Part VI: Summary of the risk management plan

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

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

This summary of the RMP for Coagadex should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Coagadex's RMP.

I. The medicine and what it is used for

Coagadex is authorised for the treatment and prophylaxis of bleeding episodes and for perioperative management in patients with hereditary Factor X deficiency (see SmPC for the full indication). It contains human coagulation factor X as the active substance and it is given by intravenous route.

Further information about the evaluation of Coagadex's benefits can be found in Coagadex's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/coagadex

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

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

II.A List of important risks and missing information

Important risks of Coagadex 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 Coagadex. 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. use in pregnancy);

Table Part VI. II.A

List of important risks and missing information	
Important identified risks	• Hypersensitivity or allergic reactions, including anaphylaxis
Important potential risks	• Inhibitor development • Virus Transmission • TSE Transmission • Inadequate Product Traceability • Thrombogenicity (under special consideration for off label use and overdose cases)
Missing information	• Very limited clinical experience in pregnancy and no experience in lactating females • No clinical data for use in patients older than 60 years • Limited clinical data on long term safety

II.B Summary of important risks

Table Part VI. II.B.1

Important identified risk : Hypersensitivity or allergic reactions, including anaphylaxis	
Evidence for linking the risk to the medicine	• Cogadex SmPC
Risk factors and risk groups	Patients sensitive to traces of human protein or any of the excipients
Risk minimisation measures	**Routine risk minimisation measures** • *SmPC sections 4.3, 4.4,4.8* • *PL sections 2,4* **Routine risk minimisation activities recommending**

	specific clinical measures to address the risk: • None **Other routine risk minimisation measures beyond the Product Information:** Legal status: Prescription only medicine **Additional risk minimisation measures** None

Table Part VI. II.B.2

Important Potential risk : Inhibitor development	
Evidence for linking the risk to the medicine	• Coagadex SmPC
Risk factors and risk groups	No evidence of inhibitor development has been identified in BPL clinical trials. In addition, little published data on inhibitor development in Factor X deficient patients has been identified. In theory, any Factor X-deficient patient receiving the BPL factor X product could develop an inhibitor. Accordingly, the following language is provided in the SmPC (section 4.4) for Coagadex : *In general, all patients treated with Coagadex® should be carefully monitored for the development of inhibitors by appropriate clinical observations and laboratory tests. If expected factor X activity levels are not attained, or if bleeding is not controlled with an expected dose, perform an assay that measures factor X inhibitor concentration.*
Risk minimisation measures	**Routine risk minimisation measures** • *SmPC section 4.4* • *PL sections 2* **Routine risk minimisation activities recommending specific clinical measures to address the risk:** • Carefully monitoring for the development of inhibitors by appropriate clinical observations and laboratory tests • Performance of assays that measure factor X inhibitor concentration, if expected factor X activity levels are not attained or if bleeding is not controlled with an expected dose

	Other routine risk minimisation measures beyond the Product Information: Legal status: Prescription only medicine **Additional risk minimisation measures** None

Table Part VI. II.B.3

Important Potential risk : Virus Transmission/TSE Transmission	
Evidence for linking the risk to the medicine	• Coagadex SmPC
Risk factors and risk groups	Not applicable, as no evidence of virus transmission/TSE transmission for Coagadex
Risk minimisation measures	**Routine risk minimisation measures** • *SmPC section 4.4* • *PL sections 2* **Routine risk minimisation activities recommending specific clinical measures to address the risk:** Appropriate vaccination (hepatitis A and B) should be considered for patients in regular/repeated receipt of human plasma derived factor X products. **Other routine risk minimisation measures beyond the Product Information:** Legal status: Prescription only medicine **Additional risk minimisation measures** None

Table Part VI. II.B.4

Important Potential risk : Inadequate Product Traceability	
Evidence for linking the risk to the medicine	• Coagadex SmPC
Risk factors and risk	Not applicable, as no evidence of inadequate product traceability has been identified in BPL clinical trials or

groups	during post marketing period with Coagadex.
Risk minimisation measures	**Routine risk minimisation measures** • *SmPC section 4.4* • *PL sections 2* **Routine risk minimisation activities recommending specific clinical measures to address the risk:** • It is strongly recommended that every time that Coagadex is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product. **Other routine risk minimisation measures beyond the Product Information:** Legal status: Prescription only medicine **Additional risk minimisation measures** None

Table Part VI. II.B.5

Important Potential risk : Thrombogenicity (under special consideration for off label use and overdose cases)	
Evidence for linking the risk to the medicine	• Coagadex SmPC
Risk factors and risk groups	Not applicable, as no evidence of thrombogenicity (under special consideration for off label use and overdose cases) has been identified in BPL clinical trials or during post marketing period with Coagadex.
Risk minimisation measures	**Routine risk minimisation measures** • *SmPC sections 4.2, 4.5, 4.9* • *PL sections 2, 3* **Routine risk minimisation activities recommending specific clinical measures to address the risk:** • Antithrombotic agents should not be used in

	patients with Factor X deficiency. • Coagadex should not be used as an antidote to the effects of direct oral anticoagulants (DOACs) in patients who do not have Factor X deficiency. **Other routine risk minimisation measures beyond the Product Information:** Legal status: Prescription only medicine **Additional risk minimisation measures** None

Table Part VI. II.B.6

Missing information: Very limited clinical experience in pregnancy and no experience in lactating females	
Risk minimisation measures	Routine risk minimisation measures • *SmPC section 4.6* **Routine risk minimisation activities recommending specific clinical measures to address the risk:** • None **Other routine risk minimisation measures beyond the Product Information:** Legal status: Prescription only medicine **Additional risk minimisation measures** None

Table Part VI. II.B.7

Missing information: No clinical data for use in patients older than 60 years	
Risk minimisation measures	**Routine risk minimisation measures** • *SmPC section 5.2*

Missing information: No clinical data for use in patients older than 60 years	
	Routine risk minimisation activities recommending specific clinical measures to address the risk: • None **Other routine risk minimisation measures beyond the Product Information:** Legal status: Prescription only medicine **Additional risk minimisation measures** None

Table Part VI. II.B.8

Missing information: No clinical data on long term safety	
Risk minimisation measures	**Routine risk minimisation measures** • *None* **Routine risk minimisation activities recommending specific clinical measures to address the risk:** • None **Other routine risk minimisation measures beyond the Product Information:** Legal status: Prescription only medicine **Additional risk minimisation measures** 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 obligations of the Coagadex Marketing Authorisation.

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

Not applicable.