Swiss Summary of the Risk Management Plan (RMP) for Juluca (Dolutegravir+Rilpivirine)

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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 Juluca 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 Juluca in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. ViiV Healthcare GmbH is fully responsible for the accuracy and correctness of the content of the published summary RMP of Juluca.

Summary of risk management plan (RMP) for JULUCA (dolutegravir/rilpivirine)

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

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

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

I. The medicine and what it is used for

JULUCA is authorised for the treatment of HIV infection (see SmPC for the full indication). It contains dolutegravir and rilpivirine as the active substances and it is given as a tablet by mouth.

Further information about the evaluation of JULUCA's benefits can be found in JULUCA'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/juluca

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

Important risks of JULUCA, together with measures to minimise such risks and the proposed studies for learning more about JULUCA'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 the case of JULUCA these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed 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 JULUCA is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of JULUCA 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 JULUCA. 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);

JULUCA is a new medicine that does not contain a new active substance. The identified and potential risks for JULUCA have been taken from the approved TIVICAY (dolutegravir (DTG)) and EDURANT (rilpivirine (RPV)) RMPs. No new risks have been identified for JULUCA.

List of important risks and missing information	
Important identified risks	**DTG/RPV** • Drug resistance
Important potential risks	**DTG** • Neural tube defects
Missing information	• Use in pregnancy and breast feeding • Long term safety

II.B Summary of important risks

JULUCA is a new medicine that does not contain a new active substance. The identified and potential risks for JULUCA have been taken from the approved TIVICAY (dolutegravir) and EDURANT (rilpivirine) RMPs. No new risks have been identified for JULUCA.

The safety information in the Product Information for JULUCA is aligned to the reference medicinal products (TIVICAY and EDURANT).

Additional pharmacovigilance and additional risk minimisation activities (where applicable) for JULUCA are provided in the table below:

Important identified risk: Drug resistance	
Additional pharmacovigilance activities	Real-world evidence for effectiveness of Two Drug Regimen, Antiretroviral therapy with integrase inhibitors plus a reverse transcriptase inhibitor (COMBINE-2 study)

Important potential risk: Neural tube defects	
Additional Risk minimisation measures	Direct health care professional communication completed in 2018
Additional pharmacovigilance activities	Antiretroviral Pregnancy Registry Study 208613 -DOLOMITE EPPICC Study Study 208759 -DOLOMITE NEAT ID Network Study

Missing information: Use in pregnancy and breast feeding	
Additional pharmacovigilance activities	Antiretroviral Pregnancy Registry Study 208613 -DOLOMITE EPPICC Study Study 208759 -DOLOMITE NEAT ID Network Study

Missing information: Long term safety data	
Additional pharmacovigilance activities	201636 (SWORD 1) / 201637 (SWORD 2): A Phase III, randomized, multicenter, parallel-group, noninferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current Integrase strand transfer inhibitor (INI)-, Non-nucleoside reverse transcriptase inhibitor (NNRTI)-, or Protease inhibitor (PI)-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed.

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 JULUCA

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

Study/Activity (including study number)	Objectives	Safety concerns/efficacy issue addressed	Status	Planned date for submission of (interim and) final study results
Study 201636 (SWORD 1) / Study 201637 (SWORD 2): A Phase III, randomized, multicenter, parallel-group, noninferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current INI-, NNRTI-, or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed.	These studies are designed to demonstrate the non-inferior antiviral activity of switching to DTG + RPV once daily compared to continuation of current antiretroviral regimen (CAR) up to 48 weeks. These studies will also characterize the long-term antiviral activity, tolerability and safety of DTG + RPV through Week 148.	Long term safety	Ongoing	Final reports: End of study CSRs anticipated November 2022
Antiretroviral Pregnancy Registry (APR)	Monitors prenatal exposures to antiretroviral (ARV) drugs to detect a potential increase in the risk of birth defects through a prospective exposure-registration cohort.	Use in pregnancy, Neural tube defects	Ongoing	A registry interim report is prepared semi-annually summarising the aggregate data. Data from the APR will be presented in the Periodic Benefit Risk Evaluation Report (PBRER).

Study/Activity (including study number)	Objectives	Safety concerns/efficacy issue addressed	Status	Planned date for submission of (interim and) final study results
Study 208613 DOLOMITE EPPICC Study	Assess “real-world” maternal and foetal outcomes following DTG use during pregnancy and to describe patterns of DTG utilization	Use in pregnancy Neural tube defects.	Ongoing	Final report June 2023
DOLOMITE NEAT ID Network Study (208759)	To assess the safety and effectiveness of DTG in pregnancy in the NEAT-ID network of approximately 40 sites across Europe.	Use in pregnancy Neural tube defects	Ongoing	Final report expected October 2023
Real-world evidence for effectiveness of Two Drug Regimen, Antiretroviral therapy with integrase inhibitors plus a reverse transcriptase inhibitor (COMBINE-2)	To evaluate the effectiveness and safety of DTG-based 2-drug regimens (DTG/RPV or DTG/3TC)	Drug resistance	Ongoing	Final report expected 31 May 2023