ZILBRYSQ®

SUMMARY OF RISK MANAGEMENT PLAN

Version 1.0

Active substance(s) (INN or common name):	Zilucoplan
Product(s) concerned (brand name(s)):	ZILBRYSQ®
Marketing authorization holder:	UCB-Pharma AG
Version number :	1.0 (summary of EU RMP v0.4 , dated 15-Sep-2023)
Date of final sign off :	15-September-2023

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 Zilbrysq® 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 Zilbrysq® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. UCB-Pharma-AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Zilbrysq®.

Date: 10 October 2024 20241010rmp summary-v1.0-pxl-ch

Contents

PART I: THE MEDICINE AND WHAT IT IS USED FOR

Pharmaceutical form(s) and strength(s)	Current: Solution for injection in a pre-filled syringe. One mL contains 40mg of zilucoplan. There are 3 different dose presentations: • 0.416mL containing zilucoplan sodium equivalent to 16.6mg of zilucoplan (rubine red pre-filled syringe) • 0.574mL containing zilucoplan sodium equivalent to 23mg of zilucoplan (orange pre-filled syringe) • 0.810mL containing zilucoplan sodium equivalent to 32.4mg of zilucoplan (dark blue pre-filled syringe)
	Proposed: Not Applicable
Is/will the product be subject to additional monitoring in the EU?	Yes
Is/will the product be subject to additional monitoring in Switzerland ?	Yes

Zilbrysq is authorised as an add-on to standard therapy for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. It contains zilucoplan as the active substance (approximately 0.3mg/kg) and it is given by subcutaneous injection once daily.
Further information about the evaluation of Zilbrysq's benefits can be found in Zilbrysq's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: Zilbrysq | European Medicines Agency (EMA) (europa.eu)

PART II: RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERISE THE RISKS

Important risks of Zilbrysq, together with measures to minimize such risks and the proposed studies for learning more about Zilbrysq'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 package leaflet 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 so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute *routine risk minimization measures*.
In the case of Zilbrysq, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including periodic safety update report assessment 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 Zilbrysq is not yet available, it is listed under 'missing information' below.

2.1 List of important risks and missing information

Important risks of Zilbrysq 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 Zilbrysq. 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 (eg, on the long-term use of the medicine).

Table 2–1: List of important risks and missing information

Important identified risks	None
Important potential risks	*Neisseria* infections, particularly meningococcal infections
Missing information	Use during pregnancy and lactation Long-term safety

2.2 Summary of important risks and missing information

Table 2–2: Summary of important risks and missing information

Important potential risk: *Neisseria* infections, particularly meningococcal infections	
Evidence for linking the risk to the medicine	This important potential risk is based on zilucoplan mechanism of action, on experience with approved drugs with a similar mechanism of action eculizumab (Soliris®) and ravulizumab (Ultomiris®), evidence from patients with genetic complement deficiencies, and our understanding of the complement system.
Risk factors and risk groups	Main risk factors for meningococcal infections include: - Congenital immunodeficiency (Taha et al, 2021) - History of hemopoietic stem cell transplantation (Taha et al, 2021) - Acquired immunodeficiency disorders (Taha et al, 2021) - Human immunodeficiency virus (Taha et al, 2021) - Asplenia or hyposplenia (Taha et al, 2021) - Chronic liver disease (Taha et al, 2021) - Acute upper and lower respiratory tract infections (Taha et al, 2021; Spyromitrou-Xioufi et al, 2020) - History of severe chronic disorders: autoimmune disease, hemophilia (Taha et al, 2021) - Low income and living in a relatively socially deprived community were both associated with an increased risk of hospitalization for invasive meningococcal disease (Taha et al, 2021) - Debilitating disease (Taha et al, 2021) - Age: incident meningococcal infections cases was higher among aged 0-2 and 15-24 years old (Taha et al, 2021) - Household crowding (Spyromitrou-Xioufi et al, 2020) - Smoking exposure (Spyromitrou-Xioufi et al, 2020) - Close relationships (Spyromitrou-Xioufi et al, 2020) - Sexual relationships between men (Folaranmi et al, 2017) - Genetic deficiency or therapeutic inhibition of terminal complement (Hodeib et al, 2020) - Lack of vaccine coverage in the developing world: meningococcal vaccination plays a major role in the control of the disease (Shaker et al, 2018).

Table 2–2: Summary of important risks and missing information

	Main risk factors for gonococcal infections include: - Age (Gale et al, 2017; Mayor et al, 2012; Bjekic et al, 1997) - Gender (Gale et al, 2017) - Low education level (Bjekic et al, 1997) - Low socioeconomic status (Bjekic et al, 1997) - Multiple sexual partners (Dela et al, 2019; Mayor et al, 2012) - Alcohol use in males (Dela et al, 2019) - Frequency of condom use in females (Dela et al, 2019) - Black race (Mayor et al, 2012) - History of previous gonococcal infection or other sexually transmitted infections (Mayor et al, 2012) - Inconsistent condom use (Mayor et al, 2012) - Men who have sex with men (Mayor et al, 2012) - Prostitution (Mayor et al, 2012) - Substance abuse (Mayor et al, 2012) No data were identified as additional risk factors for meningococcal or gonococcal infections related to gMG.
Risk minimization measures	Routine risk minimization measures: - SmPC Section 4.3 (Contraindications) and SmPC Section 4.4 (Special warnings and precautions for use) - PL Section 2 (What you need to know before you use ZILBRYSQ) Measures such as meningococcal vaccination and antibiotic prophylaxis are discussed in SmPC Section 4.4 (Special warnings and precautions for use), PL Section 2 (What you need to know before you use ZILBRYSQ), and PL Section 3 (How to use ZILBRYSQ) Signs and symptoms of meningococcal infections are listed in SmPC Section 4.4 (Special warnings and precautions for use) and PL Section 2 (What you need to know before you use ZILBRYSQ). Use under guidance and supervision by specialist HCPs experienced in the management of patients with neuromuscular disorders (SmPC Section 4.2 Posology and method of administration). Additional risk minimization measures for meningococcal infections: Controlled access program Educational materials - Guide for HCPs - Patient Alert Card - Patient/Carer Guide Vaccination reminders for prescribers
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Zilucoplan observational secondary data post-authorization safety study (MG0026). See Section 2.3 of this summary for an overview of the post-authorization plan.

Table 2–2: Summary of important risks and missing information

Missing information: Pregnancy and lactation	
Risk minimization measures	Routine risk minimization measures: - SmPC Section 4.6 (Fertility, pregnancy and lactation) - PL Section 2 (What you need to know before you use ZILBRYSQ) Use under guidance and supervision by specialist HCPs experienced in the management of patients with neuromuscular disorders (SmPC Section 4.2 Posology and method of administration). Additional risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Zilucoplan observational secondary data post-authorization safety study (MG0026). See Section 2.3 of this summary for an overview of the post-authorization plan.
Missing information: Long-term safety	
Risk minimization measures	Routine risk minimization measures: Use under guidance and supervision by specialist HCPs experienced in the management of patients with neuromuscular disorders (SmPC Section 4.2 Posology and method of administration). Additional risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Zilucoplan observational secondary data post-authorization safety study (MG0026). Open-label extension study (MG0011/RAISE-XT) See Section 2.3 of this summary for an overview of the post-authorization plan.

gMG=generalized myasthenia gravis; HCP=healthcare professional; PL=package leaflet; SmPC=summary of product characteristics

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2.3 Post-authorization development plan

2.3.1 Studies which are conditions of the marketing authorization

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

2.3.2 Other studies in post-authorization development plan

Additional pharmacovigilance activities include the following studies **:**

2.3.2.1 Zilucoplan observational secondary data post-authorization safety

study (MG0026)

Purpose of the study: The overall aim of this post-authorization safety study will be to assess the effectiveness of the risk minimization measures, as well as the incidence of important outcomes of interest in routine practice for patients with gMG receiving zilucoplan treatment.

2.3.2.2 Open-label extension study (MG0011/RAISE-XT)

Purpose of the study: the objective of the study is to evaluate the long-term safety, tolerability, and efficacy of zilucoplan in study participants with gMG.