BIMZELX®

SUMMARY OF RISK MANAGEMENT PLAN

Version 1.0

Active substance(s) (INN or common name):	Bimekizumab
Product(s) concerned (brand name(s)):	Bimzelx®
Marketing authorization holder:	UCB Pharma-AG
Version number :	1.0 (summary of EU RMP v1.0 , dated 26-Aug-2021)
Date of final sign off :	30-Nov-2022

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 Bimzelx® 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 Bimzelx® 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 Bimzelx®.

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PART I: THE MEDICINE AND WHAT IT IS USED FOR

Pharmaceutical form(s) and strength(s)	Current: Solution for injection in pre-filled syringe. Each pre-filled syringe contains 160mg bimekizumab in 1mL. Solution for injection in a pre-filled pen. Each pre-filled pen contains 160mg bimekizumab in 1mL.
	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

Bimzelx is authorized for treatment of adults with moderate to severe plaque psoriasis (PSO) who are candidates for systemic therapy (see SmPC for the full indication). It contains bimekizumab as the active substance and it is given by subcutaneous injection.

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

medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/bimzelx.

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

Important risks of Bimzelx, together with measures to minimize such risks and the proposed studies for learning more about Bimzelx'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 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*.

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

2.1 List of important risks and missing information

Important risks of Bimzelx 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 Bimzelx. 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

List of important risks and missing information	
Important identified risks	Serious infections
Important potential risks	Serious hypersensitivity reactions
	Inflammatory bowel disease (Crohn's disease and ulcerative colitis)
	Major adverse cardiovascular events
	Malignancy
Missing information	Use during pregnancy and lactation
	Long-term safety data

2.2 Summary of important risks

Table 2–2: Summary of important identified risks

Important identified risk: Serious infections	
Evidence for linking the risk to the medicine	Serious infections are considered as an important identified risk as a class effect for IL-17 inhibitors.
Risk factors and risk groups	Increasing age, diabetes mellitus, smoking, significant infection history, and PSO treatment were each associated with an increased risk (Kalb et al, 2015). Treatment with biologics or small molecules may increase risk of serious infection in PSO patients, with variability in the mechanism of action (Siegel and Winthrop, 2019).
Risk minimization measures	Routine risk minimization measures: Product labeling
Additional- pharmacovigilance activities	Additional pharmacovigilance activities: Bimekizumab real-world outcomes study Review of safety data from studies PS0014 and PS0015 See Section 2.3 of this summary for an overview of the post-authorization development plan.

IL=interleukin; PSO=psoriasis

Table 2–3: Summary of important potential risks

Important potential risk: Serious hypersensitivity reactions	
Evidence for linking the risk to the medicine	All monoclonal antibodies could potentially be associated with hypersensitivity reactions, including anaphylactic/anaphylactoid events. Data to evaluate safety concerns derive from clinical studies.
Risk factors and risk groups	Risk groups include patients who have hypersensitivity to the active substance or to any of the excipients.
Risk minimization measures	Routine risk minimization measures: Product labeling
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Bimekizumab real-world outcomes study Review of safety data from studies PS0014 and PS0015 See Section 2.3 of this summary for an overview of the post-authorization development plan.

Table 2–3: Summary of important potential risks

Important potential risk: Inflammatory bowel disease (Crohn's disease and ulcerative colitis)	
Evidence for linking the risk to the medicine	This risk is based on safety evaluation performed including pharmacoepidemiological background incidence and prevalence rates of IBD, comparison of data from other IL-17 inhibitors, and review of bimekizumab clinical data.
Risk factors and risk groups	Risk of IBD in PSO patients increases with severity of disease and systemic medication usage. Cancer, obesity, and cardiovascular disease may also be risk factors of IBD in PSO patients (Lee et al, 2019; Radtke et al, 2017; Takeshita et al, 2017; Vlachos et al, 2016; Molodecky et al, 2012; Loftus Jr 2004).
Risk minimization measures	Routine risk minimization measures: Product labeling
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Bimekizumab real-world outcomes study Review of safety data from studies PS0014 and PS0015 See Section 2.3 of this summary for an overview of the post-authorization development plan.
Important potential risk: MACE	
Evidence for linking the risk to the medicine	Data to evaluate safety concerns derive from clinical studies, comparison of data from other IL-17 inhibitors, and pharmacoepidemiological background incidence and prevalence rates.
Risk factors and risk groups	The increased cardiovascular risk in PSO patients is partly due to the association with factors that are known predictors of cardiovascular risk including hyperlipidemia, obesity, hypertension, and diabetes. In addition, PSO patients have an increased risk of vascular inflammation and MACE (defined as myocardial infarction, stroke and cardiovascular related death) beyond that attributable to known cardiovascular risk factors (Egeberg et al, 2017; Gelfand et al 2006). Observational studies have shown that if systemic inflammation is driving CVD risk then systemic treatment with methotrexate and biologic drugs may reduce elevated risk of MACE (Jindal and Jindal, 2018). Some clinical trials of IL-12/23 inhibitors have reported elevated risk of MACE; however, a recent review across 38 RCTs found no statistically elevated risk (Rungapiromnan et al, 2017; Parisi et al, 2015).

Table 2–3: Summary of important potential risks

Important potential risk: MACE	
Risk minimization measures	Routine risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Bimekizumab real-world outcomes study Review of safety data from studies PS0014 and PS0015 See Section 2.3 of this summary for an overview of the post-authorization development plan.
Important potential risk: Malignancy	
Evidence for linking the risk to the medicine	Data to evaluate safety concerns derive from clinical studies, comparison of data from other IL-17 inhibitors, and pharmacoepidemiological background incidence and prevalence rates.
Risk factors and risk groups	Several mechanisms may contribute to the increased risk of cancer among patients with PSO including chronic inflammation, impaired immunosurveillance associated with the disease itself. Other factors, such as treatment with certain pharmacologic agents or behavioral factors including smoking and alcohol consumption also may contribute to risk independently. A large meta-analysis showed that risk factors of cancer in PSO patients included alcohol and cigarette use, phototherapy, and disease severity (Pouplard et al, 2013). Two retrospective cohort studies examined severity of PSO disease and/or treatment in relation to cancer incidence (Kimball et al, 2015; Lee et al, 2012). These studies found a trend in the incidence of all cancers, lymphoma, melanoma, and NMSC associated with increased PSO disease severity defined by treatment.
Risk minimization measures	Routine risk minimization measures: None
Additional pharmacovigilance activities	Bimekizumab real-world outcomes study Review of safety data from studies PS0014 and PS0015 See Section 2.3 of this summary for an overview of the post-authorization

CVD=cardiovascular disease; IBD=inflammatory bowel disease; IL=interleukin; MACE=major adverse cardiovascular event; NMSC=nonmelanoma skin cancer; PSO=psoriasis; RCT=randomized clinical trial

Table 2–4: Summary of missing information

Missing information: Use during pregnancy and lactation	
Risk minimization measures	Routine risk minimization measures: Product labeling
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Bimekizumab pregnancy exposure and outcomes registry An observational cohort study to evaluate bimekizumab exposure during pregnancy See Section 2.3 of this summary for an overview of the post-authorization development plan.
Missing information: Long-term safety	
Risk minimization measures	Routine risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Review of safety data from studies PS0014 and PS0015 See Section 2.3 of this summary for an overview of the post-authorization development plan

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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 Bimzelx.

2.3.2 Other studies in post-authorization development plan

Additional pharmacovigilance activities include the following studies:

2.3.2.1 Bimekizumab real-world outcomes study

- **Study short name:** Bimekizumab real-world outcomes study

Purpose of the study: The primary objective of this observational cohort study will be to evaluate any potential increase in the risk of safety outcomes of interest in bimekizumab exposed PSO patients compared to other biologics indicated for moderate-to-severe PSO except for any other anti-interleukin(IL)-17 biologics (eg, anti-tumor necrosis factor[TNF], anti-IL-23) in the real-world setting.

The safety outcomes of interest will include but are not limited to major adverse cardiovascular events, malignancy, serious infections, inflammatory bowel disease, and serious hypersensitivity reactions.

2.3.2.2 Bimekizumab pregnancy exposure and outcomes registry

• **Study short name:** Bimekizumab pregnancy exposure and outcomes registry

Purpose of the study: The objective of this study is to assess maternal, fetal, and infant outcomes among women who become pregnant while exposed to bimekizumab relative to the outcomes in 2 matched comparator populations. The primary analysis will be a comparison of the birth prevalence of major structural defects in live born infants between the bimekizumab-exposed cohort and the disease comparison cohort. Additional outcome variables will be to evaluate the potential effect of bimekizumab exposure on other adverse pregnancy outcomes including, but not limited, to spontaneous abortion, elective termination, stillbirth, preterm delivery, pregnancy complications, small for gestational age, and small for postnatal growth.

2.3.2.3 Observational cohort study to evaluate bimekizumab exposure during pregnancy

• **Study short name:** Observational cohort study to evaluate bimekizumab exposure during pregnancy

Purpose of the study: The primary objective is to assess adverse pregnancy and infant outcomes, more specifically major congenital malformations, spontaneous abortions, stillbirths, small for gestational age, neonatal deaths and infant infections, in women exposed to bimekizumab during pregnancy compared to women exposed to other biologics indicated for moderate-to-severe PSO except for any other anti-IL-17 biologics (eg, anti-TNF, and-IL-23) during pregnancy using a cohort study design with data from a large electronic health database.

2.3.2.4 PS0014

• **Study short name:** A multicenter, open-label study to assess the long-term safety, tolerability, and efficacy of bimekizumab in adult study participants with moderate-to-severe chronic plaque PSO (PS0014)

Purpose of the study: To assess the long-term safety and tolerability of bimekizumab administered sc in adult study participants with moderate to severe chronic plaque PSO. This study will include 2 periods, a Treatment Period (144 weeks) and a SFU period (20 weeks after the final dose).

2.3.2.5 PS0015

• **Study short name:** A multicenter, randomized, double-blind, active comparator-controlled, parallel-group study to evaluate the efficacy and safety of bimekizumab in adult study participants with moderate-to-severe chronic plaque PSO (PS0015).

Purpose of the study: The open label extension period will allow collection of long-term efficacy and safety data from eligible study participants on open-label bimekizumab for an additional 96 weeks (after 48 of initial treatment).