Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for DARUNAVIR

This is a summary of the risk management plan (RMP) for DARUNAVIR 600 mg, 800 mg film-coated tablets, (hereinafter referred to as Darunavir). The RMP details important risks of Darunavir, how these risks can be minimised, and how more information will be obtained about Darunavir's risks and uncertainties (missing information).

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

Important new concerns or changes to the current ones will be included in updates of Darunavir's RMP.

I. The Medicine and What It is used for

Darunavir is authorised for treatment of HIV in adults and children aged three years or over, in combination with other medicines, such as ritonavir or cobicistat (see SmPC for the full indication). It contains darunavir as the active substance and it is given orally.

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

Important risks of Darunavir, together with measures to minimise such risks and the proposed studies for learning more about Darunavir'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 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 darunavir is not yet available, it is listed under ‘missing information’ below.

II.A List of Important Risks and Missing Information

Important risks of Darunavir 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 Darunavir. 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);

Table 6: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	• Severe skin reactions • Hepatotoxicity • Hyperglycaemia • Lipid abnormalities • Immune reconstitution inflammatory syndrome • Development of drug resistance • Overdose due to medication error • Drug-drug interactions
Important potential risks	• Coronary artery events • Growth abnormalities in the paediatric population • Off-Label Use of DRV/COBI in the Paediatric Population and in ARV Treatment-experienced Patients with HIV-1 RNA >100,000 copies/mL

Missing information	DRV/rtv and DRV/COBI • Elderly (65 years and above) • Pregnant and breast-feeding women • Subjects with renal impairment • Subjects with severe hepatic impairment (Child-Pugh C) DRV/rtv • Long-term safety data in children from 3 to <6 years of age DRV/COBI • Children <18 years of age • Long-term safety of DRV/COBI in adults • Subjects coinfected with HIV and HBV and/or HCV

II.B Summary of Important Risks

Table 7: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Missing information: Pregnant and breast-feeding women	
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Antiretroviral pregnancy registry (APR). See section II.C of this summary for an overview of the post-authorisation development plan.

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 Darunavir.

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

Study short name

Antiretroviral pregnancy registry (APR)

Purpose of the study

Objective of the APR is to detect any major teratogenic effect involving any of the Registry drugs to which pregnant women are exposed. The Registry is intended to provide an early signal of potential risks. Registry data are provided to supplement animal toxicology studies and assist clinicians in weighing the potential risks and benefits of treatment for individual patients.