Summary of Risk Management Plan for Idefirix

Name of medicinal product:	Idefirix
Active substance:	imlifidase
Dosage strength:	11 mg
Pharmaceutical form:	Powder for concentrate for solution for infusion
Version number of RMP summary:	1.0
Name of Marketing Authorisation Holder:	Voisin Consulting CH Sàrl
Date:	30 May 2022
Reference RMP:	EU RMP version 1.0
	Swiss Specific Addendum 1.0 to EU RMP 1.0

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 Idefirix 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 Idefirix in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Voisin Consulting CH Sàrl is fully responsible for the accuracy and correctness of the content of the published summary RMP of Idefirix.

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Part VI: Summary of the risk management plan

Summary of risk management plan for Idefirix (imlifidase)

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

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

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

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

I. The medicine and what it is used for

Idefirix is authorised for desensitization treatment of highly sensitized adult kidney transplant patients with positive crossmatch against an available deceased donor. The use of Idefirix should be reserved for patients unlikely to be transplanted under the available kidney allocation system including prioritization programmes for highly sensitized patients.

Idefirix contains imlifidase as the active substance and it is given by intravenous infusion.

Further information about the evaluation of Idefirix’s benefits can be found in Idefirix’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 minimise or further characterise the risks

Important risks of Idefirix, together with measures to minimise such risks and the proposed studies for learning more about Idefirix's 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 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 (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 PSUR 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 Idefirix is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Idefirix 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 Idefirix. 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	Severe or serious infection Infusion-related reactions
Important potential risks	None
Missing information	Long-term effectiveness and safety

II.B Summary of important risks

Important identified risk: Severe and serious infection	
Evidence for linking the risk to the medicine	Idefirix cleaves a type of antibodies called immunoglobulin G (IgG) to prevent IgG from destroying the kidney transplant. In the period when IgGs are cleaved, there may be a higher risk of some infections. Infections are very common in transplanted patients receiving immunosuppression. In a large published study in kidney-transplanted patients not treated with Idefirix, about half of the patients had at least 1 infection during the first year after transplantation. About one third of the patients had urinary tract infection, 13% had pneumonia, and 12% had sepsis (a serious infection that causes the immune system to attack the body). In clinical studies with Idefirix, 9 of 54 patients (16.7%) with chronic kidney disease (CKD), whereof 7 of 46 kidney-transplanted patients (15%), had any severe or serious infection assessed as at least possibly related to Idefirix. No patients died from infections or from any other cause in the clinical studies with Idefirix. To minimise the risk of infections, all patients should receive treatment with antibiotics.

Risk factors and risk groups	No firm conclusions can be drawn regarding subgroups due to small numbers of patients per subgroup.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.2., 4.3, 4.4 and 4.8. PL section 2 and 4.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study 17-HMedIdeS-14: An ongoing observational long-term follow-up study to evaluate long-term graft survival and clinical outcome after imlifidase. Study 20-HMedIdeS-19: A post-authorisation efficacy study (PAES) to evaluate 1-year graft survival, kidney function and safety after imlifidase (including severe and serious infections). Study 20-HMedIdeS-20: A 5-year-extension post-authorisation efficacy study (PAES) to evaluate long-term graft survival in patients who have undergone kidney transplantation after imlifidase administration. See section II.C of this summary for an overview of the post-authorisation development plan.

Important identified risk: Infusion-related reactions	
Evidence for linking the risk to the medicine	As for other biologic treatments administered intravenously (IV), infusion reactions may occur. Not only IV treatment with monoclonal antibodies and other proteins, but also IV infusion without active drug, has been associated with infusion reactions, though the exact mechanism is not known. Mild-to-moderate reactions are characterized by flushing, rash, fever, rigors, chills, shortness of breath, and low blood pressure. Severe reactions are associated with bronchospasms (narrowing of the airways), low blood pressure, heart dysfunction, severe allergic reaction, and other symptoms requiring treatment. In clinical studies with Idefirix, 3 of 54 patients (5.6%) with CKD had any infusion-related reaction assessed as related to Idefirix (whereof 2 patients were kidney-transplanted). In 2 of the 3 patients, infusion of Idefirix could be restarted within less than half an hour. No patients died from infusion-related reactions in the clinical studies with Idefirix. To minimize the risk of infusion-related reactions, all patients should receive glucocorticoid and antihistamine treatment before dosing.

Risk factors and risk groups	No firm conclusions can be drawn with regard to subgroups due to small numbers of patients per subgroup.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.2., 4.4 and 4.8. PL section 2, 3 and 4.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study17-HMedIdeS-14: An ongoing observational long-term follow-up study to evaluate long-term graft survival and clinical outcome after imlifidase. Study 20-HMedIdeS-19: A post-authorisation efficacy study (PAES) to evaluate 1-year graft survival, kidney function and safety after imlifidase (including infusion-related reactions). Study 20-HMedIdeS-20: A 5-year-extension post-authorisation efficacy study (PAES) to evaluate long-term graft survival in patients who have undergone kidney transplantation after imlifidase administration. See section II.C of this summary for an overview of the post-authorisation development plan.

Missing Information: Long-term effectiveness and safety	
Risk minimisation measures	None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Study17-HMedIdeS-14: An ongoing observational long-term follow-up study to evaluate long-term graft survival and clinical outcome after imlifidase. Study 20-HMedIdeS-19: A post-authorisation efficacy study (PAES) to evaluate 1-year graft survival, kidney function and safety after imlifidase (including infusion-related reactions). Study 20-HMedIdeS-20: A 5-year-extension post-authorisation efficacy study (PAES) to evaluate long-term graft survival in patients who have undergone kidney transplantation after imlifidase administration. See section II.C of this summary for an overview of the post-authorisation development plan.

II.C Post-authorisation development plan

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

The following studies are conditions of the marketing authorisation:

Study 17-HMedIdeS-14: Observational long-term follow-up study

Purpose of the study: To evaluate long-term graft survival in patients who have undergone kidney transplantation after imlifidase administration, and to evaluate long-term clinical outcome in terms of patient survival, kidney function, comorbidity, treatments, quality of life, safety, DSA, and immunogenicity.

Study 20-HMedIdeS-19: Post-approval efficacy study (PAES)

Purpose of the study: to assess 1-year overall graft survival rate in highly sensitized kidney transplant patients with positive crossmatch against a deceased donor and pre-treated with imlifidase. The study will include two non-comparative reference cohorts for descriptive purpose; one registry-based with kidney-transplanted patients and a second concurrent reference cohort with transplanted patients (any grade of sensitization) not enrolled to the imlifidase treatment. The study will also evaluate kidney function, patient survival, frequency of crossmatch conversion, safety profile (including serious and severe infections, and infusion-related reactions), and quality of life.

Study 20-HMedIdeS-20: Post-approval efficacy study (PAES) long-term follow-up study

Purpose of the study: A 5-year-extension post-authorisation efficacy study (PAES) to evaluate long-term graft survival in patients who have undergone kidney transplantation after imlifidase administration and in patients in the non-comparative concurrent reference cohort.

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

There are no studies required for Idefirix.