

Risk Management Plan
For
Tolvaptan Accord 7.5 mg tablets
Tolvaptan Accord 15 mg tablets
Tolvaptan Accord 30 mg tablets
(Tolvaptan)

RMP version to be assessed as part of this application:

RMP Version number	2.0
Data lock point for this RMP	06-Jul-2026
Date of final sign off	05-Aug-2026

Rationale for submitting an RMP: This Risk Management Plan (RMP) has been updated in-line with European Public Assessment Report (EPAR)-RMP of reference product Samsca (Tolvaptan) (Version 15.3, dated 05-Feb-2026) published by EMA on 01-Jun-2026.

Summary of significant changes in this RMP: Significant changes have been made in the following sections of the RMP: Part II (Module SVII and SVIII), Part VI and Part VII (Annex 7 and Annex 8).

Other RMP versions under evaluation: Not applicable

Details of the currently approved RMP:

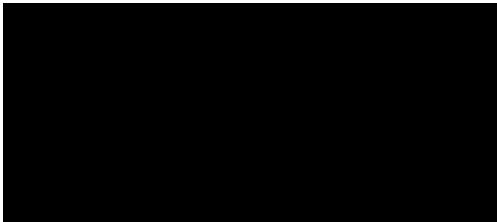
Version Number	Approved with procedure	Date of approval (opinion date)
1.2	Centralised procedure (H0005961)	26-Jan-2023

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QPPV Name: Agata Gesiewicz

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Part I: Products Overview

Table 1: Product Overview

Active substance (INN or common name)	Tolvaptan
Pharmacotherapeutic group(s) (ATC Code)	Pharmacotherapeutic group: Diuretics, vasopressin antagonists ATC code: C03XA01
Marketing Authorisation Holder	Accord Healthcare S.L.U., Spain
Medicinal products to which this RMP refers	03
Invented names in the European Economic Area (EEA)	Tolvaptan Accord 7.5 mg tablets Tolvaptan Accord 15 mg tablets Tolvaptan Accord 30 mg tablets
Marketing authorisation procedure	Centralised procedure (H0005961)
Brief description of the product	<i>Chemical class:</i> Tolvaptan is a vasopressin 2 receptor antagonist which is used for short term treatment of severe hyponatremia in patients with heart failure, cirrhosis or syndrome of inappropriate secretion of antidiuretic hormone (SIADH).
	<u>Summary of mode of action:</u> Tolvaptan is a selective vasopressin V2-receptor antagonist that specifically blocks the binding of arginine vasopressin (AVP) at

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	the V2-receptor of the distal portions of the nephron. Tolvaptan affinity for the human V2-receptor is 1.8 times that of native AVP.
	<u>Important information about its composition</u> <i>Tolvaptan Accord 7.5 mg tablets</i> Each tablet contains 7.5 mg tolvaptan. <i>Excipient with known effect:</i> 17.5 mg lactose (as monohydrate) per tablet <i>Tolvaptan Accord 15 mg tablets</i> Each tablet contains 15 mg tolvaptan. <i>Excipient with known effect:</i> 35 mg lactose (as monohydrate) per tablet <i>Tolvaptan Accord 30 mg tablets</i> Each tablet contains 30 mg tolvaptan. <i>Excipient with known effect:</i> 70 mg lactose (as monohydrate) per tablet
Hyperlink to the Product Information	Refer Module 1.3.1 for SmPC and PIL
Indications in the EEA	Current Tolvaptan is indicated in adults for the treatment of hyponatremia secondary to the syndrome of inappropriate antidiuretic hormone secretion (SIADH).
Dosage in the EEA	Current

	Due to the need for a dose titration phase with close monitoring of serum sodium and volume status, treatment with Tolvaptan Accord has to be initiated in hospital. Posology Tolvaptan has to be initiated at a dose of 15 mg once daily. The dose may be increased to a maximum of 60 mg once daily as tolerated to achieve the desired level of serum sodium. For patients at risk of overly rapid correction of sodium e.g. patients with oncological conditions, very low baseline serum sodium, taking diuretics, or taking sodium supplementation a dose of 7.5 mg should be considered. During titration, patients must be monitored for serum sodium and volume status. In case of inadequate improvement in serum sodium levels, other treatment options have to be considered, either in place of or in addition to tolvaptan. Use of tolvaptan in combination with other options may increase the risk of overly rapid correction of serum sodium. For patients with an appropriate increase in serum sodium, the underlying disease and serum sodium levels must be monitored at regular intervals to evaluate further need of tolvaptan treatment. In the setting of hyponatremia, the treatment duration is determined by the underlying disease and its treatment. Tolvaptan treatment is expected to last until the underlying disease is adequately treated or until such time that hyponatremia is no longer a clinical issue. Tolvaptan Accord must not be taken with grapefruit juice. <u>Method of administration:</u> Oral use.
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	Administration preferably in the morning, without regard to meals. Tablets must be swallowed without chewing with a glass of water.
Pharmaceutical forms and strengths	Current Pharmaceutical form: Tablets Strengths: 7.5 mg, 15 mg and 30 mg
Is the product subject to additional monitoring in EU?	No

[Redacted]

[Redacted]

[Redacted]

Part II: Safety specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

Not applicable.

Part II: Module SII - Non-clinical part of the safety specification

Not applicable.

Part II: Module SIII - Clinical trial exposure

Not applicable.

Part II: Module SIV - Populations not studied in clinical trials

Not applicable.

SIV.1 Exclusion criteria in pivotal clinical studies within the development programme

Not applicable.

SIV.2 Limitations to detect adverse reactions in clinical trial development programmes

Not applicable.

SIV.3 Limitations in respect to populations typically under-represented in clinical trial development programmes

Not applicable.

Part II: Module SV - Post-authorisation experience

SV.1 Post-authorisation exposure

Not applicable.

Part II: Module SVI - Additional EU requirements for the safety specification

SVI.1 Potential for misuse for illegal purposes

Not applicable

[Redacted]

[Redacted]

[Redacted]

Part II: Module SVII - Identified and potential risks

This Risk Management Plan (RMP) has been updated in-line with European Public Assessment Report (EPAR)-RMP of reference product Samsca (Tolvaptan) (Version 15.3, dated 05-Feb-2026) published by EMA on 01-Jun-2026. There is no change proposed by MAH in these safety concerns mentioned in Module SVIII.

Hence this section remains “Not applicable”.

SVII.1 Identification of safety concerns in the initial RMP submission

Not applicable

SVII.1.1 Risks not considered important for inclusion in the list of safety concerns in the RMP

Not applicable

SVII.1.2. Risks considered important for inclusion in the list of safety concerns in the RMP

Not applicable

SVII.2 New safety concerns and reclassification with a submission of an updated RMP

Not applicable

SVII.3 Details of important identified risks, important potential risks, and missing information

SVII.3.1. Presentation of important identified risks and important potential risks

Not Applicable

SVII.3.2. Presentation of the missing information

Not Applicable

[Redacted]

[Redacted]

[Redacted]

Part II: Module SVIII - Summary of the safety concerns

Table 2: Summary of safety concerns

Important identified risks	Volume depletion, dehydration and associated sequelae such as renal dysfunction
Important potential risks	Reproductive toxicity
Missing Information	None

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities including collection and reporting of adverse reactions and signal detection as stated in pharmacovigilance system master file are sufficient for the mentioned safety concerns.

III.2 Additional pharmacovigilance activities

None proposed

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable

Part IV: Plans for post-authorisation efficacy studies

Not applicable

[Redacted]

[Redacted]

[Redacted]

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

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

V.1. Routine Risk Minimisation Measures

Not applicable

V.2. Additional Risk Minimisation Measures

None proposed

V.3 Summary of risk minimisation measures

Not applicable

[Redacted]

[Redacted]

[Redacted]

Part VI: Summary of the risk management plan**Summary of risk management plan for Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets (Tolvaptan)**

This is a summary of the risk management plan (RMP) for Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets. The RMP details, important risks of Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets, how these risks can be minimised, and how more information will be obtained about Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets' risks and uncertainties (missing information).

Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets should be used.

Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets 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 (EPAR).

Important new concerns or changes to the current ones will be included in updates of Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets' RMP.

I. The medicine and what it is used for

Tolvaptan Accord is indicated in adults for the treatment of hyponatremia secondary to the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

It contains tolvaptan as the active substance and it is given by oral route.

Further information about the evaluation of Tolvaptan Accord 7.5mg, 15mg and 30 mg tablets' benefits can be found in Tolvaptan Accord 7.5 mg, 15mg and 30 mg tablets' EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage <https://www.ema.europa.eu/en/medicines/human/EPAR/tolvaptan-accord>

[REDACTED]

[REDACTED]

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

Important risks of Tolvaptan Accord 7.5 mg,15 mg and 30 mg tablets, together with measures to minimise such risks and the proposed studies for learning more about Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets’ 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*.

II.A List of important risks and missing information

Important risks of Tolvaptan Accord 7.5 mg, 15 mg and 30 mg tablets 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 Tolvaptan Accord 7.5 mg,15 mg and 30 mg tablets. 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 (i.e. Pregnancy outcome data);

[Redacted]

[Redacted]

[Redacted]

List of important risks and missing information	
Important identified risks	• Volume depletion, dehydration and associated sequelae such as renal dysfunction
Important potential risks	• Reproductive toxicity
Missing Information	• None

II.B Summary of important risks

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

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 authorization or specific obligation of ‘Tolvaptan Accord 7.5mg, 15mg and 30 mg tablets’

II.C.2 Other studies in post-authorisation development plan

There are no studies required for ‘Tolvaptan Accord 7.5 mg,15 mg and 30 mg tablets.’