PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR REBETOL (RIBAVIRIN)

This is a summary of the risk management plan (RMP) for Rebetol. The RMP details important risks of Rebetol, and how these risks can be minimised.

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

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

I. The Medicine and What it is Used For

Rebetol is authorised in combination with other medicines for the treatment of chronic hepatitis C (see SmPC for the full indication). It contains ribavirin as the active substance and it is given by oral route of administration.

Further information about the evaluation of Rebetol's benefits can be found in Rebetol's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: Rebetol's EPAR page

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

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

Since its approval in the EU in 1999, the safety profile of Rebetol has been well-characterized. There are no studies planned or warranted to further characterize any identified or potential risk that would alter the established risk-benefit profile for Rebetol. There are also no additional risk minimization activities planned or warranted beyond communication of the safety profile in the SmPC and package leaflet. As such, other than teratogenicity effect in the fetus, there are no important safety concerns (important identified or potential risks or missing information) for which prospective additional risk management is planned.

Table II.A.1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	Teratogenicity effect on the fetus
Important potential risks	None
Missing information	None

II.B Summary of Important Risks

The safety information for Rebetol is provided in the Product Information.

Table II.B.1: Important Identified Risk of Teratogenicity Effect on The Fetus

Evidence for linking the risk to the medicine	Animal studies indicate a teratogenic and or embryocidal effect of RBV, the risks in humans have not been evaluated systematically.
Risk factors and risk groups	Based on data from an ongoing pregnancy registry, birth defect (congenital anomaly) rates were reported in approximately 9% of live births from pregnancies in women directly exposed to ribavirin, and in approximately 6% of live births from women indirectly exposed (by male partner) to ribavirin. The observed birth defect rates are higher than the estimated background incidence of major structural or genetic birth defects affect approximately 3% of births in the general population in the United States [Ref. 5.4: 03RM4G].
Risk minimisation measures	Routine risk communication: - SmPC sections 4.3, 4.4, 4.6 and 5.3 - PL Section 2 - Contraindication in pregnancy is included in SmPC section 4.3 and PL section 2. - Recommendations for female of childbearing potential, and for men whose partners are pregnant (or childbearing potential) are included in SmPC sections 4.4 and 4.6; and in PL section 2. Additional risk minimization measures: None
Additional pharmacovigilance activities	None

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 of Rebetol.

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

There are no studies required for Rebetol.