Cluvot®/Cluviat®

Fibrogammin®

(Coagulation Factor XIII Human)

Public Summary of Risk Management Plan

(Extract from the EU Risk Management Plan Version 7.0; 30-Oct-2019)

Part VI: Summary of the risk management plan

Summary of Risk Management Plan for Coagulation Factor XIII

This is a summary of the RMP for coagulation FXIII. The RMP details important risks of coagulation FXIII, how these risks can be minimized, and how more information will be obtained about coagulation FXIII 's risks and uncertainties (missing information). Coagulation FXIII's SmPC and its package leaflet give essential information to healthcare professionals and patients on how coagulation FXIII should be used.

I. The medicine and what it is used for

Coagulation FXIII is authorized for congenital and acquired deficiency of FXIII and resulting complications and supportive therapy in case of disturbance in wound healing, especially in ulcus cruris, after large surgery or injuries (see SmPC for the full indication). It contains coagulation FXIII as the active substance and it is given by intravenous administration.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of coagulation FXIII, together with measures to minimize such risks and the proposed studies for learning more about coagulation FXIII's risks, are outlined below.

Measures to minimize 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 authorized 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 (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including periodic safety update report 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 coagulation FXIII are risks that need special risk management activities to further investigate or minimize 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 coagulation FXIII. 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 (eg, on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	• Hypersensitivity reactions • Development of FXIII inhibitors
Important potential risks	• Thromboembolic events • Transmission of infectious agents
Missing information	• None

FXIII = factor XIII

II.B Summary of important risks

Important identified risk: Hypersensitivity reactions	
Evidence for linking the risk to the medicine	Coagulation FXIII clinical trial and postmarketing data; published literature.
Risk factors and risk groups	Individuals who have had an anaphylactic or severe systemic reaction to human plasma products/preparations are at increased risk. Risk is also increased with multiple doses, and also with exposure to other plasma products. In some individuals there may be no previous history of anaphylactic reactions to plasma products.
Risk minimization measures	Routine risk minimization measures: SmPC section 4.3 SmPC section 4.4 SmPC section 4.8 Additional risk minimization measures: None
Additional pharmacovigilance activities	EUHASS, Questionnaire on allergic/anaphylactic reactions See section II.C for an overview of the postauthorization development plan.

EUHASS = European Haemophilia Safety Surveillance, FXIII = factor XIII, SmPC = summary of product characteristics

Important identified risk: Development of FXIII Inhibitors	
Evidence for linking the risk to the medicine	Coagulation FXIII clinical trial and postmarketing data; published literature.
Risk factors and risk groups	Theoretically, the risk is increased in patients receiving multiple administrations of plasma or FXIII.
Risk minimization measures	Routine risk minimization measures: SmPC section 4.4 SmPC section 4.8 Additional risk minimization measures: None
Additional pharmacovigilance activities	EUHASS See section II.C for an overview of the postauthorization development plan.

EUHASS = European Haemophilia Safety Surveillance, FXIII = factor XIII, SmPC = summary of product characteristics

Important potential risk: Thromboembolic events	
Evidence for linking the risk to the medicine	Coagulation FXIII clinical trial and postmarketing data; published literature.
Risk factors and risk groups	Individuals who have known risk factors for thrombotic events such as: • Cardiovascular risk factors • Risk factors for thrombosis eg, smoking, immobility, congestive heart failure, hypertension, advanced age, diabetes, and prior stroke.
Risk minimization measures	Routine risk minimization measures: SmPC section 4.4 Additional risk minimization measures: None
Additional pharmacovigilance activities	EUHASS, Questionnaire on thromboembolic events See section II.C for an overview of the postauthorization development plan.

EUHASS = European Haemophilia Safety Surveillance, FXIII = factor XIII, SmPC = summary of product characteristics

Important potential risk: Transmission of infectious agents	
Evidence for linking the risk to the medicine	Coagulation FXIII clinical trial and postmarketing data; published literature.
Risk factors and risk groups	Hepatitis B and C are increased with exposure to other blood products and increased in intravenous drug users and homosexuals. B19V is a common infectious pathogen in humans and is acquired during childhood.
Risk minimization measures	Routine risk minimization measures: SmPC section 4.4 Additional risk minimization measures: None
Additional pharmacovigilance activities	EUHASS, Questionnaire on transmission of infectious agents See section II.C for an overview of the postauthorization development plan.

B19V = parvovirus B19, EUHASS = European Haemophilia Safety Surveillance, FXIII = factor XIII, SmPC = summary of product characteristics

II.C Post-authorization development plan

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

There are no studies which are conditions of the marketing authorization or specific obligation of coagulation FXIII.

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

EUHASS
Purpose of the study: CSL Behring participates in this ongoing pharmacovigilance program monitoring the safety of treatments for people with inherited bleeding disorders in Europe to obtain long-term postmarketing safety data (including hypersensitivity and inhibitor development).