Part VI: Summary of the risk management plan

Summary of risk management plan for Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets (Darunavir)

This is a summary of the risk management plan (RMP) for Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets. The RMP details important risks of Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets, how these risks can be minimised, and how more information will be obtained about Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets risks and uncertainties (missing information).

Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablet's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets should be used.

Important new concerns or changes to the current ones will be included in updates of Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablet's RMP.

I. The medicine and what it is used for

Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets is authorised for following indication.

Darunavir Accord 75 mg, 150 mg, 300 mg, 600 mg film coated tablets

Darunavir Accord co-administered with low dose ritonavir is indicated in combination with other antiretroviral medicinal products for the treatment of patients with human immunodeficiency virus (HIV-1) infection.

Darunavir Accord 75 mg, 150 mg, 300 mg, 600 mg tablets may be used to provide suitable dose regimens.

- For the treatment of HIV-1 infection in antiretroviral treatment (ART)-experienced adult patients, including those that have been highly pre-treated.

- For the treatment of HIV-1 infection in paediatric patients from the age of 3 years and at least 15 kg body weight.

In deciding to initiate treatment with Darunavir Accord co-administered with low dose ritonavir, careful consideration should be given to the treatment history of the individual patient and the patterns of mutations associated with different agents. Genotypic or phenotypic testing (when available) and treatment history should guide the use of Darunavir Accord.

Darunavir Accord 400 mg and 800 mg film coated tablets

Darunavir Accord co-administered with low dose ritonavir is indicated in combination with other antiretroviral medicinal products for the treatment of patients with human immunodeficiency virus (HIV-1) infection.

Darunavir Accord, co-administered with cobicistat is indicated in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in adult patients.

Darunavir Accord 400 mg, 800 mg tablets may be used to provide suitable dose regimens for the treatment of HIV-1 infection in adult and paediatric patients from the age of 3 years and at least 40 kg body weight who are:

- antiretroviral therapy (ART)-naïve.
- ART-experienced with no darunavir resistance associated mutations (DRV-RAMs) and who have plasma HIV-1 RNA < 100,000 copies/ml and CD4+ cell count ≥ 100 cells x 10^6/l. In deciding to initiate treatment with darunavir in such ART-experienced patients, genotypic testing should guide the use of darunavir.

It contains darunavir (as darunavir propylene glycolate) as active substance and it is given by oral route.

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

Important risks of Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets, together with measures to minimise such risks and the proposed studies for learning more about Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablet'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 (if applicable) and signal management activity, 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 Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets are risks that need special risk management activities to further investigate or minimise 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 Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets. 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).

Important identified risks	• Severe skin reactions • Hepatotoxocity • 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 • Off-label use of DRV/COBI (Darunavir / Cobicistat) in the paediatric population and in ARV (Antiretroviral) treatment-experienced patients with HIV-1 (Human Immunodeficiency Virus) RNA (Ribonucleic acid) > 100,000 copies/mL
Missing information	• Older people (65 years and above) • Subjects with severe hepatic impairment (Child-Pugh C) • Subjects with renal impairment • DRV/rtv (Darunavir/Ritonavir) – Long term safety data in children from 3 to < 6 years of age • DRV/COBI (Darunavir / Cobicistat) – Children <18 years of age – Long term safety of DRV/COBI in adults – Subjects co-infected with HIV and HBV (Hepatitis B Virus) and/or HCV (Hepatitis C Virus)

II.B Summary of important risks

The safety information in the proposed product information is aligned with reference medicinal product PREZISTA® (darunavir).

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 Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets.

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

There are no studies required for Darunavir Accord 75 mg, 150 mg, 300 mg, 400 mg, 600 mg and 800 mg film coated tablets.