Swiss Summary of the Risk Management Plan (RMP) for Immune Globulin Subcutaneous [Human], 20% Solution [IGSC, 20%] (CUVITRU)

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Marketing Authorization Holder: Takeda Pharma AG

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 risk as well as to prevent or minimise them.

The RMP summary of CUVITRU 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 CUVITRU in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic. Takeda Pharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of CUVITRU.

Summary of risk management plan for CUVITRU (Immune Globulin Subcutaneous [Human], 20% Solution)

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

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

I. The medicine and what it is used for

CUVITRU is authorised for Replacement therapy in adults, and children and adolescents (0-18 years) in:

- Primary immunodeficiency syndromes with impaired antibody production.
- Secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either proven specific antibody failure (PSAF)* or serum IgG level of <4 g/l.

*PSAF = failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines.

Kindly refer to the SmPC for the full indication. CUVITRU contains human normal immunoglobulin (IG) as the active substance, and it is given by subcutaneous (SC) route.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of CUVITRU, together with measures to minimise such risks and the proposed studies for learning more about CUVITRU'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 periodic safety update report (PSUR) assessment - include PSUR statement only if product has PSUR requirements 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 CUVITRU is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of CUVITRU 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 CUVITRU. 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	• Allergic/hypersensitivity responses including anaphylactic reactions, especially in patients with IgA deficiency and IgA antibodies • Thromboembolic events
Important potential risks	• Medication error: incorrect route of administration
Missing information	• Lack of information on safety in pregnant and lactating women • Limited information on safety in neonates or infants <2 years old

II.B Summary of important risks

Important Identified Risk: Allergic/hypersensitivity responses including anaphylactic reactions, especially in patients with IgA deficiency and IgA antibodies	
Evidence for linking the risk to the medicine	On the basis of post-marketing safety data and medical literature there is sufficient evidence demonstrating potential causal association.
Risk factors and risk groups	Patients with antibodies to IgA potentially have a greater risk of developing severe hypersensitivity or anaphylactic reactions.
Risk minimization measures	**Routine risk minimisation measures:** SmPC section 4.3 SmPC section 4.4 mention that patients with anti-IgA antibodies, in whom treatment with subcutaneous IgG products remains the only option, should be treated with CUVITRU only under close medical supervision. SmPC section 4.8 **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	None.

Important Identified Risk: Thromboembolic events	
Evidence for linking the risk to the medicine	On the basis of post-marketing safety data and medical literature there is sufficient evidence demonstrating potential causal association.

Risk factors and risk groups	Patients at increased risk for thrombotic events include those with: • a history of atherosclerosis • multiple cardiovascular risk factors • advanced age • impaired cardiac output • hypercoagulable disorders • prolonged periods of immobilization • obesity • diabetes mellitus • acquired or inherited thrombophilic disorder • a history of vascular disease • a history of a previous thrombotic or thromboembolic event
Risk minimization measures	**Routine risk minimisation measures:** SmPC section 4.4 where advice is given to use drug with caution in patients with pre-existing risk factors for thrombotic events and adequate hydration should be ensure in patients before administration. **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	None.

Important Potential Risk: Medication error: Incorrect route of administration	
Evidence for linking the risk to the medicine	On the basis of post-marketing events and medical literature, there is evidence to suspect the possibility of a causal relationship between these events and CUVITRU.
Risk factors and risk groups	Medication errors are inherent risks associated with the therapeutic use of drugs and the administration process.
Risk minimization measures	**Routine risk minimisation measures:** SmPC section 4.2 mention that the patient or caregiver must be instructed in the use of a syringe driver, the infusion techniques, the keeping of treatment diary, recognition of and measures to be taken in case of severe adverse reactions. SmPC section 4.3 SmPC section 4.4 **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	None.

Missing Information: Lack of information on safety in pregnant and lactating women	
Risk minimization measures	**Routine risk minimisation measures:** SmPC section 4.6 **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	None.

Missing Information: Limited information on safety in neonates or infants <2 years old	
Risk minimization measures	**Routine risk minimisation measures:** SmPC Section 4.2 SmPC Section 4.4 SmPC Section 4.5 SmPC Section 4.8 SmPC Section 5.1 SmPC Section 5.2 **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	None.

II.C. Post-authorisation development plan

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

There are no studies which are conditions of the marketing authorisation or specific obligation of CUVITRU.

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

There are no studies required for CUVITRU.