Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for Lusutrombopag Shionogi (lusutrombopag)

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

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

This summary of the RMP for Lusutrombopag Shionogi 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 Lusutrombopag Shionogi's RMP.

I. The Medicine and What it is Used for

Platelets are needed to help you stop bleeding. Lusutrombopag Shionogi is authorised to treat thrombocytopenia (low platelet count) in patients with chronic liver disease before undergoing invasive procedures (surgery) (see SmPC for the full indication). It contains lusutrombopag as the active substance and it is given by mouth.

Further information about the evaluation of Lusutrombopag Shionogi's benefits can be found in Lusutrombopag Shionogi'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/lusutrombopag-shionogi

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

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

II.A List of Important Risks and Missing Information

Important risks of Lusutrombopag Shionogi 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 Lusutrombopag Shionogi. 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	Thrombotic/thromboembolic complications
Important Potential Risks	None
Missing Information	Use in Pregnant or lactating women; Use in patients with Child-Pugh class C liver disease Use in patients with a history of splenectomy Use in patients concomitantly receiving interferon preparations Repeated use for invasive procedures Safety in patients requiring highly invasive procedures Off label use in long term treatment

II.B Summary of Important Risks

Important Identified Risk: Thrombotic/Thromboembolic Complications	
Evidence for Linking the Risk to the Medicine	Eltrombopag publically available data including the ELEVATE study (Afdhal et al, 2012).
Risk Factors and Risk Groups	The risk for thrombosis/thromboembolism may increase in the following patient groups: • Patients with current thrombosis or thromboembolism • Patients with a history of thrombosis and thromboembolism • Patients already in a prothrombotic state • *Patients with absence of hepatopetal blood flow in the main trunk of the portal vein.*
Risk Minimisation Measures	Routine risk minimisation measures: *SmPC Section 4.4 and 4.8* *PL Section 2 and 4*

Missing Information: Use in Pregnant or lactating Women	
Risk Minimisation Measures	Routine risk minimisation measures: *SmPC Section 4.6* *PL Section 2*

Missing Information: Use in Patients with Child-Pugh Class C Liver Disease	
Risk Minimisation Measures	Routine risk minimisation measures: *SmPC Section 4.2, 4.4 and 5.2* *PL Section 2*
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Lusutrombopag Shionogi Child Pugh Class C PASS See section II.C of this summary for an overview

	of the post-authorisation development plan.

Missing Information: Use in Patients with History of Splenectomy	
Risk Minimisation Measures	Routine risk minimisation measures: *SmPC Section 4.4* *PL Section 2*

Missing Information: Use in Patients concomitantly receiving interferon preparations	
Risk Minimisation Measures	Routine risk minimisation measures: *SmPC Section 4.4* *PL Section 2*

Missing Information: Repeated Use for invasive procedures	
Risk Minimisation Measures	Routine risk minimisation measures: *SmPC Section 5.1*

Missing Information: Safety in patients requiring Highly invasive procedures	
Risk Minimisation Measures	Routine risk minimisation measures: *SmPC Section 4.4*

Missing Information: Off label use in long-term treatment	
Risk Minimisation Measures	Routine risk minimisation measures: *SmPC Section 4.2* *PL Section 2*

II.C Post-authorisation Development Plan

II.C.1 Studies which are Conditions of the Marketing Authorisation

Not Applicable

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

Lusutrombopag Shionogi Child-Pugh Class C PASS

Purpose of the study:

Limited numbers of patients with Child-Pugh class C liver disease were studied during the Lusutrombopag Shionogi clinical trials. As these patients have complex coagulation profiles, the safety of Lusutrombopag Shionogi in such patients will be assessed in this study.

The key study questions are

1. The extent to which platelets are raised in patients with Child Pugh Class C liver disease following the use of Lusutrombopag Shionogi or platelets
2. Whether the use of Lusutrombopag Shionogi or platelets in these patients is associated with elevations in liver enzymes
3. The temporal course of such elevations if they occur.