Summary of the Risk Management Plan for Kerendia®

Active substance: Finerenone

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Kerendia®
(Finerenone)
Risk Management Plan

Summary of activities in the risk management plan

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 Kerendia® 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 Kerendia® in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Bayer (Schweiz) AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Kerendia®.

1. Summary of Risk Management Plan for Kerendia®

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

Kerendia®'s Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Kerendia® should be used.

This summary of the RMP for Kerendia® 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 Kerendia®'s RMP.

2. The Medicine and what it is used for

Kerendia® is authorised for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults. It contains finerenone as the active substance and it is given by oral administration.

Further information about the evaluation of Kerendia®'s benefits can be found in Kerendia®'s European Public Assessment Report (EPAR), including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage.

3. Risks Associated with the Medicine and Activities to Minimise or further Characterise the Risks

Important risks of Kerendia®, together with measures to minimise such 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 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 Kerendia® is not yet available, it is listed under 'missing information' below.

3.1 List of Important Risks and Missing Information

Important risks of Kerendia® 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 Kerendia®. 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).

3.1.1 Summary table of safety concerns

Summary of safety concerns	
Important identified risks	Hyperkalemia
Important potential risks	Embryo-foetal toxicity
Missing information	Use in pregnancy and lactation

3.2 Summary of Important Risks

Important identified risk - Hyperkalemia	
Evidence for linking the risk to the medicine	In the pivotal Phase III study FIDELIO-DKD conducted in patients with advanced CKD and T2D, the number of subjects with treatment-emergent hyperkalemia AEs (i.e., PT hyperkalaemia and blood potassium increased) was higher in the finerenone arm (18.3%) vs in the placebo arm (9.0%). In the finerenone arm, the majority of these events were nonserious and mild or moderate in intensity. Moreover treatment-emergent hyperkalemia AEs leading to permanent discontinuation from study drug (2.3% of subjects) or hospitalisation (1.4% of subjects) constituted a small proportion of these events. There were no treatment-emergent fatal cases of hyperkalemia observed. Further, there was no evidence for an increased incidence of any severe clinical cardiac manifestations of hyperkalemia (e.g. ventricular arrhythmia or sudden cardiac death).

Important identified risk - Hyperkalemia	
	An increase from baseline in mean serum potassium in the first month of treatment of approximately 0.2 mmol/L was observed in the finerenone arm compared to placebo, with stable mean measurements from Month 4 onwards in the finerenone arm. The mean between-group difference in serum potassium of approximately 0.2 mmol/L was consistently observed across different subgroups, including baseline serum potassium and eGFR at screening. A change in potassium to >5.5 mmol/L at any time during treatment was reported for 21.4% of subjects on finerenone and 9.2% of subject on placebo. A change in potassium to >6.0 mmol/L at any time during treatment was reported for 4.5% of subjects on finerenone and 1.4% of subjects on placebo. The analysis of data collected in the context of dose-titration and interruption indicates that hyperkalemia with finerenone treatment is manageable using a serum-potassium-guided dose titration regimen. This is supported by simulation of the exposure-serum potassium model, which demonstrated that even at higher exposures, no increased risk for hyperkalemia is observed when dose-titration is applied.
Risk factors and risk groups	Hyperkalemia is a known complication of reduced renal function in patients with CKD. Besides CKD, the most common risk factors for hyperkalemia include cardiovascular disease, diabetes mellitus and concomitant use of drugs which raise the potassium concentration (e.g. ACEIs, ARBs, potassium-sparing diuretics, and beta blockers). Based on the analysis in the Phase III study FIDELIO-DKD, risk factors for hyperkalemia include low eGFR, higher baseline serum potassium and previous episodes of hyperkalemia. In addition, based on the analysis of Phase I studies, an increase in finerenone exposure e.g. in patients receiving CYP3A4 inhibitors as co-medication may be associated with a higher risk of developing hyperkalemia.
Risk minimisation measures	**Routine risk minimisation measures** • SmPC sections: 4.2, 4.4, 4.5 and 4.8 • Kerendia® is a prescription-only medicine

Important identified risk - Hyperkalemia	
	Additional risk minimisation measures None

Important potential risk - Embryo-foetal toxicity	
Evidence for linking the risk to the medicine	The evidence is based on non-clinical data in the developmental toxicity studies in the rat as well as literature data of other MRAs. There are no clinical data on the use of finerenone in pregnant women.
Risk factors and risk groups	Women of childbearing potential.
Risk minimisation measures	**Routine risk minimisation measures** • SmPC section 4.4 Special warnings and precautions for use • SmPC section 4.6 Fertility, pregnancy and lactation • SmPC section 5.3 Preclinical safety data • Kerendia® is a prescription-only medicine **Additional risk minimisation measures** None

Missing information – Use in pregnancy and lactation	
Risk minimisation measures	**Routine risk minimisation measures** • SmPC section 4.4 Special warnings and precautions for use • SmPC section 4.6 Fertility, pregnancy and lactation • SmPC section 5.3 Preclinical safety data • Kerendia® is a prescription-only medicine **Additional risk minimisation measures** None

4. Post-authorisation Development Plan

There are no studies that are conditions of the marketing authorisation or specific obligation of Kerendia®.