Summary of activities in the risk management plan by product

Summary of risk management plan for Cablivi (caplacizumab)

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

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

This summary of the RMP for Cablivi should be read in the context of all this information including the assessment report of the evaluation and in 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 the RMP.

I. The medicine and what it is used for

Cablivi is authorised for the treatment of adults experiencing an episode of acquired thrombotic thrombocytopenic purpura or aTTP as it reduces the frequency of TTP-related death, recurrence of TTP, and refractory disease. It contains caplacizumab as the active substance and it is given by injection (see SmPC for details).

aTTP is a rare blood clotting disorder in which clots form in small blood vessels. These clots can damage the brain, heart, kidneys, and other organs. Cablivi prevents blood platelets from clumping together and forming these clots.

Further information about the evaluation of Cablivi's benefits can be found in Cablivi's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage:

http://www.ema.europa.eu/ema/index.jsp?curl=/pages/medicines/human/medicines/004282/human_med_002276.jsp&mid=WC0b01ac058001d124

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

Important risks of Cablivi, together with measures to minimise such risks and the proposed studies for learning more about Cablivi'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 the case of Cablivi, the routine measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

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 Cablivi is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Cablivi 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 Cablivi. 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 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).

Table Part VI.1: List of important risks and missing information

List of important risks and missing information	
Important identified risks	• Bleeding
Important potential risks	• Serious allergy or immune reactions
Missing information	• Use during pregnancy and lactation • Use in patients with severe liver disease • Long term exposure, including inducing immune responses

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

Table Part VI.2: Important identified risks

Important identified risk: BLEEDING	
Evidence for linking the risk to the medicine	In clinical trials, bleeding events were more frequent in the caplacizumab treated group compared to the placebo group.
Risk factors and risk groups	Patients with aTTP are at increased risk for bleeding. This risk is increased by caplacizumab treatment due to its mechanism of action. Patients receiving other commonly used treatments reducing blood clotting, such as high-dose heparin, are thought to be at greater risk of bleeding, although such an association could not be found in the aggregate data. Patients with severe liver disease or other disorders affecting their hemostasis are expected to be at higher risk of bleeding when treated with products affecting blood clotting such as caplacizumab.
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.4, 4.8. and 4.9 • PIL section 2 and 4 • Legal status: subject to medical prescription

	Additional risk minimisation measures: • Patient Alert Card

Table Part VI.3: Important potential risks

Important potential risk: SERIOUS HYPERSENSITIVITY REACTIONS	
Evidence for linking the risk to the medicine	Like other biological medicinal products, Cablivi has the potential to trigger immune reactions including serious hypersensitivity reactions. No severe immune reactions have been attributed to Cablivi in the clinical trials supporting its approval.
Risk factors and risk groups	Patients with known hypersensitivity to the active ingredient caplacizumab and/or any of the excipients are at increased risk of developing hypersensitivity reaction to caplacizumab.
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.3 • PIL section 2 • Legal status: subject to medical prescription Additional risk minimisation measures: • None
Additional pharmacovigilance activities	• ALX0681-C302 (HERCULES Follow-up study). Will collect any reports of hypersensitivity reactions occurring during the study including those occurring on retreatment.

Table Part VI.4: Missing information

Missing information:	
USE IN PREGNANCY AND LACTATION	
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.6. • PIL section 2 • Legal status: subject to medical prescription Additional risk minimisation measures: • None
USE IN PATIENTS WITH SEVERE HEPATIC IMPAIRMENT	
Risk minimisation measures	Routine risk minimisation measures: • SmPC section 4.2 and 4.4 • PIL section 2 • Legal status: subject to medical prescription Additional risk minimisation measures: • None
LONG TERM EXPOSURE, INCLUDING IMMUNOGENICITY	

Risk minimisation measures	Routine risk minimisation measures: • SmPC section 5.1 Legal status: subject to medical prescription. Additional risk minimisation measures: • None
Additional pharmacovigilance activities	• ALX0681-C302 Long term HERCULES follow-up study. Designed to collect data on long term (3y) safety

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 Cablivi.

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

Study ALX0681-C302 “Prospective Follow-up Study for Patients who Completed Study ALX0681-C301 (HERCULES) to Evaluate Long-term Safety and Efficacy of caplacizumab (Post-HERCULES)" is expected to provide data on the long term safety of caplacizumab and on the safety of its repeated use for the treatment of disease recurrences.