RMP Summary

Alhemo®
(Concizumab)

Based on: Global RMP v1.0 (VV-PVG-028635)

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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 Alhemo® 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 Alhemo® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Novo Nordisk Pharma AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Alhemo®.

6 Summary of the risk management plan for concizumab

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

Alhemo® Product Information gives essential information to healthcare professionals and patients on how Alhemo® should be used.

Important new concerns or changes to the current ones will be included in updates of Alhemo® RMP.

6.1 The medicine and what it is used for

Alhemo® is authorized for routine prophylaxis to prevent or reduce the frequency of bleeding in patients ≥ 12 years of age with haemophilia A or B with inhibitors (see Product Information for the full indication). It contains concizumab as the active substance and it is given by the subcutaneous route of administration.

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

Important risks of Alhemo®, together with measures to minimise such risks and the proposed studies for learning more about Alhemo® 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 Product Information 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 public (e.g. with or without prescription) can help to minimises its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse events 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 Alhemo® is not yet available, it is listed under 'missing information' below.

6.2.1 List of important risks and missing information

Important risks of Alhemo® 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 Alhemo®.

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).

Table 6-1 List of important risks and missing information

List of important risks and missing information	
Important identified risks	• Hypersensitivity reactions
Important potential risks	• Thromboembolic events
Missing information	• Use in female patients, pregnancy and lactation • Management of patients on concizumab in connection with major surgery • The safety of concizumab in patients receiving ITI

6.2.2 Summary of important risks

An overview of important identified and important potential risks and missing information for Alhemo® is provided in Table 6-2 and Table 6-3, respectively.

Table 6-2 Important identified and potential risks

Important identified risk: Hypersensitivity reactions	
Evidence for linking the risk to the medicine	This is a class risk for all protein-based medicinal products. Anaphylactic reactions towards therapeutic monoclonal antibodies have been reported in the literature but are rare. Hypersensitivity/allergic reactions, including hypersensitivity events, injection site reactions, eczema, rash and urticaria, have been observed across the multiple-dose clinical trials in patients with haemophilia (HA, HAwI or HBwI) on treatment with concizumab. Most (97%) of the events were reported as non-serious; 3% were reported as serious.
Risk factors and risk groups	Patients with known hypersensitivity to concizumab or any of the excipients are at higher risk. The risk of hypersensitivity reactions is expected to be higher with the initial administrations compared with subsequent administrations.
Risk minimisation measures	*Routine risk minimisation measures:* The identified risk of hypersensitivity reactions is addressed in the product information including the package leaflet/patient information. Known hypersensitivity to the active substance or any of the excipients is listed under contraindications in the product information. *Additional risk minimisation measures: None*
Additional pharmacovigilance activities	*Additional pharmacovigilance activities*: Registry-based cohort study

Important potential risk: Thromboembolic events	
Evidence for linking the risk to the medicine	Thrombosis formation consistent with an exaggerated pharmacological effect was observed in repeat-dose toxicology studies conducted in normocoagulant cynomolgus monkeys at high concizumab exposures. Thromboembolic events in patients on concizumab treatment were reported in all three haemophilia subtypes (HA, HAwI and HBwI) across four multiple-dose clinical trials with no indication of an increased risk of thromboembolic events across any single haemophilia subtype (HAwI [1.3%, 0.0 events per PYE], HBwI [1.9%, 0.0 events per PYE] and HA [1.9%, 0.0 events per PYE]).
Risk factors and risk groups	Possible risk factors include a history of thromboembolic events, thromboembolism in the family, obesity, arrhythmias, hypertension, diabetes, hypercholesterolaemia, smoking, post-surgical status, immobilisation, infection, liver disease and old age. In general, patients with a pathological condition in which Tissue Factor is expressed more extensively than considered physiological, e.g., advanced atherosclerosis, cancer, crush injury, or septicaemia, may be at a higher risk of developing thromboembolic events.
Risk minimisation measures	*Routine risk minimisation measures:* Information is provided in the product information on the occurrence of non-fatal thromboembolic events in patients on concizumab in the concizumab clinical trials. The patients had multiple risk factors for the development of thromboembolic events. Information on how to detect early signs of thromboembolic events is included in the product information including the package leaflet/patient information *Additional risk minimisation measures: None*
Additional pharmacovigilance activities	*Additional pharmacovigilance activities:* *Registry-based cohort study*

Abbreviations: CCDS = company core data sheet; HA = haemophilia A; HAwI = haemophilia A with FVIII inhibitors; HBwI = haemophilia B with FIX inhibitors; PL = package leaflet; PASS = post-authorisation safety study; PYE = patient-years of exposure; RMP = risk management plan.

Table 6-3 Missing information

Use in female patients, pregnancy and lactation	
Risk minimisation measures	*Routine risk minimisation measures:* Lack of experience in this population is mentioned in the product information (Information regarding fertility, pregnancy and lactation). This section also includes the recommendation that women of childbearing potential receiving concizumab should use highly effective contraceptives during treatment with concizumab and until 7 weeks after end of treatment. *Additional risk minimisation measures: None*

Management of patients on concizumab in connection with major surgery	
Risk minimisation measures	*Routine risk minimisation measures:* The limited experience with concizumab in patients undergoing major surgery is mentioned in the product information. The product information also states that a physician experienced in treatment of haemophilia and/or bleeding disorders should be consulted in connection with major surgery and that it is generally recommended to pause concizumab prior to major surgery due to the limited experience. *Additional risk minimisation measures: None*
The safety of concizumab in patients receiving ITI	
Risk minimisation measures	*Routine risk minimisation measures:* Lack of experience with concizumab in this population is mentioned in the product information (Section on dosage). *Additional risk minimisation measures: None*

6.2.3 Post-authorisation development plan

6.2.3.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Alhemo®.

6.2.3.2 Other studies in post-authorisation development plan

There are no studies required for Alhemo®.