Public Summary of the Risk Management Plan (RMP)

SAMSCA® (tolvaptan)

Film-coated tablets: 7.5mg, 15mg, 30mg

Based on Part VI of EU RMP Version 15.0

Document Date: 02 Oct 2023

Marketing Authorisation Holder:
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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 Samsca 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 Samsca in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic. Otsuka Pharmaceuticals (Switzerland) GmbH is fully responsible for the accuracy and correctness of the content of the published RMP summary of Samsca.

1.1 Summary of the Risk Management Plan for Samsca

1.1.1 VI.1: Summary of the Risk Management Plan for Samsca

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

Samsca's prescribing information and its package leaflet give essential information to healthcare professionals and patients on how this product should be used.

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

1.1.2 I: The Medicine and What it is Used for

Samsca is authorised in Switzerland under indication to be used in adults to treat hyponatremia as a secondary consequence of the syndrome of inadequate secretion of antidiuretic hormone (SIADH). It contains tolvaptan as the active substance and it is given by oral tablet administration.

1.1.3 II: Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Samsca, together with measures to minimise such risks and the proposed studies for learning more about its 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 prescribing 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 patient (eg, prescription only) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In the case of Samsca, these 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 Samsca is not yet available, it is listed under 'missing information' below.

1.1.3.1 II.A: A List of Important Risks and Missing Information

Important risks of Samsca 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 Samsca. 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 1.1.3.1-1 II.A-1: List of Important Risks and Missing Information for Samsca (from Part II: Module SVIII)	
Important identified risks	• Volume depletion, dehydration and associated sequelae such as renal dysfunction
Important potential risks	• None
Missing information	• Pregnancy outcome data • Off-label use • Use in hepatic impaired patients

1.1.3.2 II.B: Summary of Important Risks for Samsca

Table 1.1.3.2-1 Important Identified Risk: Volume Depletion, Dehydration and Associated Sequelae such as Renal Dysfunction	
Evidence for linking the risk to the medicine	**Hyponatraemia** Tolvaptan Clinical Trials: All Heart Failure and Hyponatraemia subjects from controlled Phase 2 and 3 multiple dose trials. CTD Modules 2.5 Clinical Overview and 2.7.4 Summary of Clinical Safety.
Risk factors and risk groups	Patients with an inability or a compromised capacity to perceive and communicate thirst would be at risk of severe dehydration without appropriate medical intervention. This would include bedridden and unconscious subjects. Patients who are concomitantly treated with diuretics may be at risk of severe dehydration and subsequent renal impairment. Special populations which may be at higher risk also include those with a fluid overload in extravascular compartments, but with intravascular contraction. These groups include subjects with hepatic cirrhosis, and potentially some subjects with heart failure.
Risk minimisation measures	**Routine risk minimisation measures:** **Samsca Prescribing Information** • **Section: Contraindications** • **Section: Warnings and Precautions**

Table 1.1.3.2-1	Important Identified Risk: Volume Depletion, Dehydration and Associated Sequelae such as Renal Dysfunction
	Samsca Package Leaflet (PL) • **Section: When should Samsca not be taken?** • **Section: When is caution advised when taking Samsca?** • **Section: What side effects can Samsca have?** • Prescription only medicine **Additional risk minimization measures**: • None **Additional pharmacovigilance activities**: • None

Table 1.1.3.2-2	Missing Information: Pregnancy Outcome Data
Risk minimisation measures	**Routine risk minimisation measures:** **Samsca Prescribing Information** • **Section: Contraindications** • **Section: Pregnancy, lactation** **Samsca Package Leaflet (PL)** • **Section: When should Samsca not be taken?** • **Section: When is caution advised when taking Samsca?** • **Section: Can Samsca be taken during pregnancy or while breastfeeding?** • Prescription only medicine **Additional risk minimisation measures:** • None **Additional pharmacovigilance activities**: • None

Table 1.1.3.2-3 Missing Information: Off-label Use	
Risk minimisation measures	**Routine risk minimisation measures:** **Samsca Prescribing Information** • **Section: Indication/Uses** • **Section: Dosage/Administration** **Samsca Package Leaflet (PL)** • **Section: What is Samsca and what is it used for** • Prescription only medicine **Additional risk minimisation measures:** • None **Additional pharmacovigilance activities**: • None

Table 1.1.3.2-4 Missing Information: Use in Hepatic Impaired Patients	
Risk minimisation measures	**Routine risk minimisation measures:** **Samsca Prescribing Information** • **Section: Dosage/Administration** • **Section: Warnings and Precautions** • **Section: Pharmacokinetics** **Samsca Package Leaflet (PL)** • **Section: When should Samsca not be taken?** • **Section: When is caution advised when taking Samsca?** • **Section: What side effects can Samsca have?** • Prescription only medicine **Additional risk minimisation measures:** • None **Additional pharmacovigilance activities:** • None

1.1.4 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 for Samsca.