NCPE Assessment

Technical Summary

Finerenone/Kerendia®

HTA ID 22012

22.08.2023

Applicant: Bayer

Finerenone for the treatment of Chronic Kidney Disease (Stage 3 & 4 with Albuminuria) associated with Type 2 Diabetes in Adults.

NCPE
National Centre for Pharmacoeconomics, Ireland

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of finerenone (Kerendia®).

Following assessment of the Applicant's submission, the NCPE recommends that finerenone (Kerendia®) be considered for reimbursement if cost effectiveness can be improved relative to existing treatments*.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Bayer) Health Technology Assessment of finerenone. The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In January 2023, Bayer submitted a dossier which investigated the clinical effectiveness, cost-effectiveness and budget impact of finerenone (Kerendia®) for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults. The licence for finerenone has recently been extended to include adults with all stages of chronic kidney disease associated with type 2 diabetes. This NCPE evaluation, and recommendation, pertains to the indication for which the submission was made. Bayer is seeking reimbursement of finerenone on the community drug scheme.

In Ireland, standard of care (SoC) consists of angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin receptor blockers (ARBs) which should be optimised. While SGLT2 inhibitors (i.e. use in addition to ACEi/ARB therapy) have been recently added into the international guidelines, use in Ireland is currently low, albeit increasing.

1. Comparative effectiveness of finerenone

Clinical evidence supporting the use of finerenone was from the FIDELIO-DKD trial (n=5,734). FIDELIO-DKD was a phase III, randomized, double-blind, placebo-controlled, parallel-group, multicentre, event-driven study of finerenone compared with placebo in patients with chronic kidney disease and type 2 diabetes mellitus. The majority of patients were on an ACEi or an ARB. A small proportion were also on a SGLT2 inhibitor. Patients were randomized (1:1) to finerenone (10 mg or 20 mg once daily) or placebo and stratified by region, eGFR category at screening, and albuminuria level at screening. Finerenone or placebo were given as an add-on treatment.

The primary composite endpoint was time to first occurrence of the 40% renal composite endpoint and comprised onset of kidney failure, a sustained decrease of eGFR greater than or equal to 40% from baseline over at least 4 weeks, or renal death. Patient characteristics were balanced between arms. The primary endpoint occurred in 17.8% and 21.1% of the finerenone and placebo groups, respectively, and the hazard ratio (HR) was 0.825 (95% CI 0.73 to 0.93; P = 0.0014) in favour of finerenone. The HR for sustained decrease in eGFR greater than or equal to 40% from baseline was 0.815 (95% CI 0.722 to 0.920). This was the main driver of the

composite endpoint result. Treatment effect was assessed across the subgroups: history of cardiovascular disease, eGFR category at baseline, albuminuria level at baseline, and SGLT2 inhibitor treatment at baseline. The treatment effect of finerenone on the primary endpoint was consistent, with the primary analysis, across subgroups except for the subgroup treated with SGLT2 inhibitors at baseline where placebo was favoured. The Review Group note that this data is derived from a small sample size and is uncertain.

Supporting evidence was also presented from the FIGARO-DKD trial (n= 7,437; randomisation (1:1) to finerenone (10 mg or 20 mg once daily) or placebo given as an add-on to background treatment). The primary composite end point comprised cardiovascular death, nonfatal MI, nonfatal stroke, or hospitalization for heart failure. The composite outcome occurred in 13% and 14.8% of the finerenone and placebo groups, respectively; HR was 0.86 (95% CI, 0.75 to 0.99; P = 0.0339) in favour of finerenone. The only individual component of statistical significance was hospitalization for heart failure, which had an HR of 0.71 (95% CI, 0.56 to 0.90) in favour of finerenone. The treatment effect of finerenone was consistent with the primary analysis across patient subgroups except for the subgroup treated with SGLT2 inhibitors at baseline. Health related quality of life (HRQoL) was assessed using the Kidney Disease Quality of Life-36 and the EQ-5D-5L questionnaires. The impact of finerenone on HRQoL is uncertain due to difficulty interpreting the results.

Data was also presented from the FIDELITY pooled analysis – a prespecified pooled analysis of the FIDELIO-DKD and FIGARO-DKD trials. It should be noted that patients in FIDELIO had a lower eGFR at baseline than FIGARO, and the mean treatment duration was longer in FIGARO (approximately 35 months) than in FIDELIO (approximately 27 months). The statistical analysis in FIDELITY was exploratory and descriptive in nature however pooling was considered appropriate. Results showed that treatment with finerenone was associated with a reduction in the relative risk of the composite kidney outcome and the composite CV outcome.

2. Safety of finerenone

In the FIDELIO-DKD study, the mean and median durations of treatment in the finerenone

and placebo groups was approximately 27 months. Any treatment-emergent adverse event (AE) was reported by 87% (2,468/2,827) of patients in the finerenone group and 88% (2,478/2,831) in the placebo group and these were considered treatment-related in 23% and 16% respectively. In the finerenone and placebo groups respectively, the proportions of patients with a reported serious AE were 32% versus 34% and the proportions of patients discontinuing therapy due to an AE were 7.3% versus 5.9%.

The most frequently reported treatment-emergent AEs of any grade in the finerenone and placebo group respectively were: hyperkalaemia (16% versus 7.8%), nasopharyngitis (8.5% versus 8.8%), hypertension (7.5% versus 9.5%). Using investigator-reported hyperkalaemia, the incidence was doubled in the finerenone versus placebo group (18% versus 9.0%) and this was considered related to the mode of action of finerenone. Hyperkalaemia led to more discontinuations (2.3% versus 0.9%) and hospitalisations (1.4% versus 0.3%) with finerenone than placebo. There were no deaths due to hyperkalaemia. The SPC notes that finerenone should not be started in patients with a serum potassium >5.0 mmol/L. For patients receiving finerenone, it is recommended that serum potassium and eGFR are remeasured 4 weeks after starting and that the dose is guided by remeasured serum potassium levels and recent changes in eGFR.

3. Cost effectiveness of finerenone

The Applicant submitted a lifetime cost-utility analysis of finerenone compared to standard of care (SoC) in adults with Stage 3 or 4 chronic kidney disease and type 2 diabetes mellitus. Patient baseline characteristics and direct comparative efficacy data (finerenone in combination with SoC (finerenone + SoC) versus Soc were derived from FIDELIO-DKD.

Methods

A Markov model with 13 health states, which were defined by chronic kidney disease stages and history of cardiovascular events, was submitted, with a cycle length of 4 months. Chronic kidney disease stages were defined based on eGFR level. Patients enter the model distributed across chronic kidney disease Stages 3 and 4. The model assumes that the probability of moving between chronic kidney disease states (i.e., kidney function improving

or worsening) is only based on the patient's current chronic kidney disease state. Patients in Stages 4 and 5 can move to the dialysis state. Patients in Stages 4 or 5 can receive a kidney transplant without dialysis or from dialysis. Patients can transition to death from all health states.

Model inputs were derived mainly from FIDELIO-DKD and the literature. Costs included treatment acquisition, event treatment, follow-up costs, and death costs. Health state utility values were derived from the EQ-5D-5L data, from FIDELIO-DKD, mapped to a 3-level value set.

Results

The results of the Applicant base case deterministic cost-effectiveness analysis are presented in Table 1.

Table 1 Applicant base case incremental cost-effectiveness results [a]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
Finerenone + SoC	65,424	5.52			
SoC	65,527	5.44	- 103	0.08	Finerenone + SoC is Dominant

Abbreviations: QALY= quality adjusted life year; SoC= standard of care.

[a] Corresponding probabilistic ICER using 1000 iterations = finerenone + SoC dominant (i.e. finerenone + SoC is more effective and less costly than SoC). Figures in the table are rounded, and so calculations may not be directly replicable. Discount rate of 4% applied to costs and outcomes.

The Review Group made the following adjustments to the Applicants base case model;

1. Use of trial data for both arms (instead of the Applicant's method, which applied a HR to the SoC arm to derive an estimate for treatment arm).
2. Adjusting for effect of SGLT2i's (the Applicant assumed that 41.3% of patients receiving SoC receive SGLT2 inhibitors, however there was no treatment effect applied).
3. Baseline risk (the Applicant assumed that patients had no prior risk of CV events, however 45.9% of patients in the Fidelio-DKD trial had a prior history of CV events).
4. Utility decrement associated with hyperkalemia (the Review Group considered the estimate of 0.03 to be more plausible as it was in line with estimates from the literature).

Results of the NCPE-adjusted base case are presented in Table 2.

Table 2: NCPE adjusted base case incremental cost-effectiveness results[a]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
Finerenone + SoC	67,353	5.39			

SoC	65,627	5.35	1,726	0.04	46,625

Abbreviations:
[a] Corresponding probabilistic ICER using 1000 iterations =€52,137/QALY. Figures in the table are rounded, and so calculations may not be directly replicable. Discount rate of 4% applied to costs and outcomes.

Of note, the Applicant did not investigate the cost effectiveness of finerenone +SoC versus SGLT2 inhibitors +SoC. The Review Group note that the use of SGLT2 inhibitors for this indication is increasing (in line with international guidance). The limited evidence available does not suggest that a treatment benefit exists for finerenone +SoC versus SGLT2 inhibitors +SoC.

Sensitivity analysis

Model functionality did not allow the relative efficacy of finerenone, the relative efficacy of the SGLT2 inhibitors and and CKD progression rates to be varied in the probabilistic analysis. Therefore, full uncertainty in the model is not reflected. The probabilities of cost-effectiveness for finerenone + SoC versus SoC, in the NCPE-adjusted base case analyses, were 2.3% and 38% at a threshold of €20,000/QALY and €45,000/QALY, respectively.
In scenario analyses of the NCPE adjusted base case, the incremental cost-effectiveness ratio (ICER) increased (i) when the starting age of the modelled cohort was increased and (ii) when the impact of finerenone on preventing cardiovascular events was decreased. The Review Group estimate that a total rebate of 10% on the price to wholesaler (PtW) is required to reduce the NCPE-adjusted base case ICER below the €45,000/QALY threshold. A total rebate in excess of 40% is required to reduce the ICER below €20,000/QALY.

4. Budget impact of finerenone

The PtW of one 28-day pack containing 10mg or 20mg of finerenone is €56. Reimbursement has been requested through the community drug scheme. The annual cost per patient of finerenone is €803.81 (inclusive of wholesale margin, pharmacy fees and Framework Agreement Rebate of 7.75%).

For the budget impact model, prevalence and incidence rates of Stage 3 and 4 chronic kidney disease and type 2 diabetes mellitus were estimated from the literature. Market sharem based on estimates provided by clinical experts in Ireland, ranged from 5% in year 1

to 27.5% in year 5. Discontinuation rates were based on data from the FIDELIO-DKD trial. The Applicant estimated that 1,134 patients would be treated with finerenone in year 1, increasing to 6,630 patients in year 5. It was assumed that finerenone would not replace any current treatments because it is an add-on therapy to SoC. Therefore the net drug budget impact was the same as the gross drug budget impact. In the Applicant budget impact analysis, the cumulative five-year gross drug budget impact was estimated to be €15.5 million (including VAT). The budget impact was most sensitive to the cost of the intervention.

5. Patient Organisation Submission

No patient organisation submissions were received during the course of the assessment.

6. Conclusion

Following assessment of the Applicant's submission, the NCPE recommends that finerenone, be considered for reimbursement, for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults, if cost-effectiveness can be improved relative to existing treatments*.

* This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013