WAINZUA®

Solution for injection
45 mg/0.8 ml (56 mg/ml)

Summary of the Risk Management Plan (RMP) for WAINZUA® (eplontersen)

Document version: 1.0

Document date: 14 February 2025

Based on EU RMP version 1.2 (DLP 07 Apr 2023)

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 eplontersen WAINZUA® 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 eplontersen WAINZUA® in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. AstraZeneca AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of eplontersen WAINZUA®.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR WAINZUA® (EPLONTERSEN)

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

WAINZUA's SmPC and its package leaflet give essential information to healthcare professionals and patients on how WAINZUA should be used.

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

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

I.1 THE MEDICINE AND WHAT IT IS USED FOR

The indication of WAINZUA is for the treatment of adult patients with stage 1 and 2 polyneuropathy associated with hereditary transthyretin-mediated amyloidosis (ATTRv). It contains eplontersen as the active substance and is administered as subcutaneous injection solution.

I.2 RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

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

I.2.1 List of important risks and missing information

Important risks of WAINZUA 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 WAINZUA. 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 1 List of important risks and missing information

Important identified risks	None
Important potential risks	Ocular Adverse Events due to Vitamin A Deficiency
Missing information	Use in pregnancy Long-term use safety

I.2.2 Summary of important risks

Table 2 Important potential risk: Ocular Adverse Events due to Vitamin A Deficiency

Evidence for linking the risk to the medicine	The assessment of ocular adverse events due to vitamin A deficiency was conducted through a non-specific, concatenated MedDRA search that included a predefined set of PTs for either vitamin A deficiency or ocular adverse events. This search strategy was used as a screening tool for potential events and is non-specific, so none of the events identified were definitively ocular adverse events specifically related to vitamin A deficiency. Based on the search strategy, the incidence of ocular adverse events potentially related to vitamin A deficiency (adverse events of special interest) was 27.1% (n = 39) in the Up to Week 66 Eplontersen group compared with 15.0% (n = 9) in the external placebo group. Main contributors to the imbalance were vitamin A deficiency and vitamin A decreased. It should be noted that vitamin A laboratory values were available to the Investigator in the eplontersen group in Study ION-683844-CS3 while they were blinded to the investigator during ISIS 420915-CS2 (External Placebo). Hence no TEAEs of vitamin A decreased or vitamin A deficiency were reported in the external placebo group. Excluding these two PTs, the incidence of ocular AESIs was similar between the Up to Week 66 Eplontersen group (16.7 % [n=24])) and the external placebo group (15.0 % [n=9]).
Risk factors and risk groups	Patients with a clinical history of vitamin A deficiency.

Table 2 Important potential risk: Ocular Adverse Events due to Vitamin A Deficiency

Risk minimisation measures	Routine risk minimisation measures: • SmPC Section “Warnings and precautions” • PIL section “When is caution required when using WAINZUA?” • Guidance on the investigation of signs and symptoms of vitamin A deficiency and the need for evaluation of ocular signs or symptoms of vitamin A deficiency prior to initiation of eplontersen treatment in SmPC Section “Warnings and precautions” and PIL Section “When is caution required when using WAINZUA?” • Recommendation for oral supplementation of vitamin A in SmPC Section “Warnings and precautions” and PIL Section “When is caution required when using WAINZUA?” • Guidance on the ocular symptoms that should trigger an ophthalmology referral in SmPC “Warnings and precautions” • Legal status (prescription only medication) Additional risk minimisation measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • None

AESI = Adverse Event of Special Interest; MedDRA = Medical Dictionary for Regulatory Activities; PIL = Patient Information Leaflet; PT = Preferred Term; SmPC = Summary of Product Characteristics; TEAE = Treatment-Emergent Adverse Event.

Table 3 Missing information: Use in Pregnancy

Risk minimisation measures	Routine risk minimisation measures: • SmPC Sections “Warnings and precautions” and ‘‘Pregnancy, lactation” • PIL Section “Can WAINZUA be used during pregnancy and breast-feeding?” • Recommendation that pregnancy should be excluded prior to initiation of treatment, that women of childbearing potential should practice effective contraception during treatment, and details of actions that should be taken should a woman intend to become pregnant or should an unplanned pregnancy occur during eplontersen treatment in SmPC Section ”Pregnancy, lactation” and PIL Section ”Can WAINZUA be used during pregnancy and breast-feeding?” • Legal status (prescription only medication) Additional risk minimisation measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities • D8451R00002: EPPRO - Surveillance Program of Women and Their Offspring Exposed to Eplontersen During Pregnancy

Table 4 Missing information: Long-term Safety

Risk minimisation measures	Routine risk minimisation measures: • None Additional risk minimisation measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities • ION-682884-CS13 - An Open-Label, Extension Study to Assess the Long-Term Safety and Efficacy of ION-682884 in Patients with Hereditary Transthyretin-Mediated Amyloid Polyneuropathy

I.2.3 Post-authorisation development plan

I.2.3.1 Studies that are conditions of the marketing authorisation

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

I.2.3.2 Other studies in post-authorisation development plan

D8451R00002

EPPRO - Surveillance Program of Women and Their Offspring Exposed to Eplontersen During Pregnancy.

The primary objective is to estimate the proportion (incidence proportion) of major congenital malformations in offspring and adverse pregnancy outcomes of women with ATTRv-PN exposed to eplontersen.

The secondary objective is to describe the socio-demographic and health-related characteristics of the study population and estimate the proportion (incidence proportion) of minor congenital malformations and foetal/neonatal adverse outcomes in offspring of women with ATTRv-PN exposed to eplontersen.

Eplontersen open-label extension study (ION-682884-CS13)

Study title: An Open-Label, Extension Study to Assess the Long-Term Safety and Efficacy of ION-682884 in Patients with Hereditary Transthyretin-Mediated Amyloid Polyneuropathy

Purpose of the study: The study continues to collect and monitor events of interest (i.e., thrombocytopenia, renal impairment, hepatic impairment) and other events of special interest similar to those that were evaluated in the ION-682884-CS3 study. The objectives of the study are the following:

- to evaluate the safety and tolerability of extended dosing with eplontersen in patients with ATTRv-PN.
- to evaluate the efficacy of extended dosing with eplontersen.