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For the safe and optimal use of human proteins

Swiss Summary of the Risk Management Plan (RMP) for *fibryga* (human fibrinogen)

Document Version	01 (based on RMP version 04)
Marketing Authorisation Holder	OCTAPHARMA AG
Pharmaceutical form and strength	Each bottle of *fibryga* contains 1 g human fibrinogen. After reconstitution with 50 ml water for injections, *fibryga* contains approximately 20 mg/ml human fibrinogen.
Date of Document	24-Aug-2018

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 *fibryga* 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 *fibryga* 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 *fibryga*.

Summary of risk management plan for *fibryga* (human fibrinogen)

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

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

I. The medicine and what it is used for

fibryga is authorised for treatment of bleeding and peri-operative prophylaxis in patients with congenital hypo- or afibrinogenaemia with bleeding tendency (see SmPC for full indication). It contains human fibrinogen as the active substance and it is given by intravenous infusion or injection.

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

Important risks of *fibryga*, together with measures to minimise such risks and the proposed studies for learning more about *fibryga*'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, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

II.A List of important risks and missing information

Important risks of *fibryga* 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 *fibryga*. 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
Important Potential Risks	- Suspected transmission of infectious agents
Missing Information	- None

II.B Summary of important risks

Important identified risk: Hypersensitivity reactions, including anaphylactic reactions	
Evidence for linking the risk to the medicine	As with any protein product given into a vein, allergic-type hypersensitivity reactions may occur. In some cases, allergic reactions may be life-threatening, therefore this risk is considered as important identified risk. Usually patients recover fully after treatment.
Risk factors and risk groups	Patients with a history of previous allergic reactions or known hypersensitivity to any of the constituents of the drug.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.3, 4.4 and 4.8 Package leaflet section 2 and 4

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 fibrinogen that are potentially life-threatening. In patients with existing cardiovascular risk factors, substitution therapy with fibrinogen may increase the cardiovascular risk. Rarely, patients may experience heart attacks or strokes.
Risk factors and risk groups	Risk groups for thromboembolic events include patients who have known clinical or laboratory risk factors for thromboembolic events, such as obesity, 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, or increased blood viscosity. The most important behavioural risk factors of heart disease and stroke are unhealthy diet, physical inactivity, tobacco use and harmful use of alcohol. These risk factors may show up in individuals as raised blood pressure, raised blood glucose, raised blood lipids, and overweight and obesity.
Risk minimisation measures	Routine risk minimisation measures: SmPC section 4.4, 4.8 and 4.9 Package leaflet section 2 and 4

Important identified risk: Suspected transmission of infectious agents	
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 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 viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, 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: SmPC section 4.4 PL section 2

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 *fibryga*.

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

There are no studies required for *fibryga*.

Summary of changes to the Summary of the RMP for Switzerland over time

Version	Date	Safety Concerns	Comment
01	24-Aug-2018	**Identified Risks** - Hypersensitivity reactions, including anaphylactic reactions - Thromboembolic events **Potential Risks** - Suspected transmission of infectious agents **Missing information** - None	First version of RMP Summary for Switzerland