

# Health Technology Briefing

## May 2024

### Finerenone for treating heart failure

Company/Developer

Bayer AG

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 30105

NICE ID: Not available

UKPS ID: 673441

### Licensing and Market Availability Plans

Currently in phase III clinical development.

### Summary

Finerenone is currently in clinical development for treating heart failure in adults. Heart failure is a combination of symptoms and signs that indicate that the heart is pumping blood around the body less efficiently. Left ventricular ejection fraction is calculated as the percentage of how much blood in a part of the heart called the left ventricle is pumped out with each contraction. The prevalence of heart failure increases slowly with age until about 65 years of age, and then more rapidly. Symptoms of heart failure include breathlessness, fatigue and swelling caused by excess fluid build-up in bodily tissues. There is an unmet need for well-tolerated treatment options for patients with heart failure.

Finerenone is a non-steroidal tablet that is taken orally. It binds to a target known as the mineralocorticoid receptor (MR). MR is involved in starting processes that cause inflammation. By binding to MR, finerenone stops the start of these processes and prevents inflammation. If licensed, finerenone will offer an additional treatment option for adults with heart failure.

## Proposed Indication

Treatment of adults with heart failure and left ventricular ejection fraction (LVEF) of  $\geq 40\%$ .<sup>1</sup>

## Technology

### Description

Finerenone (Kerendia) is a nonsteroidal, selective antagonist of the mineralocorticoid receptor (MR), which is activated by aldosterone and cortisol and regulates gene transcription.<sup>2</sup> The MR consists of three functional domains: N-terminal domain; DNA-binding domain; and C-terminal ligand binding domain.<sup>3</sup> Finerenone binding to the MR leads to a specific receptor-ligand complex that blocks recruitment of transcriptional coactivators implicated in the expression of pro-inflammatory and pro-fibrotic mediators.<sup>2</sup> It has been shown to suppress specific profibrotic cardiac genes that are less efficaciously regulated by eplerenone and spironolactone, resulting in a markedly stronger antifibrotic action in the left ventricle.<sup>3</sup>

Finerenone is currently in clinical development for the treatment of heart failure in adults with LVEF  $\geq 40\%$ . In a phase III clinical trial (FINEARTS-HF, NCT04435626), patients either received 10, 20 or 40 milligrams finerenone tablets orally, once daily or a matched placebo.<sup>1</sup>

### Key Innovation

Currently available steroidal MR antagonists have been associated with intolerable side-effects including hyperkalaemia. Non-steroidal MR antagonists, such as finerenone, are compounds that have been developed to improve the side-effect profile of current steroidal MR antagonists while maintaining clinical efficacy. They have so far demonstrated significant risk reduction in cardiovascular diseases. Potent antihypertrophic, antiproliferative, anti-inflammatory and antifibrotic actions by finerenone were corroborated in different rodent models, which often showed a stronger protection by finerenone compared with MR antagonists.<sup>3</sup> If licensed, finerenone will offer a treatment option for adults with heart failure.

### Regulatory & Development Status

Finerenone currently has Marketing Authorisation in the UK for the treatment of chronic kidney disease (stage 3 and 4 with albuminuria) associated with type 2 diabetes in adults.<sup>2</sup>

Finerenone is also in phase II and III clinical development for the following indications:<sup>4</sup>

- Type 1 diabetes mellitus and chronic kidney disease
- Non-diabetic chronic kidney disease
- Paediatric chronic disease

## Patient Group

### Disease Area and Clinical Need

Heart failure occurs when the heart is unable to pump blood around the body properly. It usually happens because the heart has become too weak or stiff. Heart failure is often the results of multiple problems affecting the heart at the same time. Conditions such as coronary heart disease, high blood pressure or obesity can cause heart failure. Symptoms of heart failure include breathlessness, constant fatigue and swollen ankles or legs.<sup>5</sup> Heart failure is classified by measurement of the left ventricular ejection fraction (LVEF). People with a LVEF between 41–49% have a mildly reduced ejection fraction. People who have

symptoms of heart failure, cardiac structure or function abnormalities, and/or raised levels of natriuretic peptides with a preserved LVEF of 50% or more, have heart failure with preserved ejection fraction (HF-PEF).<sup>6</sup>

The prevalence of heart failure increases slowly with age until about 65 years of age, and then more rapidly. The prevalence of heart failure in the UK is estimated to be 1 in 35 people aged between 65 and 74 years, 1 in 15 people aged between 75 and 84 years, and 1 in 7 people aged 85 years and older. It is estimated that in people with heart failure, about 50% have preserved or mildly reduced ejection fraction.<sup>7</sup> In England, 2022-23, there were 34,890 finished consultant episodes (FCE) and 16,796 admissions for left ventricular failure (ICD-10 code I50.1), which resulted in 135,389 FCE bed days and 3,034 day cases.<sup>8</sup>

### Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following for treating heart failure with reduced ejection fraction in adults:<sup>9</sup>

- angiotensin-converting-enzyme inhibitors and a beta blocker;
- angiotensin receptor blockers;
- beta-blockers;
- mineralocorticoid receptor antagonists;
- other specialist treatments (hydralazine with nitrate and digoxin)

NICE also recommends empagliflozin and dapagliflozin for treating heart failure with preserved or mildly reduced ejection fraction.<sup>10,11</sup>

### Clinical Trial Information

<b>Trial</b>	<b>FINEARTS-HF, <a href="#">NCT04435626</a>, <a href="#">EudraCT 2020-000306-29</a></b> ; A Multicenter, Randomized, Double-blind, Parallel-group, Placebo-controlled Study to Evaluate the Efficacy and Safety of Finerenone on Morbidity and Mortality in Participants With Heart Failure (NYHA II-IV) and Left Ventricular Ejection Fraction $\geq$ 40% (LVEF $\geq$ 40%) <b>Phase III</b> – Active, not recruiting <b>Location(s)</b> : 17 EU countries, UK, USA, Canada, and other countries <b>Primary completion date</b> : May 2024
<b>Trial Design</b>	Randomised, parallel assignment, placebo-controlled, quadruple-blind
<b>Population</b>	N = 6016; adults aged 40 years and older, diagnosis of heart failure with New York Heart Association (NYHA) class II-IV and documented LVEF of $\geq$ 40% measured by any modality within the last 12 months.
<b>Intervention(s)</b>	Finerenone oral, immediate release tablets <ul style="list-style-type: none"> <li>• For participants with an eGFR <math>\leq</math>60 mL/min/1.73 m<sup>2</sup>: Starting dose is 10 mg OD and maximum dose 20 mg OD.</li> <li>• For participants with an eGFR <math>&gt;</math>60 mL/min/1.73 m<sup>2</sup>: Starting dose is 20 mg OD and maximum dose 40 mg OD.</li> </ul>
<b>Comparator(s)</b>	Matched placebo administered orally.
<b>Outcome(s)</b>	Primary outcome: number of cardiovascular deaths and heart failure events [Time Frame: Up to 42 months]

	See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

### Estimated Cost

Finerenone (Kerendia) is already marketed in the UK for the treatment of chronic kidney disease. A pack of 28 x 10 mg or 28 x20 mg tablets cost £36.68.<sup>12</sup>

### Relevant Guidance

#### NICE Guidance

- NICE technology appraisal guidance. Empagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction (TA929). November 2023.
- NICE technology appraisal guidance. Dapagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction (TA902). June 2023.
- NICE guideline in development. Chronic heart failure in adults: diagnosis and management - Pharmacological treatment of chronic heart failure (GID-NG10405). Expected date to be confirmed.
- NICE guideline. Chronic heart failure in adults: diagnosis and management (NG106). September 2018.
- NICE quality standard. Chronic heart failure in adults (QS9). June 2011. Updated January 2023.

#### NHS England (Policy/Commissioning) Guidance

No relevant guidance identified.

#### Other Guidance

- European Society of Cardiology (ESC). Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. 2023.<sup>13</sup>
- American Heart Association (AHA). Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. 2022.<sup>14</sup>
- Scottish Intercollegiate Guidelines Network (SIGN). SIGN 147: Management of chronic heart failure. 2016.<sup>15</sup>

### Additional Information

## References

- 1 Clinicaltrials.gov. *A Multicenter, Randomized, Double-blind, Parallel-group, Placebo-controlled Study to Evaluate the Efficacy and Safety of Finerenone on Morbidity and Mortality in Participants With Heart Failure (NYHA II-IV) and Left Ventricular Ejection Fraction  $\geq$  40% (LVEF  $\geq$  40%)*. 2017. Available from: <https://clinicaltrials.gov/study/NCT04435626> [Accessed 22 March 2024].
- 2 Electronic Medicines Compendium (EMC). *Kerendia*. 2023. Available from: <https://www.medicines.org.uk/emc/product/13437/smpc> [Accessed 22 March 2024].
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- 4 Clinicaltrials.gov. *Search for: Finerenone | Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies | Phase 2, 3*. 2024. Available from: [https://classic.clinicaltrials.gov/ct2/results?cond=&term=finerenone&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age\\_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd\\_s=&strd\\_e=&prcd\\_s=&prcd\\_e=&sfpd\\_s=&sfpd\\_e=&rfpd\\_s=&rfpd\\_e=&lupd\\_s=&lupd\\_e=&sort=](https://classic.clinicaltrials.gov/ct2/results?cond=&term=finerenone&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort=) [Accessed 25 March 2024].
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**NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.**