PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for DOVATO (dolutegravir/lamivudine)

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

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

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

I. The medicine and what it is used for

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

Further information about the evaluation of DOVATO's benefits can be found in DOVATO'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/dovato

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

Important risks of DOVATO, together with measures to minimise such risks and the proposed studies for learning more about DOVATO'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 DOVATO, these measures are supplemented with *additional risk minimization 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 DOVATO is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of DOVATO 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 DOVATO. 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);

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

List of important risks and missing information	
Important identified risks	None
Important potential risks	<>Dolutegravir ➢ Neural tube defects
Missing information	<>Dolutegravir/lamivudine ➢ Use in pregnancy/ breastfeeding

II.B Summary of important risks

DOVATO is a new medicine that does not contain a new active substance. The identified and potential risks for DOVATO have been taken from the approved TIVICAY (dolutegravir) EU-RMP. No new risks have been identified for DOVATO.

The safety information in the proposed Product Information for DOVATO is aligned to the reference medicinal product (TIVICAY).

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

Important potential risk: Neural tube defects	
Additional Risk minimisation measures	Direct health care professional communication completed in 2018
Additional pharmacovigilance activities*	Antiretroviral pregnancy registry (APR)

* The risk of NTD has additional pharmacovigilance activities collecting data on the dolutegravir component of the DTG/3TC FDC; these studies are described in the Dolutegravir RMP

Missing information: Use in pregnancy and breast feeding	
Additional pharmacovigilance activities	Antiretroviral pregnancy registry (APR)

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 DOVATO.

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
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).

*The NTD risk has ongoing additional pharmacovigilance activities collecting data on the dolutegravir component of the DTG/3TC FDC; these studies are described in the Dolutegravir RMP