content of this published summary RMP of Omvoh.

I. The Medicine and What It Is Used For

Mirikizumab is indicated for ulcerative colitis (UC) (see SmPC for the full indication). Mirikizumab is the active substance, and it is given by IV infusion (after dilution) and by subcutaneous injection.

Further information about the evaluation of mirikizumab's benefits can be found in mirikizumab's European Public Assessment Report, including in it's plain-language summary, available on the European Medicines Agency website, under the medicine's webpage.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

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

Measure to minimise the risks identified for medicinal products can be specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and health care professionals.

This constitutes *routine risk minimisation* measure.

In addition to this measure, 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. This measure constitutes *routine pharmacovigilance activities.*

II.A. List of Important Risks and Missing Information

Important risks of mirikizumab 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 mirikizumab. 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	• Serious infections • Severe liver injury • Malignancies • MACE
Missing information	• Safety of mirikizumab in pregnant women and lactating women

Abbreviation: MACE = major adverse cardiac event.

II.B. Summary of Important Risks

Important potential risk: Serious infections	
Evidence for linking the risk to the medicine	In patients with UC across the Phase 2 and Phase 3 studies, serious infections (n = 33, 2.3%) were reported commonly during treatment with mirikizumab. When including time-off mirikizumab and the post-treatment follow-up period, serious infections (n = 39, 2.7%) were also reported commonly. Although the majority of patients recovered, serious infections due to coronavirus or COVID-19 infections resulted in the deaths of 3 patients with UC, 1 while receiving mirikizumab and 2 while off mirikizumab. Across all mirikizumab exposures in Phase 2 and Phase 3 clinical trials for UC, CD, and Ps, serious infections (n = 99, 2.6%) have been reported commonly during treatment with mirikizumab. When including time-off mirikizumab and the post-treatment follow-up time, serious infections (n = 108, 2.8%) were also reported commonly. Although the majority of patients recovered, serious infections due to COVID-19 or coronavirus infections or sequelae of COVID-19 infection resulted in the deaths of 7 patients, 5 patients while receiving mirikizumab and 2 patients while off mirikizumab. All deaths due to coronavirus or COVID-19 infection or sequelae of COVID-19 infection in the mirikizumab programme occurred early in the COVID-19 pandemic, prior to the availability of effective treatments and vaccinations. Furthermore, these patients with fatal COVID-19 infections were at increased risk for hospitalization, severe disease, and/or death due to COVID-19 based on one or more of the following criteria: age ≥65 years, BMI ≥25 kg/m^2, diabetes mellitus, cardiovascular disease, and/or arterial hypertension. None of these deaths from severe COVID-19/coronavirus infection or sequelae of COVID-19 infection were determined by the investigator or sponsor to be related to mirikizumab.
Risk factors and risk groups	Risk groups or specific risk factors for serious infections have not been identified from the clinical development programme. Due to the immunomodulatory effect of medicines in the anti-IL23 class, patients with evidence of untreated latent TB or other active, chronic, or recurrent infections or a history thereof may be at greater risk of reactivation or exacerbation of their underlying infection, even though this has not been reported in the mirikizumab clinical development programme.
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.3, Contraindications • SmPC Section 4.4, Special Warnings and Precautions for Use

	• PL Section 2 Additional risk minimisation measures: None proposed
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Observational Secondary Database Study to Assess the Long-Term Safety of Mirikizumab. See Section II.C of this summary for an overview of the post-authorisation development plan.
Important potential risk: Severe Liver Injury	
Evidence for linking the risk to the medicine	For the UC population exposed to mirikizumab in the Phase 2 and Phase 3 clinical trials, elevated ALT ≥5xULN and ≥10xULN were reported by 0.4 % and 0.1% of patients in the mirikizumab treatment group respectively. Elevated AST ≥5xULN and ≥10xULN were reported by 0.7% and 0.1% of patients in the mirikizumab treatment group respectively. For all mirikizumab exposures in Phase 2 and Phase 3 clinical trials for UC, CD, and Ps, elevated ALT and AST ≥10xULN was reported for each analyte in 0.1% of mirikizumab-treated patients. Most of these liver enzyme elevations/increases were considered mild to moderate in severity and 3 patients with Ps had AST and or ALT elevations that were reported as serious. None were associated with an adverse clinical outcome. Overall, 0.34% of patients discontinued due to a TEAE of liver enzyme elevation. Most recovered from the liver enzyme elevations while continuing on mirikizumab treatment and with no further adverse effects. One patient with UC met Hy's law criteria with a maximum ALT of 17.9xULN, maximum AST of 9.9xULN, and maximum bilirubin of 2.4xULN. This TEAE of "hepatic enzyme increased" was reported as moderate severity and as non-serious. As no alternative aetiology for LFT elevation could be determined, an association with mirikizumab treatment could not be excluded. Therefore, based on the potential of significantly elevated aminotransferases being indicative of possible severe liver injury, it is considered an important potential risk.
Risk factors and risk groups	In the UC, CD, and Ps programmes, no specific risk groups or specific risk factors have been identified, although concurrent use of alcohol and/or medications with a known risk of liver enzyme elevation or DILI may result in a higher frequency of liver enzyme elevations and possible liver injury. Additionally, clinical observations of transient elevations of liver enzymes with no known cause and persistent elevations most commonly due to PSC, AIH, cholelithiasis, and NAFLD, and some herbal, dietary, and traditional healing and supplemental products may also contribute to a higher frequency of liver enzyme elevations and possible liver injury. In the UC programme, no specific risk factors have been identified
Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.4, Special Warnings and Precautions for Use • SmPC Section 4.8, Undesirable Effects • PL Section 2 Additional risk minimisation measures: None proposed

Additional pharmacovigilance activities	Additional pharmacovigilance activities: Observational Secondary Database Study to Assess the Long-Term Safety of Mirikizumab. See Section II.C of this summary for an overview of the post-authorisation development plan.
Important potential risk: Malignancies	
Evidence for linking the risk to the medicine	There are theoretical considerations which could link the pharmacologic mode of action of mirikizumab to the development of tumours; however, the current clinical and non-clinical data do not suggest that mirikizumab causes malignant tumours or promotes tumour growth.
Risk factors and risk groups	No specific risk factors for malignancy in relation to treatment with mirikizumab have been identified.
Risk minimisation measures	None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Observational secondary database study to assess the long-term safety of mirikizumab. See Section II.C of this summary for an overview of the post-authorisation development plan.
Important potential risk: MACE	
Evidence for linking the risk to the medicine	There is no conclusive mechanism of action for cerebrocardiovascular disease with IL-23p19 inhibition. A risk may exist due to a therapeutically induced acute change in the immunologic environment, specifically inhibition of helper T cell sub-type 17, which may disrupt homeostasis between pro-atherogenic and protective effects. Because IL-23 plays a key role in maintaining homeostasis within the cerebrocardiovascular (CCV) system, it has been hypothesised that inhibition of IL-23 may result in pathogenic shifts which destabilise atherosclerotic plaques; however, clinical relevance of these hypotheses are uncertain.
Risk factors and risk groups	No specific risk factors for MACE in relation to treatment with mirikizumab have been identified.
Risk minimisation measures	None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Observational secondary database study to assess the long-term safety of mirikizumab. See Section II.C of this summary for an overview of the post-authorisation development plan.

Abbreviation: AIH = autoimmune hepatitis; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; CD = Crohn's disease; COVID-19 = coronavirus disease 2019; DILI = drug-induced liver injury; IL = interleukin; LFT = liver function test; MACE = major adverse cardiovascular event; n = number of patients in the specified category; NAFLD = non-alcoholic fatty liver disease; Ps = psoriasis; PSC = primary sclerosing cholangitis; SmPC = summary of product characteristics; TB = tuberculosis; TEAE = treatment-emergent adverse event; UC = ulcerative colitis; ULN = upper limit of normal.

Missing information: Safety of mirikizumab in pregnant women and lactating women	
Risk minimisation measures	Routine risk minimisation measures • SmPC Section 4.6, Fertility, Pregnancy, and Lactation • PL Section 2 Additional risk minimisation measures: None proposed
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Observational Secondary Database Cohort Study on Mirikizumab Exposure and Pregnancy See Section II.C of this summary for an overview of the post-authorisation development plan.

Abbreviation: PL = package leaflet; SmPC = summary of product characteristics.

II.C. Post-authorisation Development Plan

II.C.1. Studies that Are Conditions of the Marketing Authorisation

There are no studies that are conditions of the marketing authorisation or specific obligation of mirikizumab.

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

Study short name: Observational Secondary Database Cohort Study on Mirikizumab Exposure and Pregnancy.

Purpose of the study: Pregnant women were not included in the mirikizumab clinical development programme. However, the indicated population for mirikizumab of patients with UC includes women of childbearing age. Therefore, exposure to mirikizumab during pregnancy may occur during post-marketing setting. Although there were no mirikizumab-related adverse effects on embryo-foetal development, pregnancy outcome, and peri- and post-natal development in pregnant monkeys administered mirikizumab, effects on pregnancy and foetal or infant outcomes in humans have not been fully determined. Therefore, the purpose of this study is to determine the pregnancy, and foetal or infant outcomes among pregnant women with a diagnosis of UC who are exposed to mirikizumab.

The pregnancy, maternal and foetal or infant outcomes of interest include:

1. Pregnancy outcomes: recognized spontaneous abortions, stillbirths, elective terminations, and preterm delivery.
2. Foetal or infant outcomes: small for gestational age, and major and minor congenital malformations.

Study objectives

1. To monitor the use of mirikizumab among women of childbearing age.
2. To determine the incidence of pregnancy and foetal or infant outcomes among pregnant women with a diagnosis of UC who are exposed to mirikizumab during pregnancy.
3. If sufficient sample size of women exposed to mirikizumab during pregnancy and infants linked to the exposed pregnancies are identified, to compare the incidence of pregnancy and foetal or infant outcomes of pregnant women with a diagnosis of UC who are exposed to mirikizumab during pregnancy to pregnant women with a diagnosis of UC who are not exposed to mirikizumab and/or who are exposed to other medications indicated for the treatment of UC.

Study short name: Observational Secondary Database Study to Assess the Long-Term Safety of Mirikizumab.

Purpose of the study: Data from clinical trials demonstrate that mirikizumab is effective in the treatment of patients with moderate to severe UC. However, the long-term safety of mirikizumab exposure in terms of events with a low frequency and/or long latency among patients with ulcerative colitis in routine clinical practice has not been fully characterised.

Study Objectives

The objective of this study is to examine the incidence of severe liver injury, serious infections, including opportunistic infections, malignancies excluding non-melanoma skin cancer (NMSC), and MACE among patients with a diagnosis of UC who are exposed to mirikizumab compared to patients with UC who are not exposed to mirikizumab and/or who are exposed to other medications indicated for the treatment of UC in real world clinical practice in the US. The incidence of the study outcomes will also be examined among subgroups of interest including elderly patients 65 years of age and older.

Major Changes to the Risk Management Plan over Time

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This summary was last updated in 11-2023