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For the safe and optimal use of human proteins

Swiss Summary of the Risk Management Plan (RMP) for Octagam (human normal immunoglobulin (IVIG))

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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 *octagam* 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 *octagam* 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 *octagam*.

Summary of risk management plan for *octagam* (human normal immunoglobulin (IVIG))

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

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

The medicine and what it is used for

octagam is authorised for replacement therapy in primary immunodeficiency (PID) 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 or serum IgG level of <4g/l. It is also authorised for immunomodulation in primary immune thrombocytopenia (ITP), Guillain Barré syndrome, Kawasaki disease, chronic inflammatory demyelinating polyneuropathy (CIDP) and/or for multifocal motor neuropathy (MMN) (see SmPC for the full indication). It contains human normal immunoglobulin (IgG) as the active substance and it is given by intravenous infusion.

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

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

List of important risks and missing information

Important risks of *octagam* 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 *octagam*. 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	− Thromboembolic events − Aseptic meningitis − Hypersensitivity reactions, including anaphylactic reactions − Renal failure − Interference with certain blood glucose tests − Haemolysis
Important potential risks	− Suspected transmission of pathogen infection − Interaction with live attenuated virus vaccines and serological testing − Transfusion-related acute lung injury (TRALI) − Neutropenia/Leukopenia
Missing information	− none

Summary of important risks

Important identified risk: Thromboembolic events	
Evidence for linking the risk to the medicine	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	Caution should be exercised in prescribing and infusing IVIG in obese patients and in patients with pre-existing risk factors for thromboembolic events, such as: • age (elderly) • hypertension • diabetes mellitus • hyperlipidaemia • history of vascular disease • history of thrombotic episodes • acquired or inherited thrombophilic disorders • prolonged periods of immobilisation • hypovolaemia • renal insufficiency • liver disease (cirrhosis, impaired liver function, etc.) • atrial fibrillation • severe muscle haemorrhage, crush injury, or orthopaedic surgery in haemophilia patients • increased blood viscosity • dermatomyositis.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (sections 4.2, 4.4 and 4.8) and in the PL (sections 2 and 4)

Important identified risk: Aseptic meningitis	
Evidence for linking the risk to the medicine	Certain drugs including human normal immunoglobulins such as *octagam* 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	Individuals treated with drugs that potentially cause drug-induced aseptic meningitis, such as antimicrobials, NSAIDs, vaccines and intravenous immunoglobulins. Patients with pre-existing migraine receiving high-dose IVIG.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (sections 4.4 and 4.8) and in the PL (sections 2 and 4)

Important identified risk: Hypersensitivity reactions, including anaphylactic reactions	
Evidence for linking the risk to the medicine	As with any plasma-derived protein product administered intravenously, 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 plasma-derived products or known hypersensitivity to any of the constituents of the drug. Patients presenting with anti-IgA antibodies or IgA deficiency.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (sections 4.3, 4.4 and 4.8) and in the PL (sections 2 and 4)

Important identified risk: Renal failure	
Evidence for linking the risk to the medicine	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) 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: Mentioned in the SmPC (sections 4.4 and 4.8) and in the PL (sections 2 and 4)

Important identified risk: Interference with certain blood glucose tests	
Evidence for linking the risk to the medicine	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.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (sections 4.4, 4.5 and 4.8) and in the PL (sections 2 and 4)

Important identified risk: Haemolysis	
Evidence for linking the risk to the medicine	IVIG 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 usually 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 IVIG dose, high isoagglutinin titre in IVIG product, and underlying inflammatory state.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (sections 4.4 and 4.8) and in the PL (sections 2 and 4)

Important potential risk: Suspected transmission of pathogen infection	
Evidence for linking the risk to the medicine	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	Any virus: immunocompromised patients Additional risk groups for parvovirus B19: pregnant women (foetus up to 20 weeks of gestation) and patients with haemoglobinopathies.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (section 4.4) and in the PL (section 2)

Important potential risk: Interaction with live attenuated virus vaccines and serological testing	
Evidence for linking the risk to the medicine	Interference of IVIG with life attenuated virus vaccines results in lack of protection against the respective virus in an individual. This can lead to a serious or even fatal disease caused by the virus despite previous vaccination.
Risk factors and risk groups	Patients receiving live attenuated virus vaccines such as measles, rubella, mumps and varicella, etc. Passively transferred antibodies in immunoglobulin preparations can confound the results of serological testing.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (sections 4.4 and 4.5) and in the PL (section 2)

Important potential risk: Transfusion-related acute lung injury (TRALI)	
Evidence for linking the risk to the medicine	TRALI is a serious complication and is characterised by severe respiratory distress, collection of fluid in the lung (pulmonary oedema), and low blood oxygen level TRALI mainly occurs as a result of transfusions of whole blood, packed red blood cells (RBCs), platelets, granulocytes, FFP and cryoprecipitate. Only few cases have been reported in connection with IVIG.
Risk factors and risk groups	Published recipient risk factors for TRALI include: • Chronic alcohol abuse, history of heavy alcoholism • Positive fluid balance pre-transfusion • Mechanical ventilation • Shock pre-transfusion • Current smoker • Liver surgery (transplant) • [IL-8] pre-transfusion, • (End-stage) Liver disease

	• Emergency coronary artery bypass grafting (CABG) • Haematologic malignancy • Massive transfusion • Sepsis • Patient age • Time on cardiopulmonary bypass.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (sections 4.4 and 4.8) and in the PL (sections 2 and 4)

Important potential risk: Neutropenia/Leukopenia	
Evidence for linking the risk to the medicine	Since the introduction of IVIG therapy in various immunological diseases, neutropenia/leukopenia has been reported as a rare adverse event. Neutropenia/leukopenia after IVIG was first recognized in patients with ITP. In a 1992 report, a patient with active systemic lupus erythematosus received 2 courses of IVIG infusion, with marked neutropenia/leukopenia developing repeatedly after each IVIG course and so confirming the association between IVIG infusion and the neutropenic event.
Risk factors and risk groups	Risk factors for the development of neutropenia/leukopenia include: • Blood cell or bone marrow conditions • Cancer and cancer treatments • Congenital problems • Infectious diseases • Autoimmune diseases • Malnutrition • Medications.
Risk minimisation measures	Routine risk minimisation measures: Mentioned in the SmPC (sections 4.4 and 4.8) and in the PL (sections 2 and 4)

Post-authorisation development plan

Studies which are conditions of the marketing authorisation

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

Other studies in post-authorisation development plan

There are no studies required for *octagam*.

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

Version	**Date**	**Change**
01	16-Nov-2022	Not applicable. First version of RMP Summary for Switzerland.