PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR SIBNAYAL

This is a summary of the risk management plan (RMP) for SIBNAYAL® also called during development ADV7103. The RMP details important risks of SIBNAYAL, how these risks can be minimised, and how more information will be obtained about SIBNAYAL's risks and uncertainties (missing information).

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

This summary of the RMP for SIBNAYAL 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 SIBNAYAL's RMP.

I. The medicine and what it is used for

SIBNAYAL is indicated for treatment of distal renal tubular acidosis (dRTA) in patients aged one year and older (see SmPC for the full indication). It is a fixed combination of two active substances, potassium citrate and potassium hydrogen carbonate, as prolonged release granules which when orally administered, are slowly released throughout the gastro-intestinal tract, providing a prolonged effect for 12 hours after administration allowing a twice daily administration.

Further information about the evaluation of SIBNAYAL's benefits can be found in SIBNAYAL's 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/sibnayal.

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

Important risks of SIBNAYAL, together with measures to minimise such risks and the proposed studies for learning more about SIBNAYAL'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.

ADVICENNE does not plan to perform any risk minimisation activities in relation to the use of SIBNAYAL other than routine risk minimisation 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*.

ADVICENNE does not plan to perform any pharmacovigilance activities outside of routine activities and measures in relation to SIBNAYAL nor has ADVICENNE received any request to perform any such activity.

II.A List of important risks and missing information

Important risks of SIBNAYAL 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 SIBNAYAL.

Potential risks of SIBNAYAL 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).

List of important risks and missing information	
Important identified risks	Risk of hyperkalaemia when used in patients with comorbidities such as renal impairment
Important potential risks	None
Missing information	None

II.B Summary of important risks

Important identified risks

Risk of hyperkalaemia when used in patients with comorbidities such as renal impairment	
Evidence for linking the risk to the medicine	The use of SIBNAYAL in patients with severe renal impairment, or any other condition which may significantly reduce renal potassium excretion, may lead to accumulation of potassium leading to hyperkalaemia, which can be life threatening in severe cases.
Risk factors and risk groups	Certain groups, particularly those with impaired kidney excretion of potassium, are sensitive to adverse effects of increasing potassium intake on heart function associated with increases in plasma potassium. The effects of potassium are seen earlier and are more pronounced when underlying conduction defects are already present, such as in the elderly with cardiac disease and those patients taking pharmacological cardiac depressants.

Risk minimisation measures	Routine risk minimisation measures • *SmPC section 4.2* • *SmPC section 4.4* • *SmPC section 4.6* • *SmPC section 4.9* • *PL section 2 (Warnings and precautions)*

Important potential risks

Not applicable.

II.C Post-authorisation development plan

Not applicable.