Summary of the Risk Management Plan (RMP) for REKAMBYS® (Rilpivirine prolonged-release suspension)

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Disclaimer:

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of REKAMBYS® is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of REKAMBYS® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Janssen-Cilag AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of REKAMBYS®.

Summary of risk management plan for REKAMBYS®

This is a summary of the Risk Management Plan (RMP) for REKAMBYS®. The RMP details important risks of REKAMBYS®, how these risks can be minimized, and how more information will be obtained about REKAMBYS®'s risks and uncertainties (missing information).

REKAMBYS®'s Summary of Product Characteristics (SmPC) and its Package Leaflet (PL) provide essential information to healthcare professionals (HCPs) and patients on how REKAMBYS® should be used.

This summary of the RMP for REKAMBYS® 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 REKAMBYS®'s RMP.

I. The medicine and what it is used for

REKAMBYS® is authorized, in combination with cabotegravir injection, for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen, without present or past evidence of viral resistance to, and no prior virological failure with, agents of the non-nucleoside reverse transcriptase inhibitor and integrase inhibitor class (see SmPC for the full indication). It contains rilpivirine (RPV) as the active substance. REKAMBYS® and cabotegravir (CAB) injections should be administered at separate gluteal injection sites during the same visit.

Further information about the evaluation of REKAMBYS®'s benefits can be found in REKAMBYS®'s EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage.

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

Important risks of REKAMBYS®, together with measures to minimize such risks and the proposed studies for learning more about REKAMBYS®'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 HCPs;
- 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 patient (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 Benefit-Risk Evaluation Report (PBRER)/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 REKAMBYS® is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of REKAMBYS® 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 REKAMBYS®. 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	Medication errors (ie, non-adherence to the dosing schedule, incorrect route of administration)
Missing information	Use in pregnancy

II.B Summary of important risks

Important Potential Risk: Medication errors (ie, non-adherence to the dosing schedule, incorrect route of administration)	
Evidence for linking the risk to the medicine	In the RPV long acting (LA) + CAB LA clinical development program, investigators could report identified medication errors of any type; medication errors were reported infrequently during the clinical trials. It is known that documentation of medication errors from the clinical trials is imperfect and may not represent the true rate of errors. Human factor studies were conducted, assessing the monthly injection regimen, using commercially representative medicinal product kits. These included representative drug product vials, delivery devices and packaging, and to-be-marketed prescribing information with instructions for use (IFU) for the dosing of RPV LA under simulated use conditions. The objective was to provide evidence that the user requirements were adequately met. Errors observed during the human factor studies were associated with incorrect dose selection, incorrect dose measured in syringe, and incorrect injection site chosen. The studies suggest that medication errors for the every 2 months injection regimen will be similar to those for the monthly injection regimen.
Risk factors and risk groups	The injectable RPV LA + CAB LA regimen will initially be novel. Both the monthly and every 2 months injection regimens have 3 stages for dosing; oral lead-in dosing, intramuscular (IM) initiation dosing, and IM continuation dosing, with both RPV LA and CAB LA being administered as separate injections. However, the initiation injection dose of RPV LA consists of a single injection for the monthly regimen, while it consists of 2 injections given 1 month apart for the every 2 months regimen. There is a risk of administering an incomplete regimen potentially resulting in sub-optimal therapeutic levels. There is also a risk of bypassing the oral lead-in stage, since the oral formulations are supplied separately from the suspension for injection. Accidental (partial) intravenous injection is an uncommon, but inherent, risk of IM administration.
Risk minimization measures	Routine risk minimization measures: • SmPC Sections 4.2 and 4.4 • PL Sections 2 and 3 • IFU Routine risk minimization activities recommending specific

	clinical measures to address the risk: • SmPC Sections 4.2 and 4.4 provide detailed instructions on the correct administration of the regimen, importance of adherence to the injection schedule, and how to handle treatment discontinuation. • PL Sections 2 and 3 include instructions on what to do when stopping treatment. • IFU are provided in the PL and include detailed information on the preparation and administration of an IM injection. Other routine risk minimization measures beyond the Product Information: • Administered by HCPs. • Different packaging designs to differentiate between dose and medication. Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Drug Utilization, Adherence, Effectiveness and Resistance: A Prospective Observational Cohort Study in Patients Initiating ARV Regimen of RPV LA+CAB LA, in Collaboration With EuroSIDA See section II.C of this summary for an overview of the postauthorization development plan.

Missing Information: Use in pregnancy	
Risk minimization measures	Routine risk minimization measures: • SmPC Sections 4.4 and 4.6 • PL Section 2 Routine risk minimization activities recommending specific clinical measures to address the risk: • Recommendation regarding the use of REKAMBYS® during pregnancy is provided in SmPC Sections 4.4 and 4.6, and PL Section 2. Other routine risk minimization measures beyond the Product Information: • This is a prescription only medicine. • Prescribed by HCPs. Additional risk minimization measures:

	• None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Review of Antiretroviral Pregnancy Registry (APR). See section II.C of this summary for an overview of the postauthorization development plan.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

Drug Utilization, Adherence, Effectiveness and Resistance: A Prospective Observational Cohort Study in Patients Initiating ARV Regimen of RPV LA+CAB LA, in Collaboration With EuroSIDA

Purpose of the Study: To better understand the patient population receiving RPV LA and/or CAB LA containing injection regimens in routine clinical practice, usage patterns, adherence, postmarketing clinical effectiveness of this regimen, discontinuations, and monitor for resistance among virologic failures for whom data on resistance testing are available. The Drug Utilization Study will also evaluate the effectiveness of routine risk minimization measures for the safety concern of medication errors and assess the use of RPV LA and/or CAB LA containing injection regimens according to the SmPC recommendations.

COMBINE-2 for RPV LA+CAB LA Regimen: A Prospective Cohort Study to Monitor Effectiveness, Adherence and Resistance

Purpose of the Study: To gather data from 1,000 patients to assess clinical effectiveness, adherence, durability, and discontinuations after initiating the RPV LA + CAB LA regimen, and monitor for resistance and response to subsequent ARV regimen among patients who switched from the RPV LA + CAB LA regimen.II.C.2 Other studies in post-authorisation development plan

II.C.2. Other Studies in Postauthorization Development Plan

Antiretroviral Pregnancy Registry (APR)

Purpose of the Study: Monitor prenatal exposures to antiretroviral drugs to detect a potential increase in the risk of birth defects through a prospective exposure-registration cohort.