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For the safe and optimal use of human proteins

Swiss Summary of the Risk Management Plan (RMP) for Cutaquig (human normal immunoglobulin (SCIG))

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Disclaimer:

The Risk Management Plan (RMP) is 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 *cutaquig* 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 *cutaquig* in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Octapharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of *cutaquig*.

Summary of risk management plan for *cutaquig* (human normal immunoglobulin (SCIG))

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

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

The medicine and what it is used for

cutaquig is authorised for antibody replacement therapy in primary and some types of secondary immunodeficiency syndromes (see SmPC for the full indication). It contains human normal immunoglobulin as the active substance and it is given by the subcutaneous route of administration.

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

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

List of important risks and missing information

Important risks of *cutaquig* 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 *cutaquig*. 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	− Hypersensitivity reactions, including anaphylactic reactions − Thromboembolic events − Aseptic meningitis − Renal dysfunction / failure
Important potential risks	− Interference with certain blood glucose tests − Potential for transmission of infectious agents − Haemolysis − Increased or unknown risks in home-based SC (self) administration
Missing information	− Safety in pregnant or breastfeeding women

Summary of important risks

Important identified risk: Allergic (hypersensitivity) reactions, including severe, sudden allergic (anaphylactic) reactions	
Evidence for linking the risk to the medicine	As with any protein product that is administered under the skin, allergic-type hypersensitivity reactions may occur. In very rare cases, allergic reactions may be life-threatening. Usually, patients recover fully following treatment.
Risk factors and risk groups	Patients with a history of previous reactions to a human plasma-derived product or a known hypersensitivity to any of the ingredients of *cutaquig*.
Risk minimisation measures	<u>Routine risk minimisation measures:</u> SmPC sections 4.3, 4.4 and 4.8 Package leaflet sections 2 and 4

Important identified risk: Blood clots (Thromboembolic events)	
Evidence source(s) and strength of evidence	Blood clots (thromboembolic events) are serious adverse reactions associated with the use of human immunoglobulin products that are potentially life-threatening. Blood clots may affect the arteries or veins. In the veins this may lead to a painful swelling of the legs (deep vein thrombosis) and very occasionally life threatening or fatal clots may occur in the lungs. Clots in the arteries may lead to a heart attack or stroke – particularly in patients who already have problems with their arteries.
Risk factors and risk groups	Known risk factors for thromboembolic events (blood clots) include: advanced age, immobility, (major) surgery, obesity, multiple trauma, hip fracture, lower extremity paralysis caused by spinal cord injury, cardiac or respiratory failure, presence of central venous lines, oestrogens, and a wide variety of inherited and acquired haematological conditions.

Important identified risk: Blood clots (Thromboembolic events)	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 4.8 Package leaflet sections 2 and 4

Important identified risk: Inflammation of the membranes that cover the brain and spinal cord not caused by bacteria or viruses (Aseptic meningitis)	
Evidence source(s) and strength of evidence	Certain drugs including human normal immunoglobulins such as *cutaquig* have been implicated in causing noninfective (aseptic) meningitis. Patients with aseptic meningitis may experience among other symptoms persistent fatigue, light-headedness, and asthenia which might impair daily activities. Most cases of aseptic meningitis syndrome are benign and patients fully recover.
Risk factors and risk groups	Patients receiving high doses of *cutaquig*.
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 4.8 Package leaflet sections 2 and 4

Important identified risk: Renal dysfunction / failure	
Evidence source(s) and strength of evidence	In the case of (acute) renal failure, the kidneys are no longer able to filter waste products from the blood. Consequently, waste products may accumulate and reach toxic levels. Cases of (acute) renal failure are usually serious. In most cases of acute renal failure at least 1 day of renal dialysis is required.
Risk factors and risk groups	Risk factors include pre-existing renal insufficiency, hypertension, dehydration or volume depletion, paraproteinaemia, sepsis, diabetes mellitus, hypovolaemia, concomitant nephrotoxic medicinal products, and age over 65 years (elderly patients).
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4

Important identified risk: Interference with certain blood glucose tests	
Evidence source(s) and strength of evidence	Falsely elevated glucose readings may lead to the inappropriate administration of insulin, resulting in life-threatening or even fatal hypoglycaemia. Similarly, cases of true hypoglycemia may be masked.
Risk factors and risk groups	Use of non-glucose-specific blood glucose testing systems.

Important identified risk: Interference with certain blood glucose tests	
Risk minimisation measures	Routine risk minimisation measures: SmPC sections 4.4 and 4.5 Package leaflet section 2

Important potential risk: Potential for transmission of infectious agents	
Evidence source(s) and strength of evidence	When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of the blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove the viruses. Despite these measures, when medicines prepared from human blood or plasma are administrated, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.
Risk factors and risk groups	Patients with a weakened immune system.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4 Package leaflet section 2

Important potential risk: Destruction of red blood cells (Haemolysis)	
Evidence source(s) and strength of evidence	IG administration may result in mild haemolytic reactions which are usually subclinical and self-limiting. In very rare cases, significant haemolysis may occur. Cases of haemolysis with clinically observable symptoms are serious. Severe haemolysis may result in renal failure, thus requiring haemodialysis. In some patients also blood transfusions may be necessitated.
Risk factors and risk groups	Risk factors include non-group O blood, large cumulative IG dose, high isoagglutinin titre in IG product, and underlying inflammatory state.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.8 Package leaflet section 2

Important potential risk: Increased or unknown risks in home-based subcutaneous (self) administration	
Evidence source(s) and strength of evidence	There have been reports of product leakage due to inappropriately sized needles used in home therapy setting during post-marketing use of *cutaquig*. Underdosing, may render the therapy with *cutaquig* ineffective. Consequences of an overdose with *cutaquig* are not known.
Risk factors and risk groups	Not applicable
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.2 Package leaflet section 3

Missing information: Safety in pregnant or breastfeeding women	
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.6 Package leaflet section 2

Post-authorisation development plan

There are no studies required for *cutaquig*.

Overview of changes in the Summary of the RMP for Switzerland over time

Version	Date	Change
01	06-Jul-2022	Not applicable. First version of RMP Summary for Switzerland.