

Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for TOLVAPTAN 15 mg and 30 mg oral tablets

This is a summary of the risk management plan (RMP) for TOLVAPTAN 15 mg and 30 mg oral tablets, (hereinafter referred to as Tolvaptan). The RMP details important risks of Tolvaptan, how these risks can be minimised, and how more information will be obtained about Tolvaptan's risks and uncertainties (missing information).

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

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

I. The Medicine and What It is used for

Tolvaptan is authorised for the treatment of hyponatremia secondary to the syndrome of inappropriate antidiuretic hormone secretion (see SmPC for the full indication). It contains tolvaptan as the active substance and it is given orally.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

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

II.A List of Important Risks and Missing Information

Important risks of Tolvaptan are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. 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 Tolvaptan. 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 4: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	<ul style="list-style-type: none"> • Volume depletion, dehydration and associated sequelae such as renal dysfunction • Too rapid rise of serum sodium and neurologic sequelae (encephalopathy, osmotic demyelination) • Interaction with CYP3A4 inhibitors
Important potential risks	<ul style="list-style-type: none"> • Raised intraocular pressure/glaucoma
Missing information	<ul style="list-style-type: none"> • Paediatric use • Pregnancy outcome data • Use in breastfeeding • Off-label use • Use in hepatic impaired patients

II.B Summary of Important Risks

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

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 obligation of Tolvaptan.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Tolvaptan.