Summary of risk management plan for CABLIVI®

Cablivi® (caplacizumab)
Marketing Autorisation Holder : sanofi-aventis (suisse) sa
RMP version 3.0
Date: 6 Sep 2022

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 minimize them. The RMP summary of Cablivi® 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 medicament" 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 Cablivi® in Switzerland is the "Arzneimittelinformation/ Information sur le medicament" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic. Sanofi-aventis (suisse) sa is fully responsible for the accuracy and correctness of the content of this published summary RMP of Cablivi®.

I. THE MEDICINE AND WHAT IT IS USED FOR

According to Swiss label

Cablivi is used to treat adults and adolescents aged 12 years and older and weighing at least 40 kg who have an episode of acquired thrombotic thrombocytopenic purpura (aTTP) in combination with plasmapheresis and immunosuppression.

According to EU SmPC

CABLIVI is authorized for the treatment of adults and adolescents of 12 years of age and older weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP), in conjunction with plasma exchange (PE) and immunosuppression (see SmPC for the full indication). It contains caplacizumab as the active substance and it is given by intravenous (IV) or subcutaneous (SC) injection.

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 European Medicines Agency (EMA) website, under the medicine's webpage:
https://www.ema.europa.eu/en/medicines/human/EPAR/cablivi

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERIZE THE RISKS

Important risks of CABLIVI, together with measures to minimize such risks and the proposed studies for learning more about CABLIVI's risks, are outlined in the next sections.

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 HCPs;
- 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 the case of CABLIVI, these measures are supplemented with additional risk minimization measures mentioned under relevant important risks, outlined in the next sections.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including periodic safety update report (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" outlined in the next section.

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 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 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 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);

Table 27 - List of important risks and missing information

Important identified risk	Major bleeding
Important potential risk	Serious hypersensitivity reactions
Missing information	Use in patients with severe hepatic impairment

II.B Summary of important risks

Table 28 - Important identified risk with corresponding risk minimization activities: Major bleeding

Major 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. The risk of bleeding is expected, based on the pharmacologic mode of action of caplacizumab. Cases of Major bleeding, including life-threatening and fatal bleeding have been reported in patients receiving caplacizumab in the postmarketing setting, mainly in those using concomitant anti-platelet agents or anticoagulants.
Major bleeding	
Risk factors and risk groups	Patients with aTTP are at increased risk for bleeding due to the profound thrombocytopenia caused by the disease itself. This risk is increased by caplacizumab treatment due to its mechanism of action. A further increase of the bleeding risk through concomitant administration of anticoagulant medications such as heparin, DOACs or vitamin K antagonists is supported by the evidence of spontaneous reports from the postmarketing experience. Patients with underlying coagulopathies (eg, hemophilia, other coagulation factor deficiencies) are also at increased risk of bleeding, as are patients undergoing surgery, invasive dental procedures, or other invasive interventions. Patients with severe liver disease or other disorders affecting coagulation status are expected to be at higher risk of bleeding when treated with products affecting blood clotting such as caplacizumab.
Risk minimization measures	**Routine risk minimization measures:** SmPC sections 4.4, 4.8 and 4.9 PIL sections 2 and 4 Legal status: Medicinal product subject to restricted medical prescription. **Additional risk minimization measures:** Patient alert card

aTTP: Acquired Thrombotic Thrombocytopenic Purpura; DOAC: Direct Oral Anticoagulant; PIL: Patient Information Leaflet; SmPC: Summary of Product Characteristics.

Table 29 - Important potential risk with corresponding risk minimization activities: Serious hypersensitivity reactions

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 minimization measures	**Routine risk minimization measures:** SmPC section 4.3 PIL sections 2 and 4 Legal status: Medicinal product subject to restricted medical prescription. **Additional risk minimization measures:** None

PIL: Patient Information Leaflet; SmPC: Summary of Product Characteristics.

Table 30 - Missing information with corresponding risk minimization activities: Use in patients with severe hepatic impairment

Use in patients with severe hepatic impairment	
Risk minimization measures	**Routine risk minimization measures:** SmPC section 4.2 and 4.4 PIL section 2 Legal status: Medicinal product subject to restricted medical prescription **Additional risk minimization measures:** None

PIL: Patient Information Leaflet; SmPC: Summary of Product Characteristics.

II.C Post-authorization development plan

II.C.I *Studies which are conditions of the marketing authorization*

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

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

There are no studies required for CABLIVI.