PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

A summary of the RMP for evolocumab is presented below.

Summary of Risk Management Plan for Repatha® (Evolocumab)

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

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

This summary of the RMP for Repatha should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of 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 Repatha's RMP.

I. The Medicine and What it is Used for

Repatha is authorized for homozygous familial hypercholesterolaemia, hypercholesterolaemia and mixed dyslipidaemia, and established atherosclerotic cardiovascular disease (see SmPC for the full indication). It contains evolocumab as the active substance and it is given by subcutaneous injection.

Further information about the evaluation of Repatha's benefits can be found in Repatha's EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/Repatha.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of Repatha, together with measures to minimize such risks and the proposed studies for learning more about Repatha's risks, are outlined below.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorized 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 public (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute *routine risk minimization* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed including periodic safety update report (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 Repatha is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Repatha are risks that need special risk management activities to further investigate or minimize 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 Repatha. 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).

List of important risks and missing information	
Important identified risks	None
Important potential risks	None
Missing information	• Use in pregnant/lactating women • Long-term use including effects of low-density lipoprotein cholesterol < 40 mg/dL (< 1.03 mmol/L)

II.B. Summary of Important Risks

Missing information: Use in pregnant/lactating women	
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.6, where advice is given that Repatha should not be used during pregnancy unless the clinical condition of the woman requires treatment with evolocumab • PL Section 2 Additional risk minimization measures: • None

Missing information: Long-term use including effects of low-density lipoprotein cholesterol < 40 mg/dL or < 1.03 mmol/L	
Risk minimization measures	Routine risk minimization measures: • Section 5 Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Study 20130295 • Study 20160250 See Section II.C of this summary for an overview of the postauthorization development plan.

II.C. Postauthorization Development Plan

II.C.1. Studies Which Are Conditions of the Marketing Authorization

There are no studies which are conditions of the marketing authorization or specific obligation of Repatha.

II.C.2 Other Studies in Postauthorization Development Plan

Study Short Name	Purpose of the Study
Study 20130295	To characterize the safety and tolerability of extended long-term administration of evolocumab in subjects having received evolocumab or placebo in the completed FOURIER trial Safety concerns addressed: Long-term use including effects of LDL-C < 40 mg/dL or < 1.03 mmol/L
Study 20160250	To describe the safety and tolerability of long-term administration of evolocumab in a cohort of Western European subjects having received evolocumab or placebo in the completed FOURIER trial Safety concerns addressed: Long-term use including effects of LDL-C < 40 mg/dL or < 1.03 mmol/L