Swiss Summary of the Risk Management Plan (RMP)

for Rukobia (Fostemsavir)

Document Number:	Version 1.0
Based on EU RMP:	Version 1.0
Marketing Authorisation Holder:	ViiV Healthcare GmbH
Date:	27.11.2021

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 Rukobia 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 Rukobia 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 Rukobia.

Summary of risk management plan for fostemsavir

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

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

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

I. The medicine and what it is used for

Fostemsavir, in combination with other antiretrovirals, is authorised for treatment of adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen (see SmPC for the full indication). It contains temsavir as the active substance and it is given by a tablet by mouth.

Further information about the evaluation of fostemsavir’s benefits can be found in fostemsavir’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/rukobia.

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

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

II.A List of important risks and missing information

Important risks of fostemsavir 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 fostemsavir. 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);

List of important risks and missing information	
Important identified risks	None
Important potential risks	Ventricular tachyarrhythmias due to QT prolongation
Missing information	Use in pregnant and lactating women Long term safety data

II.B Summary of important risks

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

Important potential risk: Ventricular tachyarrhythmias due to QT prolongation	
Evidence for linking the risk to the medicine	The risk of ventricular tachyarrhythmias due to QT prolongation, which can be life-threatening, is considered an important potential risk based on the finding that a supra-therapeutic dose of FTR prolonged QTc interval in the thorough QT (TQT) clinical study in healthy volunteers. Based on modelling of TQT clinical data, the threshold for clinically significant QTc prolongation (≥10 ms) is 7,500 ng/mL TMR, which is 4.2x higher than the Cmax associated with FTR 600 mg BID regimen in HTE HIV-1 infected patients

	enrolled in the Phase 3 study. This safety threshold for QT prolongation is sufficiently high to cover the Cmax increase due to co-administration of pharmacoenhancers. No significant clinical events relating to this risk have been identified to date in clinical studies involving FTR.
Risk factors and risk groups	No additional risk factors have been identified in HTE HIV infected-patients beyond those previously described for the general population.
Risk minimisation measures	**Routine risk minimisation:** • SmPC section 4.4, 4.5 and 4.8. • PL section 2 and 4. **Other routine risk minimization measures beyond the Product Information:** • This is a prescription only medicine. • Prescribed by physicians experienced in the treatment of HIV. **Additional risk minimization measures**: None.
Additional pharmacovigilance activities	**Additional pharmacovigilance activity:** **Short study name:** A Clinical Trial to Investigate the Efficacy and Safety of Fostemsavir in HTE Subjects Infected with Multi-drug Resistant HIV-1 (BRIGHTE Study). See section II.C of this summary for an overview of the post-authorisation development plan.

Important missing information 1: Use in pregnant and lactating women	
Risk minimisation measures	**Routine risk minimisation measures:** SmPC section 4.6. PL section 2. **Other routine risk minimisation measures beyond the Product Information**: • This is a prescription only medicine. • Prescribed by physicians experienced in the treatment of HIV. **Additional risk minimization measures**: None.
Additional pharmacovigilance activities	**Additional pharmacovigilance activity:** **Short study title:** Antiretroviral Pregnancy Registry (APR) See section II.C of this summary for an overview of the post-authorisation

	development plan.

Important missing information 2: Long term safety data	
Risk minimisation measures	None.
Additional pharmacovigilance activities	**Additional pharmacovigilance activity:** **Short study title:** A Clinical Trial to Investigate the Efficacy and Safety of Fostemsavir in HTE Subjects Infected with Multi-drug Resistant HIV-1 (BRIGHTE Study) 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 fostemsavir.

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

Study Short Name: Antiretroviral Pregnancy Registry (APR).

Purpose of the Study: The APR is an international registry that monitors prenatal exposures to ARV drugs to detect a potential increase in the risk of birth defects through a prospective exposure-registration cohort.

Study Short Name: A Multi-arm, Phase 3, Randomized, Placebo Controlled, Double Blind Clinical Trial to Investigate the Efficacy and Safety of Fostemsavir (BMS-663068/GSK3684934) in Heavily Treatment Experienced Subjects Infected with Multi-drug Resistant HIV-1 (BRIGHTE Study).

Purpose of the Study: This ongoing Phase 3 study is designed assess the efficacy and safety of fostemsavir in heavily treatment-experienced patients**.**