Summary of risk management plan for Efavirenz/Emtricitabine/Tenofovir disoproxil Krka

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

Efavirenz/Emtricitabine/Tenofovir disoproxil Krka 's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Efavirenz/Emtricitabine/Tenofovir disoproxil Krka should be used.

This summary of the RMP for Efavirenz/Emtricitabine/Tenofovir disoproxil Krka 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 Efavirenz/Emtricitabine/Tenofovir disoproxil Krka 's RMP.

I. The medicine and what it is used for

Efavirenz/Emtricitabine/Tenofovir disoproxil Krka is authorised for for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults aged 18 years and over with virologic suppression to HIV-1 RNA levels of < 50 copies/ml on their current combination antiretroviral therapy for more than three months. Patients must not have experienced virological failure on any prior antiretroviral therapy and must be known not to have harboured virus strains with mutations conferring significant resistance to any of the three components contained in Efavirenz/Emtricitabine/Tenofovir disoproxil Krka prior to initiation of their first antiretroviral treatment regimen (see sections 4.4 and 5.1).

It contains Efavirenz/Emtricitabine/Tenofovir disoproxil as the active substance and it is given orally.

Further information about the evaluation of Efavirenz/Emtricitabine/Tenofovir disoproxil Krka's benefits can be found in Efavirenz/Emtricitabine/Tenofovir disoproxil Krka's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage *http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/004274/human_med_002233.jsp&mid=WC0b01ac058001d124*.

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

Important risks of Efavirenz/Emtricitabine/Tenofovir disoproxil Krka, together with measures to minimise such risks and the proposed studies for learning more about Efavirenz/Emtricitabine/Tenofovir disoproxil Krka'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 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 Efavirenz/Emtricitabine/Tenofovir disoproxil Krka is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Efavirenz/Emtricitabine/Tenofovir disoproxil Krka 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 Efavirenz/Emtricitabine/Tenofovir disoproxil Krka. 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);

Summary of safety concerns	
Important identified risks:	Liver disease (High-grade hepatic enzyme elevation and severe hepatic events)
	Spinal cord and brain birth defects (Neural tube developmental abnormalities)
	Psychiatric and nervous system symptoms
	Skin rashes and severe skin reactions
	Higher levels of efavirenz in the bloodstream caused by a genetic characteristic (Alteration in efavirenz blood levels and CYP2B6 genetic polymorphisms)
	Kidney problems (Renal toxicity)
	Bone problems (Bone events due to proximal renal tubulopathy/loss of BMD)
Important potential risks:	Kidney stones (Urolithiasis/nephrolithiasis)
Missing information:	Limited information on use in pregnant and breastfeeding women

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

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 Efavirenz/Emtricitabine/Tenofovir disoproxil Krka.

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

There are no studies required for Efavirenz/Emtricitabine/Tenofovir disoproxil Krka.