

Part VI: Summary of the risk management plan

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

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

I. The medicine and what it is used for

MANASA is indicated for:

secondary prevention of cardiovascular events, as substitution therapy for adult patients who are adequately controlled therapy with the components administered concomitantly at equivalent therapeutic doses.

Posology

The recommended dose of Rosuvastatin calcium/ Acetylsalicylic acid 5 mg/100 mg, 10 mg/100 mg, 20 mg/100 mg, hard capsules is one capsule per day.

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

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

If important information that may affect the safe use of MANASA is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of MANASA 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 MANASA. 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);

List of important risks and missing information	
Important identified risks	– None
Important potential risks	- Hepatic failure (including hepatic necrosis and fulminant hepatitis)
Missing information	– None

II.B Summary of important risks

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

Liver impairment (Hepatic failure, including hepatic necrosis and fulminant hepatitis)	
Evidence for linking the risk to the medicine	Liver toxicity is a well recognized adverse effect of treatment with statins[1]. However pre-marketing studies have suggested that rosuvastatin may have a lesser potential to cause liver toxicity as compared with other statins.
Risk factors and risk groups	The mild ALT elevations associated with rosuvastatin therapy are usually self-limited and do not require dose modification; rosuvastatin should be stopped if ALT levels rise above 10-fold the ULN, or persist in being above 5-fold elevated or are associated with symptoms. In the clinically apparent liver injury attributed to rosuvastatin, recovery is usually complete within 1 to 2

	months. Recurrence of injury with rechallenge has been reported and should be avoided. Cases of chronic hepatitis, but no instances of acute liver failure or vanishing bile duct syndrome, attributable to rosuvastatin have been reported. In cases of autoimmune hepatitis-like injury, corticosteroids have been used when recovery does not occur promptly. If corticosteroids are used, the dose and duration of treatment should be kept to a minimum, and careful followed up after stopping is essential.
Risk minimisation measures	<p><i>Routine risk minimisation measures</i></p> <p>The safety information in the proposed product information is aligned to the reference medicinal product.</p> <p>SmPC section 4.3.</p> <p>PIL section Contraindications, Undesirable effects</p> <p>No risk minimisation measure</p>

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 MANASA.

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

There are no studies required for MANASA.