REPUBLIC OF BULGARIA
NATIONAL COUNCIL ON PRICES AND REIMBURSEMENT OF MEDICINAL PRODUCTS

HEALTH TECHNOLOGY ASSESSMENT

Kerendia

10 mg film-coated tablet x 28 (blister)

20 mg film-coated tablet x 28 (blister)

INN Finerenone

Therapeutic indication	Kerendia is indicated for the treatment of chronic kidney disease (with albuminuria) associated with type 2 diabetes mellitus in adult patients.
Start - end of the procedure	14.03.2023 – 13.12.2023
Final decision	Inclusion in Annex 1 of the Positive Drug List (PDL) for home treatment of diseases reimbursed by the National Health Insurance Fund (NHIF). Inclusion in Annex 2 of the Positive Drug List (PDL) for purchase by the healthcare facilities with state and/or municipality ownership and under Article 5 of the Medical Establishments Act, and reimbursement by the NHIF.

Summary of the report on the clinical and pharmacoeconomic assessment of the health technology of the medicinal product Kerendia

Health problem

Chronic kidney disease (CKD) is a progressive and irreversible kidney disease that causes a gradual loss of kidney function. The early stages of the disease are usually asymptomatic and diagnosed through laboratory tests, and for this reason patients are often undiagnosed and untreated. The gradual loss of kidney function is manifested by a reduced ability to filter blood in the nephrons and can lead to a complete loss of organ function, i.e. end stage kidney disease (ESKD). One of the main risk factors for the development of CKD is type 2 diabetes.

CKD in T2DM patients is managed with lifestyle changes (e.g. smoking cessation, healthy diet, exercise, and weight reduction among overweight or obese patients) and pharmacological approaches targeting metabolic pathway risk factors (e.g. hyperglycemia) and the hemodynamic pathway (factors stimulated by the RAAS and affecting blood pressure).

Finerenon is a nonsteroidal selective antagonist of the mineralocorticoid receptor (MR), which is activated by aldosterone and cortisol and regulates gene transcription. Its binding to MR leads to the formation of a specific receptor-ligand complex, which blocks the recruitment of transcriptional coactivators involved in the expression of proinflammatory and profibrotic mediators.

Efficacy data

The safety profile of finerenone was evaluated in 27 phase I trials, 5 phase II trials and 2 phase III trials. The two phase III trials were designed to evaluate the renal and cardiovascular effects of finerenone in patients with CKD and T2DM - **FIDELIO-DKD (NCT02540993)** and **FIGARO-DKD (NCT02545049)**. The trials were separate, but complementary, and aimed to evaluate the effect of finerenone versus placebo in patients with CKD and T2DM treated with standard therapy including a maximum dose ACE inhibitor or ARB. Both trials were randomized, double-blind, placebo-controlled, parallel-group trials with a median follow-up of 2.6 years (FIDELIO) and 3.4 years (FIGARO).

In the **FIDELIO** clinical trial, finerenone demonstrated clinically meaningful effects in patients with CKD and T2DM when added to standard of care (SoC), both in delaying CKD progression and in reducing cardiovascular morbidity and mortality. The treatment benefit was statistically significant (p=0.0014), was observed 12 months after randomization and was maintained throughout the trial period (median follow-up 2.6 years). Treatment benefit was consistent across endpoint components and was supported by a significant improvement in sustained ≥40% reduction in eGFR from baseline (p=0.0009). Finerenone significantly reduced the risk of the key secondary composite CV endpoint by 14 % and the number of patients to be treated to prevent a key secondary event was 42.

The therapeutic effect of finerenone on the key secondary composite renal endpoint in the **FIGARO** clinical trial was similar to that in the FIDELIO trial, but significance was not reached (p=0.0689). Treatment with finerenone resulted in a lower risk of the key secondary composite renal endpoint, assessed as time to onset of renal failure, sustained ≥40% decrease in eGFR from baseline for at least 4 weeks, or renal death compared with placebo. The incidence of each of the components of the combined renal outcome was observed less frequently in the finerenone group compared to the placebo group. Finerenone significantly reduced the risk of the primary composite CV endpoint by 13% compared with the placebo group, and the number of patients needed to be treated to prevent a key secondary event was 47.

Safety data

Finerenone was well tolerated by patients with CKD and T2DM and demonstrated a safety profile consistent with its mechanism of action. The most common adverse event is hyperkalemia.

Data on comparators

A comparable alternative to the health technology Kerendia is the standard therapy. The standard therapy in finerenone's target population includes ACE-inhibitors, ARBs, beta-blockers, diuretics, Ca-antagonists and statins. Glucose-lowering therapy includes insulin, metformin, acarbose, sulfonylureas, DPP4-i, GLP-1 agonists, and SGLT2i.

Pharmacoeconomic indicators

Published health technology assessments performed by governmental institutions intended for the health care systems of other countries

Two positive assessments have been published by other governmental institutions - Haute Autorité de santé - HAS (France) and Tandvårds- och läkemsförmånsverket - TLV (Sweden).

Applied analysis

The cost effectiveness pharmacoeconomic analysis (CEA) was applied, in which the final result in terms of health benefits is presented in the form of life years gained (LYG) and cost utility analysis (CUA), where the final outcome in terms of health benefits is expressed as a quality-adjusted life years (QALY) gained. A comparable alternative is the standard therapy. The chosen time horizon in the model is lifetime. The perspective of the analysis is that of the paying institution - National Health Insurance Fund (NHIF). Health benefits and costs are discounted with an annual discount factor of 3.5%. A Markov model was used for modeling, which reflects 2 important health conditions - cardiovascular and renal events.

The results of the applied cost-effectiveness and cost-utility analysis show that compared to standard therapy, the medicinal product Kerendia is below the recommended profitability threshold of 3 times GDP for Bulgaria - BGN 60,636.

Costs for the assessed health technology
Costs included in the model are costs of drug therapy with Kerenida and the alternatives, costs of hemodialysis, kidney transplantation, and cardiovascular complications.

Subgroup analysis
Not attached.

Budget impact analysis
The analysis of the budget impact was conducted from the perspective of a paying institution - NHIF. The time horizon is 5 years. The target population includes patients with chronic kidney disease (with albuminuria) associated with type 2 diabetes mellitus. The estimated number of patients in the first year is 1,500, and in the fifth year - 6,000. Two scenarios "World with Kerendia" and "World without Kerendia" have been developed.

The analysis forecasts increase in costs over a five-year period for the NHIF, excluding risk-sharing agreements and patient access schemes.

Conclusion

Finerenone demonstrated clinically meaningful effects in patients with CKD and T2DM, both in delaying the progression of CKD and in reducing cardiovascular morbidity and mortality. In the treatment algorithm, Kerendia was cost-effective when compared to standard therapy in terms of additional costs per one additional life year gained and per one QALY gained. The inclusion of the medicinal product Kerendia for the treatment of CKD+ZDT2 will result in additional costs for the paying institution.