Finerenone for treating heart failure with preserved or mildly reduced ejection fraction [ID6514]

PART 1

For public – contains no confidential information

Technology appraisal committee C [9 June 2026, ACM1]

Chair: James Fotheringham

Lead team: Alastair Dickson, Ugochi Nwulu, Jon Tosh

External assessment group: School of Health and Related Research (SCHARR)

Technical team: Anita Sangha, Samuel Slayen, Adam Brooke

Company: Bayer

Finerenone for treating heart failure with preserved or mildly reduced ejection fraction [ID6514]

- ✓ **Background and key issues**
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ❑ Summary

NICE National Institute for Health and Care Excellence

Heart failure with preserved or mildly reduced ejection fraction

Chronic condition, heart is unable to pump enough blood to meet body's needs

Causes of heart failure (HF): structural or functional abnormalities of heart

- Common causes: coronary heart disease, hypertension, heart valve disease and cardiomyopathy

Symptoms: include breathlessness, fatigue, swollen ankles and legs

Prognosis: HF usually gets worse over time, typically cannot be cured, often results in repeated hospitalisations

- Treatment can control symptoms and prolong life, but prognosis is poor: 5-year survival for HF is ~48%*

Classification: New York Heart Association (NYHA) classification often defines severity in clinical practice

- Classification is based on limitations of physical activity → 1 = least severe and 4 = most severe

Epidemiology: ~650,000 with HF in England, ~50% have preserved or mildly reduced ejection fraction**

- Characteristics of people with HFpEF in England†: mean age ~80 years, ~55% female, ~88% White ethnicity

Heart failure (HF) subtype	Left ventricular ejection fraction (LVEF) (% of blood ejected from the left ventricle per heartbeat)
Preserved ejection fraction (HFpEF):	**50% or higher**
Mildly reduced ejection fraction (HFmrEF)	**41 to 49%**
Reduced ejection fraction (HFrEF)	40% or lower

*Taylor et al (2019): Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population based cohort ** Company BIA submission

†Fletcher et al (2024): Contemporary epidemiology of hospitalised heart failure with reduced versus preserved ejection fraction in England: a retrospective, cohort study of whole-population electronic health records

Abbreviations: HF, heart failure; HFpEF, heart failure with preserved ejection fraction

Patient perspectives

HF significantly impacts QoL, finerenone offers benefits over current treatment

Submissions from 1 patient expert and Pumping Marvellous Foundation

- HF is often associated with multiple co-morbidities, poor QoL and high mortality
- Evidence base for HFpEF is limited (compared with HFrEF) which has meant that there are lack of treatment options for this population
    - often limited to management of co-morbidities which can be challenging
    - concerns about side effects with steroidal MRAs (higher risk of hyperkalaemia, renal decline and hormonal side effects with spironolactone)
- Finerenone is more targeted and better tolerated [than steroidal MRAs] with key trial suggesting significant reductions in hospital admissions in people with HFpEF
    - benefits are likely largest for people who also have CKD and/or diabetes

"The key benefit [of finerenone] is the reduction in hospital admissions which improves people's quality of life coupled with the benefits of reduction in CKD and diabetic risk along with no hormonal side effects"

Further comments on evidence base and care pathway for relevant population in key issue and equality considerations slides

Abbreviations: CKD, chronic kidney disease; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist

Clinical perspectives

HFpEF and HFmrEF can be debilitating, treatment options are limited for this population

Submissions from 1 clinical expert, British Cardiovascular Society, British Society for Heart Failure and UK Clinical Pharmacist Association

- HFpEF/HFmrEF is associated with a substantial symptom burden and recurrent hospitalisations → detrimental QoL impact for patients and caregivers
- SGLT2 inhibitors are the only approved disease-modifying therapy for HFpEF, but additional effective therapies are needed to improve outcomes and care pathway
- Key trial for finerenone (HFmrEF/HFpEF) showed a significant and clinically meaningful reduction in total worsening HF events
- Finerenone is an additional option for people who 1) remain symptomatic despite existing treatment 2) cannot tolerate steroidal MRAs or have diabetic CKD
    - risk of hyperkalaemia and change in renal function → monitored as part of usual care, hyperkalaemia often easily managed in most people

"Current treatment options are limited in HFpEF and there remains a substantial residual burden of symptoms and hospitalisations… potential benefits provided by addition of finerenone are clinically important… and will help reduce variability in care."

Further comments on evidence base and care pathway for relevant population in key issue and equality considerations slides

Abbreviations: CKD, chronic kidney disease; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; MRA, mineralocorticoid receptor antagonist, SGLT2, sodium-glucose co-transporter-2

Finerenone (Kerendia, Bayer)

<table>
<tr><td>Marketing authorisation (MA)</td><td>

Finerenone is indicated for the treatment of symptomatic chronic heart failure with left ventricular ejection fraction (LVEF) ≥40% in adults
Also licensed for CKD (stage 3 and 4 with albuminuria) associated with T2DM in adults (NICE TA877 recommends optimised use within this population)

</td></tr>
<tr><td>Mechanism of action</td><td>

Selective non-steroidal mineralocorticoid receptor antagonist (MRA)

no relevant affinity for sex-hormone receptors → reduces risk of hormonal side effects (such as gynecomastia in men) often associated with some steroidal MRAs

</td></tr>
<tr><td>Administration</td><td>

Oral tablet taken once daily (maximum recommended dose is 40mg daily)
Appropriate dosage is based on serum potassium and renal function (eGFR)

<table>
<tr><th>Treatment phase</th><th>Initial daily dosing schedule (if serum potassium is ≤5.0 mmol/L)</th></tr>
<tr><td>Titration dose</td><td>10 mg if eGFR ≥25 to <60 mL/min/1.73 m^2</td></tr>
<tr><td>Titration dose</td><td>20 mg if eGFR ≥60 mL/min/1.73 m^2</td></tr>
<tr><td>Target dose</td><td>20 mg if eGFR ≥25 to <60 mL/min/1.73 m^2</td></tr>
<tr><td>Target dose</td><td>40 mg if eGFR ≥60 mL/min/1.73 m^2</td></tr>
</table>

If serum potassium >5.0 mmol/L: dose adjustment or discontinuation may be needed

</td></tr>
<tr><td>Price</td><td>

List price is £36.68 per pack of 28 tablets (10 mg and 20 mg, company expects price for new 40 mg strength to be the same), ~£476.84 for 12 months treatment (13 packs)
No confidential commercial arrangement

</td></tr>
</table>

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MRA, mineralocorticoid receptor antagonist; T2DM, type 2 diabetes mellitus

Treatment pathway

HFmrEF and HFpEF treatment pathway based on NG106 (published 2018, updated September 2025)

Mildly reduced ejection fraction (LVEF: 41- 49%)

Consider:

ACE inhibitor (or ARB)**

+

Beta-blocker

+

MRA
Steroidal (spironolactone or eplerenone) or non-steroidal

+

SGLT2 inhibitor
- Dapagliflozin (TA902)
- Empagliflozin (TA929)

In all settings and stages:
- ensure people have rehabilitation and education
- give diuretics* if needed for congestion and fluid retention

Company's proposed positioning of finerenone (non-steroidal MRA option added to SoC)

Preserved ejection fraction (LVEF: ≥50%)

Consider:

MRA
Steroidal (spironolactone or eplerenone) or non-steroidal

+

SGLT2 inhibitor
- Dapagliflozin (TA902)
- Empagliflozin (TA929)

*lowest available dose **if ACE inhibitor not tolerated

- Consider lower starting doses or smaller dose increments if the person has CKD and eGFR≤45 mL/min/1.73 m²
- Specialist heart failure team should consider liaising with renal physician if CKD and eGFR<30 mL/min/1.73 m²

Does treatment in NHS clinical practice follow the treatment pathway?

Abbreviations: ACE; angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium-glucose co-transporter-2; SoC, standard of care

Basis for MRA recommendations in NG106

Population: HF with reduced EF

- '**Offer**' MRA class-based recommendation informed by several RCTs: EMPHASIS-HF, J-EMPHASIS HF, EARLIER, compared eplerenone vs placebo.
- Economic evaluation initiated MRA as part of quadruple therapy up front, rather than in sequence
- Trials suggested clinical benefit for MRA + SoC* vs placebo + SoC:
  - all-cause mortality (EMPHASIS-HF): HR 0.76 (95% CI 0.62 to 0.93)
  - CV mortality (EMPHASIS-HF): HR 0.76 (95% CI 0.61 to 0.94)
  - HF-related hospitalisation or visit (meta-analysis of all 3 RCTs): HR 0.60 (95% CI 0.50 to 0.72)

*ACE inhibitor/ARB + Beta-blocker

Population: HF with preserved or mildly reduced EF

- '**Consider**' MRA recommendation informed by meta-analysis of FINEARTS-HF and TOPCAT RCTs:
  - FINEARTS-HF (see key clinical trial for finerenone)
  - TOPCAT (2014): n=3,445, symptomatic HF (LVEF ≥45%), compared spironolactone vs placebo
  - No economic analysis completed
- Pooled results suggested some clinical benefit for MRAs (class-level efficacy) vs placebo
  - HFmrEF → all-cause and CV mortality: HRs 0.91 and 0.81 (results not significant), first HF-related hospitalisation or visit: HR 0.77 (95% CI 0.64 to 0.93)
  - HFpEF → all-cause and CV mortality: HRs 0.89 and 0.90 (results not significant), HF-related hospitalisation: HR 0.77 (95% CI 0.69 to 0.87)

Abbreviations: ACE; angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CI, confidence interval; CV, cardiovascular; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; RCT, randomised controlled trial; SoC, standard of care

Key issues

Issue	Resolved?	ICER impact
Primary key issue: comparators 1a) Exclusion of steroidal MRAs as a comparator 1b) Evidence for comparison (finerenone vs spironolactone): ITCs or RWE	**No – for discussion**	**Large**
Secondary key issue: survival analysis methods Estimation of all-cause and CV mortality for finerenone and placebo arms using FINEARTS-HF data: • Company: used jointly fitted models with covariates controlling for treatment arm and time varying KCCQ-TSS quartile • EAG: preferred independently fitted models without covariates • Company response to TE: agree with EAG's preferred approach	Yes	Small (reduces ICER)

Abbreviations: CV, cardiovascular; ICER, incremental cost-effectiveness ratio; ITC, indirect treatment comparison; KCCQ-TSS; Kansas City Cardiomyopathy Questionnaire total symptom score; MRA, mineralocorticoid receptor antagonist; RWE, real-world evidence; TE, technical engagement

Finerenone for treating heart failure with preserved or mildly reduced ejection fraction [ID6514]

- ❑ Background and key issues
- ✓ **Clinical effectiveness**
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ❑ Summary

NICE National Institute for Health and Care Excellence

Key clinical trial: FINEARTS-HF

Phase 3, double-blind RCT, randomisation (1:1) stratified by country/region and LVEF (<60%, ≥60%)	
Population	Adults aged ≥40 years with HFmrEF or HFpEF (LVEF ≥40%), NYHA class 2-4
Intervention (FAS, n=3,003)	Finerenone titrated to 20mg once daily (if baseline eGFR <60 mL/min/1.73 m²) or 40 mg once daily (if baseline eGFR≥60 mL/min/1.73 m²) + SoC (as placebo arm)
Comparator (FAS, n=2,998)	Matched placebo + SoC (may have included diuretics, beta-blockers, RAAS inhibitors, statins, SGLT2 inhibitors)
Duration	Median duration of follow-up: 32 months, study duration up to 43 months
Primary outcome	Composite of CV death and total worsening HF events (hospitalisation or urgent HF visit)
Key secondary outcomes	Total worsening HF events, KCCQ-TSS at 6,9 and 12 months, renal composite outcome, NYHA class at 12 months, all-cause mortality, AEs
Locations	37 countries across Americas, Asia, Europe (including UK, n=[redacted] in FAS), Oceania

EAG comments: FINEARTS-HF is at low risk of bias

- Exclusion criteria: continuous (≥90 days) treatment with an MRA within 12 months prior to screening
  - comparator arm likely only relevant to population who are unable to have steroidal MRAs
- SGLT2 inhibitors only approved for chronic HF part way through the FINEARTS-HF study
  - likely overrepresents use for other indications (e.g. T2DM) rather than for HFmrEF or HFpEF

Abbreviations: AE, adverse events; CV, cardiovascular; eGFR, estimated glomerular filtration rate; FAS, full analysis set; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; KCCQ-TSS; Kansas City Cardiomyopathy Questionnaire total symptom score; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NYHA; New York Heart Association; RAAS, renin-angiotensin-aldosterone signalling; RCT, randomised controlled trial; SGLT2, sodium-glucose co-transporter-2; SoC, standard of care; T2DM, type 2 diabetes mellitus

FINEARTS-HF primary outcome results

Finerenone significantly reduces the primary composite end point of total worsening HF events and cardiovascular death (CV) compared with placebo

Primary outcome and components (FAS)	Finerenone (n=3,003)	Placebo (n=2,998)
Primary outcome composite: total worsening HF events and death from CV causes		
Number of events	1,083	1,283
Rate ratio (finerenone vs placebo)	0.84 (95% CI 0.74 to 0.95), p=0.007	
Component: total worsening HF events (first and recurrent hospitalisation for HF or urgent HF visit)		
Rate ratio (finerenone vs placebo)	0.82 (95% CI 0.71 to 0.94), p=0.006	
Component: death from CV causes		
Hazard ratio (finerenone vs placebo)	0.93 (95% CI 0.78 to 1.11), p=[redacted]	

Finerenone treatment effect on primary composite end point is largely driven by significant reduction in total worsening HF events, with no significant reduction in death from CV causes

Abbreviations: CI, confidence interval; CV, cardiovascular; FAS, full analysis set; HF, heart failure

Key issues 1a: Exclusion of steroidal MRAs as a comparator (1)

Company and EAG disagree on whether steroidal MRAs are a relevant comparator to finerenone

Background – company: steroidal MRAs not included as a comparator in the decision problem*

- Company clarification response: limited evidence to support use of steroidal MRAs in HFmrEF and HFpEF
- EAG: steroidal MRA use was an exclusion criteria in FINEARTS-HF → comparator arm may not reflect clinical practice or NG106 recommendations

*see – decision problem back-up slide

Company response to TE – steroidal MRA use is limited in clinical practice (1)

- CE opinion: historical use of steroidal MRAs does not mean it is an evidence-based comparator to finerenone
  - TOPCAT did not meet its primary endpoint** and has well-recognised concerns (see back-up slide)
  - steroidal and non-steroidal MRAs should not be considered interchangeable in this population due to meaningful differences in pharmacology, evidence strength and tolerability
- Post-hoc analysis using TOPCAT Americas subgroup suggests signal of benefit* but is hypothesis generating and lacks robustness of adequate statistical power → aligns with NG106 (2018) committee view
- NG106 (2025) recommendation to consider steroidal MRAs is due to high quality FINEARTS-HF evidence
- Current use of steroidal MRAs in HFpEF and HFmrEF varies on setting and is often less than optimal
  - CE opinion: initial prescribing remains low, due to hyperkalaemia concerns and managing side effects

**composite of cardiovascular death, aborted cardiac arrest or HF hospitalisation → full population: HR 0.89 (95% CI 0.77 to 1.04, p=0.14), Americas subgroup: HR 0.82 (95% CI 0.69 to 0.98, p=0.026)

Abbreviations: CE, clinical expert; CI, confidence interval; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; MRA, mineralocorticoid receptor antagonist, TE, technical engagement

Large ICER impact

Key issues 1a: Exclusion of steroidal MRAs as a comparator (2)

Stakeholder comments – steroidal MRA use is low, variable and often for alternative indications

- MRAs generally not considered interchangeable → treatment decisions based on evidence and tolerability
- No robust evidence of a disease modifying effect for steroidal MRAs in people with HFpEF or HFmrEF
  - TOPCAT evidence is uncertain → low and highly variable uptake of steroidal MRAs in practice
  - very limited evidence for eplerenone in HFpEF
- Steroidal MRAs are being used in relevant population often for alternative indications such as resistant hypertension or adjunctive diuretic therapy rather than as a primary heart failure treatment
- Current use of steroidal MRAs in HFpEF and HFmrEF difficult to estimate and varies
- Tolerability issues with steroidal MRAs and side effects with spironolactone limit usage in practice

Source (TE responses)	Estimate of steroidal MRA use in HFpEF/HFmrEF (before NG106 update)
Company: market research	~[redacted]% in primary care to ~[redacted]% in secondary care
Company: UK retrospective cohort study*	15.5% in HFpEF, 20.6% in HFmrEF (prescribed at hospital discharge)
Company: NICOR National HF Audit 2024	68% of hospitalised patients had an MRA (informative for HFrEF only)
Stakeholder comments	~10-20% overall (<10% with HFpEF), ~20-30% in primary care, ~60% after new diagnosis/recent hospital admission with HF specialist input

*Migas et al (2024) Missed opportunities in heart failure diagnosis and management: study of an urban UK population

NICE

Abbreviations: HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ICER, incremental cost-effectiveness ratio; MRA, mineralocorticoid receptor antagonist; NICOR, National Institute for Cardiovascular Outcomes Research

Large ICER impact

Key issues 1a: Exclusion of steroidal MRAs as a comparator (3)

EAG comments – steroidal MRAs should remain a relevant comparator

- NG106 recommends to consider an MRA (as a class) in both HFmrEF and HFpEF
- Steroidal MRAs are used in clinical practice in a subgroup of people with HFmrEF and HFpEF
- Acknowledge that steroidal MRAs would not be suitable for all people → EAG base case ICER is an appropriate estimate of cost effectiveness for finerenone vs SoC (from FINEARTS-HF) in this subgroup
- FINEARTS-HF may have strengthened evidence base for steroidal MRAs in NG106 update → if so, this indicates a strong prior held by clinical experts that finerenone results can be generalised to steroidal MRAs

Are steroidal MRAs a relevant comparator to finerenone?
Will the use of steroidal MRAs change following the updated recommendations in NG106?

Abbreviations: HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; ICER, incremental cost-effectiveness ratio; MRA, mineralocorticoid receptor antagonist; SoC, standard of care

Large ICER impact

Key issues 1b: Evidence for comparison (1): ITCs using RCTs

Relative efficacy of finerenone compared with spironolactone depends on the choice of analyses

Background – no direct evidence comparing finerenone vs steroidal MRAs in HFmrEF or HFpEF

- EAG: requested ITC comparing finerenone vs steroidal MRAs in relevant population at clarification
- Company clarification response: ITC not appropriate largely due to weakness in available evidence base

Company response to TE (1) – ITCs to estimate relative efficacy of finerenone vs spironolactone

- Did Bucher ITC for relevant endpoints from FINEARTS-HF and TOPCAT using SoC as common comparator by assuming transitivity of treatment effects

ITC results	Finerenone vs spironolactone (TOPCAT full analysis set)		Finerenone vs spironolactone (TOPCAT Americas subgroup)	
Outcome	Mean	95% CI	Mean	95% CI
Hospitalisation due to heart failure (HR)	1.036	0.833 to 1.288	1.049	0.833 to 1.320
All-cause mortality (HR)	1.022	0.829 to 1.259	1.120	0.884 to 1.420
Cardiovascular mortality (HR)	1.033	0.783 to 1.364	1.257	0.913 to 1.729
Serious adverse events (OR)	0.968	0.817 to 1.146	NR	NR
Hyperkalaemia (OR)	0.979	0.820 to 1.169	0.649	0.467 to 0.902
Treatment discontinuation (IRR)	0.923	0.792 to 1.074	NR	NR

ITC results: no statistically significant differences in key outcomes between finerenone and spironolactone, significantly lower odds of hyperkalaemia with finerenone in TOPCAT Americas subgroup only

Outcome data not available for all endpoints in the TOPCAT Americas subgroup → complete set of results could not be derived for this subgroup
Values <1 indicate lower risk/odds/rate with finerenone versus spironolactone, values >1 indicate higher risk/odds/rate with finerenone versus spironolactone

Abbreviations: CI, confidence interval; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; IRR, incidence rate ratio; ITC, indirect treatment comparison; MRA, mineralocorticoid receptor antagonist; NR, not reported; OR, odds ratio; RCT, randomised controlled trial; SoC, standard of care; TE, technical engagement

Key issues 1b: Evidence for comparison (2): ITCs using RCTs

Company response to TE (2) – ITCs using TOPCAT are not appropriate

- TOPCAT has well-recognised concerns (see back-up slide)→ uncertain effect estimates
- Significant heterogenicity between TOPCAT and FINEARTS-HF (differences in clinical eras and settings, geographical regions, inclusion criteria and underlying SoC, see back-up slide)
- Restricted to Bucher ITC: cannot incorporate wider network of evidence or explore heterogeneity formally

EAG comments - Bucher ITC is a robust measure of relative treatment effect if there are no treatment effect modifiers in a study arm

- Company has not explained why outlined differences between studies would be treatment effect modifiers
  - if no treatment effect modifiers → estimate of relative effectiveness from ITC should be appropriate
  - CE opinion: non-Americas subgroup data has limitations → analysis comparing with the Americas subgroup would be informative, providing all caveats related to a post-hoc analysis are considered
- NG106 (2025) committee was content to pool steroidal MRAs and finerenone efficacy estimates indicating a prior belief that effectiveness is similar

Stakeholder comments – ITCs using TOPCAT likely lack validity

- Differences in patient selection, background therapy and regional variation in TOPCAT limits comparability with FINEARTS-HF → ITCs are subject to significant uncertainty and risk of bias

Abbreviations: CE, clinical expert; ICER, incremental cost-effectiveness ratio; ITC, indirect treatment comparison; MRA, mineralocorticoid receptor antagonist; RCT, randomised controlled trial; SoC, standard of care; TE, technical engagement

Large ICER impact

Key issues 1b: Evidence for comparison (3): RWE

Company response to TE (3) – RWE to estimate relative efficacy of finerenone vs spironolactone

- 2 retrospective, observational cohort studies (Almas et al. 2026 and Wu et al. 2025) compared efficacy of non-steroidal vs steroidal MRAs in adults with HF based on use within a 1-year period of diagnosis
  - propensity score matching was used to balance baseline characteristics between non-steroidal and steroidal MRA groups identified from a global database of patient health records (TriNetX)

		Almas et al. 2026	Wu et al. 2025
Population		HFpEF	HFpEF and HFrEF
N = before matching	nsMRA	Finerenone, n=497	Finerenone, n=1,632
	sMRA	Spironolactone, n=253,920	Spironolactone or eplerenone, n=374,370
N = after matching	nsMRA and sMRA	n=491	n=1,619, HFpEF subgroup: n=628

Endpoint used in model	Hazard ratio finerenone vs. spironolactone	
	Almas et al. 2026	Wu et al. 2025 (HFpEF subgroup)
All-cause mortality	0.38 (95% CI 0.23, 0.64)	0.51 (95% CI 0.32, 0.81)
All-cause hospitalisation	Not reported	0.83 (95% CI 0.67, 1.02)
Worsening HF/HF exacerbation*	0.63 (95% CI 0.54, 0.74)	0.6 (95% CI 0.45, 0.79)
Hyperkalaemia	0.96 (95% CI 0.69, 1.33)	0.89 (95% CI 0.68, 1.17)**

Values <1 indicate lower risk with finerenone versus spironolactone

RWE results: direction of effect favours finerenone for all outcomes, statistically significant for all-cause mortality and worsening HF/HF exacerbation across both studies

*Reported as "HF exacerbation" in Almas et al. 2026, reported as "worsening HF" in Wu et al. 2025 **Reported for full HFpEF and HFrEF population only
Note: These studies either had funding not declared or no external funding received. Mostly USA, unclear if any UK patients were in the TriNetX database.

Abbreviations: CI, confidence interval; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ICER, incremental cost-effectiveness ratio; MRA, mineralocorticoid receptor antagonist; nsMRA, non-steroidal MRA; RWE, real-world evidence; sMRA, steroidal MRA; TE, technical engagement

Key issues 1b: Evidence for comparison (4): RWE

Company response to TE (4) – limitations of RWE restrict suitability for robust comparison

- RWE and FINEARTS-HF populations do not closely align due to differences in baseline risk, comorbidities and background therapy* (RWE cohorts: more co-morbid and heavily treated at baseline)
  - may introduce additional effect modification when applying HRs to FINEARTS-HF outcomes
- Wu et al. 2025 included mixed steroidal MRA exposure → additional clinical heterogeneity may be present

EAG comments – RWE studies are subject to inaccuracy and results may lack face validity (1)

- Exclusion of Habib et al. 2025 based on smaller sample size is not appropriate → finerenone demonstrated broadly comparable effectiveness and safety to spironolactone in study (at odds with the 2 studies included)
- RWE studies can be prone to selection bias, particularly due to unmeasured confounding
- Agree that RWE and FINEARTS-HF populations differ as outlined by company
  - treatment effect estimated in the RWE cohorts for finerenone vs spironolactone may be different in FINEARTS-HF population due to potential effect modification
  - substantial difference in all-cause mortality observed in the finerenone group between Almas et al. 2026 (4.1% after matching) and FINEARTS-HF (16.4%) likely reflects differences in the study populations

*See back-up slides:

1. Baseline characteristics (before and after matching) vs FINEARTS-HF
2. Company critique on RWE
3. Notes from NICE's RWE framework

Abbreviations: HR, hazard ratio; ICER, incremental cost-effectiveness ratio; MRA, mineralocorticoid receptor antagonist; RWE, real-world evidence; TE, technical engagement

Large ICER impact

Key issues 1b: Evidence for comparison (5): RWE

EAG comments – RWE studies are subject to inaccuracy and results may lack face validity (2)

- All-cause mortality midpoint HRs for finerenone vs spironolactone (0.38, Almas et al. 2026) compared with finerenone vs placebo (0.93, FINEARTS-HF), imply that placebo has better efficacy than spironolactone
  - comparisons for hospitalisations and urgent HF hospitalisation visits [redacted]
  - does not align with NG106 → presented combined efficacy for both steroidal MRA and finerenone

NICE technical team comments

- Almas et al. 2026: finerenone not licensed for HFpEF at the time of the study → most likely prescribed for CKD and/or T2DM in people who also had HFpEF (~50% had diabetes in spironolactone group, matched to 91% in finerenone group)

Company conclusions	EAG conclusions
Neither ITC and RWE analyses provide a sufficiently robust basis for a reliable quantitative comparison between finerenone and spironolactone	**Relative efficacy estimated by the ITCs are likely to be more accurate than those produced by the RWE studies**

How appropriate are the company's ITCs and RWE analyses for estimating the relative treatment effect of finerenone versus spironolactone?

Abbreviations: CKD, chronic kidney disease; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; ITC, indirect treatment comparison; MRA, mineralocorticoid receptor antagonist; RWE, real-world evidence; T2DM, type 2 diabetes mellitus

Finerenone for treating heart failure with preserved or mildly reduced ejection fraction [ID6514]

- ❑ Background and key issues
- ❑ Clinical effectiveness
- ✓ **Modelling and cost effectiveness**
- ❑ Other considerations
- ❑ Summary

NICE National Institute for Health and Care Excellence

No key issues relating to company model

- EAG: model structure and inputs appropriate for decision making
- No difference between company and EAG base case assumptions (post technical engagement)

Company and EAG base case results of finerenone vs SoC (FINEARTS-HF)

- Company and EAG agree that no additional QALY weighting for severity should be applied

Deterministic incremental base case results

Technology	Total costs (£)	Total QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)
Finerenone + SoC	[redacted]	[redacted]	[redacted]	[redacted]	12,756
SoC	[redacted]	[redacted]			

Probabilistic incremental base case results

Technology	Total costs (£)	Total QALYs	Inc. costs (£)	Inc. QALYs	ICER (£/QALY)
Finerenone + SoC	[redacted]	[redacted]	[redacted]	[redacted]	12,764
SoC	[redacted]	[redacted]			

EAG scenario analyses → all ICERS below £16,000/QALY gained
EAG: ICERs are only relevant to population for whom steroidal MRAs are unsuitable

Company: finerenone would likely be used with SGLT2 inhibitors (13.6% use in FINEARTS-HF at baseline) → presented alternative base case including SGLT2 inhibitor use at baseline, significantly reduces ICER

EAG: SGLT2 inhibitor use in FINEARTS-HF likely due to other indications rather than HF → subgroup is not a reasonable 'alternative base case' that is generalisable to HF patients who are taking SGLT2 inhibitors

NICE technical team: ~51% of people with HFmrEF or HFpEF prescribed SGLT2 inhibitor in 2024/25*

*National Institute for Cardiovascular Outcomes Research (NICOR) National Heart Failure Audit. Annual Report 2025

NICE

Abbreviations: HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; Inc, incremental; ICER, incremental cost-effectiveness ratio; MRA, mineralocorticoid receptor antagonist; QALY, quality-adjusted life year; SGLT2, sodium-glucose co-transporter-2; SoC, standard of care

CE results of finerenone vs spironolactone (Bucher ITC)

Deterministic incremental key scenario results (TOPCAT full analysis set)

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)	INMB (£25k/QALY)
Finerenone + SoC	12,917	5.387	4,636	-0.083	Dominated	-6,721
Spironolactone + SoC	8,281	5.470				

Deterministic incremental key scenario results (TOPCAT Americas subgroup)

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)	INMB (£25k/QALY)
Finerenone + SoC	12,917	5.387	4,487	-0.182	Dominated	-9,043
Spironolactone + SoC	8,431	5.569				

Finerenone is dominated by spironolactone in all additional company scenario analyses

Company: ICERs not supported by robust evidence → not appropriate for decision making
EAG: relative efficacy estimated by ITCs likely more accurate than RWE studies → ICER comparing finerenone vs spironolactone will likely be nearer to those generated by ITC (vs RWE studies)

Abbreviations: ICER, incremental cost-effectiveness ratio; INMB; incremental net monetary benefit; ITC, indirect treatment comparison; QALY, quality-adjusted life years; RWE, real-world evidence

CE results of finerenone vs spironolactone (RWE studies)

Deterministic incremental key scenario results (Wu et al. 2025)

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)	INMB (£25k/QALY)
Finerenone + SoC	12,917	5.387	5,809	0.806	7,208	14,338
Spironolactone + SoC	7,108	4.581				

Deterministic incremental key scenario results (Almas et al. 2026)

Technology	Total costs (£)	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)	INMB (£25k/QALY)
Finerenone + SoC	12,917	5.387	6,762	1.189	5,687	22,962
Spironolactone + SoC	6,155	4.198				

Company additional scenario analyses: ICERs all below £8,000/QALY gained

Company: ICERs not supported by robust evidence → not appropriate for decision making
EAG: relative efficacy estimated by ITCs likely more accurate than RWE studies → ICER comparing finerenone vs spironolactone will likely be nearer to those generated by ITC (vs RWE studies)

Abbreviations: ICER, incremental cost-effectiveness ratio; INMB; incremental net monetary benefit; ITC, indirect treatment comparison; QALY, quality-adjusted life year; RWE, real-world evidence

Finerenone for treating heart failure with preserved or mildly reduced ejection fraction [ID6514]

- ❑ Background and key issues
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ✓ **Other considerations**
- ❑ Summary

NICE National Institute for Health and Care Excellence

Equality considerations

People with HFpEF are highly disadvantaged, steroidal MRAs may not be suitable for all people

Potential equality issue raised	

HF subtype	• Inequitable access to care for HFpEF and HFmrEF subtypes (compared with HFrEF):
	  ○ many specialist HF services (access to MDT/HF nurses and cardiac rehab) not commissioned for LVEF>40% → treatment variation, limited medicines optimisation
	  ○ often managed in primary care → finerenone prescribing needed across settings
	  ○ HFpEF disproportionality affects older people, potentially more women → symptoms often mistaken for ageing/comorbidities, can delay diagnosis/treatment

Key trial population	• FINEARTS-HF: 45% female (lower than expected in LVEF >40%), ~80% white ethnicity ○ no rationale to restrict finerenone use based on sex or ethnicity
Socioeconomic deprivation	• Higher HF risk, lower HF diagnosis age, less likely to have specialist HF care • Higher obesity levels → may impact QoL and potential prognostic benefits of finerenone
Subgroups less suitable for steroidal MRAs	• HFpEF/HFmrEF with hyperkalaemia, CKD, hypotension, frail with multimorbidity • Anti-androgenic side effects (e.g. gynaecomastia) with spironolactone* may limit uptake and treatment continuation in men

*eplerenone is a selective steroidal MRA with reduced affinity for androgen receptors → lower risk of anti-androgenic side effects

• Can these issues be considered within a technology appraisal and if so, how?

Abbreviations: CKD, chronic kidney disease; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MDT, multidisciplinary team; QoL, quality of life

Managed access

Criteria for a managed access recommendation

The committee can make a recommendation with managed access if:

- the technology cannot be recommended for use because the evidence is too uncertain
- the technology has the **plausible potential** to be cost effective at the **currently agreed price**
- new evidence that could **sufficiently support the case for recommendation** is expected from ongoing or planned clinical trials, or could be collected from people having the technology in clinical practice
- data could feasibly be collected within a reasonable timeframe (up to a **maximum of 5 years**) without **undue burden**.

Managed access (MA) feasibility assessment for finerenone

- Company has not submitted a managed access proposal
- Not likely potential candidate for MA – multiple other treatment options, used as an add-on to SoC
- Further data collection unlikely to resolve uncertainties relating to a lack of comparator in decision problem
- Ongoing clinical trials assess finerenone in other HF populations (not fully relevant to this evaluation)

Stakeholder highlighted SPIRIT-HF (due for publication later this year)

- RCT comparing spironolactone vs placebo in HFmrEF/HFpEF (n=730)
- Trial did not meet primary endpoint [composite of CV death and total HF hospitalisations at 2 years, rate ratio 1.32 (95% CI 0.79 to 2.21)], study included fewer than half of planned number of participants

Abbreviations: CI, confidence interval; CV, cardiovascular; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; MA, managed access; RCT, randomised controlled trial; SoC, standard of care

Finerenone for treating heart failure with preserved or mildly reduced ejection fraction [ID6514]

- ❑ Background and key issues
- ❑ Clinical effectiveness
- ❑ Modelling and cost effectiveness
- ❑ Other considerations
- ✓ **Summary**

NICE National Institute for Health and Care Excellence

Key issues

Key issue	ICER impact	Slide(s)
Primary key issue: comparators 1a) Exclusion of steroidal MRAs as a comparator 1b) Evidence for comparison (finerenone vs spironolactone): ITCs or RWE	**Large**	13 to 20

Abbreviations: ICER, incremental cost-effectiveness ratio; ITCs, indirect treatment comparisons; MRA, mineralocorticoid receptor antagonist; RWE, real-world evidence

Finerenone for treating heart failure with preserved or mildly reduced ejection fraction [ID6514]

Supplementary appendix

NICE National Institute for Health and Care Excellence

NICE's Real World Evidence framework

On assessing external validity

- An explicit definition of the target population is needed with suitable reference information
- Averages and distributions of variables compared separately or simultaneously using propensity scores
- Differences between populations do not necessarily lead to concerns about external validity unless those differences are in variables considered to be important treatment effect modifiers

On minimising external validity bias

- Matching and weighting methods to balance individual characteristics between populations
- Regression methods to standardise model predictions to the target population
- If the sample is drawn from an entirely different population to the target judgements of similarity will require assessments of "transportability"

In this appraisal (ID6514)

- How similar are the trial, real world and target populations?
- Is there transportability between different "ejection fraction" groups that would allow evidence from eplerenone trials in a reduced ejection fraction group to be used in this appraisal?

Link back to key issue slide

Decision problem

Link back to key issue slide

	Final scope	Company	EAG comments
Population	People with heart failure with preserved or mildly reduced ejection fraction	As per NICE final scope	FINEARTS-HF did not recruit people aged <40 years → not problematic given average age of HF patients
Intervention	Finerenone plus SoC	As per NICE final scope	Agree with company
Comparators	Established clinical management without finerenone, including but not limited to SGLT2 inhibitors, loop diuretics and treatments for co-morbidities	Placebo added on to SoC	• NG106 recommends considering MRAs (and SGLT2 inhibitors) as part of SoC → use of steroidal MRAs should be accounted for in the appraisal of finerenone • Comparison between finerenone and steroidal MRAs is necessary
Outcomes	• Symptoms of HF • Hospitalisation for HF • All-cause hospitalisation • Mortality, CV mortality • Kidney function • AEs, HRQoL	As per NICE final scope	Agree with company

Abbreviations: AEs, adverse events; CV, cardiovascular; HF, heart failure; HRQoL, health-related quality of life; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium-glucose co-transporter-2; SoC, standard of care

Differences between finerenone vs steroidal MRAs

Company response to TE

- Finerenone is a highly selective, non-steroidal MRA with unique physicochemical properties that differentiate it from traditional steroidal MRAs such as spironolactone
  - translate into consistent and clinically meaningful benefits across a broad range of cardio-renal outcomes → relevant for people with multiple co-morbidities
  - more favourable effects on potassium levels and eGFR
- Spironolactone is a non-selective steroidal MRA and can cause anti-androgenic side effects in men (such as gynecomastia and sexual dysfunction)

Stakeholder comments

- Finerenone has a more favourability profile, including fewer off-target endocrine effects
  - suggestion that non-steroidal MRAs (such as finerenone) confer a lower risk of hyperkalaemia
  - also licensed for CKD and T2DM, whereas steroidal MRAs are generally avoided in those with eGFR <30 mL/min/1.73 m^2

TEAEs	FINEARTS-HF safety analysis set (n=2,993 in both finerenone and placebo arms)
Hyperkalaemia	• [redacted]% finerenone vs [redacted]% placebo, serious events: 0.6% finerenone vs 0.2% placebo • Number of cases requiring hospitalisation: 0.5% finerenone vs 0.2% placebo • No fatal hyperkalaemia events reported

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MRA, mineralocorticoid receptor antagonist; SoC, standard of care; TE, technical engagement; TEAEs, treatment-emergent adverse events; T2DM, type 2 diabetes mellitus

Key issues 1b: Evidence for comparison (1): ITCs using RCTs

Company response to TE: summary of critical analysis of TOPCAT and FINEARTS-HF

	TOPCAT	FINEARTS-HF
Clinical era	2006 to 2012	Enrolment 2020–2023, more contemporary treatment era
Background therapies	No SGLT2 inhibitors available	SGLT2 inhibitors available (used by 13.6% of participants at baseline)
Location	Americas (North America, Latin America), Eastern Europe only (Russia and Georgia)	Wider Europe, Asia, North America, Latin America, and Oceania
LVEF criteria	LVEF ≥45%	LVEF ≥40% (both HFpEF and HFmrEF)
HF diagnosis criteria and pathology	Elevated NT-proBNP levels (criteria not uniformly specified) or prior HF hospitalisation. Evidence of limited objective HFpEF pathology in many participants	Elevated NT-proBNP levels (clearly defined criteria) and evidence of structural heart disease at baseline
Regional consistency and data integrity	Differences in patient characteristics and event rates between regions • implausibly low event rates and spironolactone adherence concerns in Eastern Europe	Patient characteristics and event rates were consistent across regions

Link back to key issue slides

Abbreviations: ICER, incremental cost-effectiveness ratio; ITC, indirect treatment comparison; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RCT, randomised controlled trial; SGLT2, sodium-glucose co-transporter-2; TE, technical engagement

Key issues 1b: Evidence for comparison (2): RWE

Company response to TE: critical analysis of Almas et al. 2026 and Wu et al. 2025

Topic	Almas et al. 2026	Wu et al. 2025
ESS (after matching)	n=491 → less than FINEARTS-HF	FAS n=1,619, HFpEF subgroup: n=628 → less than FINEARTS-HF
Population	HFpEF → partially aligned with FINEARTS-HF (HFpEF in TriNetX database likely corresponds to some people with HFmrEF*)	FAS population includes both HFrEF and HFpEF → not directly aligned with FINEARTS-HF but HFpEF subgroup analysis is available
Treatments investigated	Spironolactone only within sMRA arm	Spironolactone and eplerenone within sMRA arm. May introduce heterogeneity if clinically meaningful differences between sMRAs
Outcomes	All-cause mortality, HF exacerbation and hyperkalaemia. Outcomes for hospitalisation not captured (key endpoint in the model)	All-cause mortality, all-cause hospitalisation, worsening HF and hyperkalaemia
Baseline characteristics compared with FINEARTS-HF	Both studies: more comorbid (higher prevalence of diabetes and greater use of background therapies) and population is also more ethnically diverse Wu et al. 2025: baseline characteristic not reported separately for HFpEF subgroup, reducing transparency regarding comparability with FINEARTS-HF	

*Almas et al. 2026 note potential misclassification of patients within the HFpEF category, with the possibility of those with HF with improved or mid-range ejection fraction being labelled as HFpEF.

Link back to key issue slides

Abbreviations: ESS, effective sample size; FAS, full analysis set; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ICER, incremental cost-effectiveness ratio; RWE, real-world evidence; sMRA, steroidal mineralocorticoid receptor antagonist; TE, technical engagement

Key issues 1b: Evidence for comparison (3): RWE

Company response to TE: Almas et al. 2026 → baseline characteristics before and after propensity score matching (1)

Characteristic	Almas et al. 2026 (before matching)		Almas et al. 2026 (after matching)		FINEARTS-HF	
	Finerenone (n=497)	Spironolactone (n=253,920)	Finerenone (n=491)	Spironolactone (n=491)	Finerenone (n=3,003)	Placebo (n=2,998)
Age (mean ±SD)	70.26 ± 11.26	69.49 ± 14.05	70.25 ± 11.3	69.68 ± 12.37	71.9 ± 9.6	72.0 ± 9.7
Sex: female	41.4%	52.9%	41.8%	40.3%	45.1%	45.9%
Race: White	52.9%	68.2%	53.6%	55.4%	78.8%	79.0%
Race: Asian	17.9%	2.2%	16.9%	15.5%	16.6%	16.6%
Race: Black	15.1%	18.8%	15.3%	14.9%	1.6%	1.3%
Comorbidities/medical history						
Diabetes	91.1%	50.3%	91.0%	91.0%	40.5%	40.8%
Atrial fibrillation	38.6%	49.9%	38.9%	39.9%	38.8%	37.6%
MI	20.7%	18.5%	20.8%	22.4%	26.1%	25.3%
Hypertension	90.1%	82.9%	90.2%	90.8%	87.9%	89.6%

Link back to key issue slides

Abbreviations: ICER, incremental cost-effectiveness ratio; MI, myocardial infarction; RWE, real-world evidence; SD, standard deviation; TE, technical engagement

Key issues 1b: Evidence for comparison (4): RWE

Company response to TE: Almas et al. 2026 → baseline characteristics before and after propensity score matching (2)

Characteristic	Almas et al. 2026 (before matching)		Almas et al. 2026 (after matching)		FINEARTS-HF	
	Finerenone (n=497)	Spironolactone (n=253,920)	Finerenone (n=491)	Spironolactone (n=491)	Finerenone (n=3,003)	Placebo (n=2,998)
Medication use						
Beta-blocker	87.7%	85.8%	87.8%	87.8%	84.6%	85.2%
ACE inhibitor	46.5%	48.5%	46.4%	49.1%	36.1%	35.8%
ARB	64.6%	43.9%	64.4%	65.0%	34.9%	35.2%
SGLT2 inhibitor	53.7%	15.0%	53.2%	57.0%	13.1%	14.1%
Loop diuretic	82.5%	89.9%	83.3%	85.5%	87.2%	87.4%
Thiazide diuretic	53.5%	44.9%	53.8%	59.7%	14.3%	13.4%
GLP-1	40.0%	6.3%	39.3%	39.5%	2.6%	2.9%

Link back to key issue slides

Abbreviations: ACE; angiotensin-converting enzyme; ARB, angiotensin receptor blocker; GLP-1, glucagon-like peptide-1 receptor agonist; ICER, incremental cost-effectiveness ratio; RWE, real-world evidence; SGLT2, sodium-glucose co-transporter-2; TE, technical engagement

Key issues 1b: Evidence for comparison (5): RWE

Company response to TE: Wu et al. 2025 → baseline characteristics before and after propensity score matching (1)

Characteristic	Wu et al. 2025 (before matching)		Wu et al. 2025 (after matching)*		FINEARTS-HF	
	nsMRA (n=1,632)	sMRA (n=374,370)	nsMRA (n=1,619)	sMRA (n=1,619)	Finerenone (n=3,003)	Placebo (n=2,998)
Age (mean ±SD)	69.8 ± 11.5	66.5 ± 14.7	69.8 ± 11.5	70.1 ± 12.5	71.9 ± 9.6	72.0 ± 9.7
Sex: female	38.1%	42.2%	38.3%	40.3%	45.1%	45.9%
Race: White	45.0%	55.7%	45.3%	45.6%	78.8%	79.0%
Race: Asian	22.7%	4.3%	22.2%	21.3%	16.6%	16.6%
Race: Black	15.1%	19.2%	15.2%	16.3%	1.6%	1.3%
LVEF (mean ±SD)	57.1 ± 12.2	43.1 ± 17.8	57.1 ± 12.2	52.4 ± 15.2	52.6 ± 7.8	52.5 ± 7.8
Comorbidities/medical history						
Diabetes	68.3%	31.4%	68.0%	69.0%	40.5%	40.8%
Atrial fibrillation	27.9%	32.6%	28.0%	28.1%	38.8%	37.6%

*Wu et al. (2025) baseline characteristics presented for full analysis set i.e. HFpEF and HFrEF. Baseline characteristics were not available for the HFpEF subgroup

Link back to key issue slides

Abbreviations: ICER, incremental cost-effectiveness ratio; nsMRA, non-steroidal mineralocorticoid receptor antagonist; RWE, real-world evidence; SD, standard deviation; sMRA, steroidal mineralocorticoid receptor antagonist; TE, technical engagement

Key issues 1b: Evidence for comparison (6): RWE

Company response to TE: Wu et al. 2025 → baseline characteristics before and after propensity score matching (2)

Characteristic	Wu et al. 2025 (before matching)		Wu et al. 2025 (after matching)*		FINEARTS-HF	
	nsMRA (n=1,632)	sMRA (n=374,370)	nsMRA (n=1,619)	sMRA (n=1,619)	Finerenone (n=3,003)	Placebo (n=2,998)
Medication use						
Beta-blocker	57.7%	57.3%	57.7%	55.7%	84.6%	85.2%
ACE inhibitor	14.6%	23.6%	14.7%	14.9%	36.1%	35.8%
ARB	45.3%	28.0%	45.0%	45.5%	34.9%	35.2%
Calcium-channel blocker	40.4%	30.4%	40.4%	39.7%	31.9%	33.7%
SGLT2 inhibitor	41.5%	9.1%	41.0%	40.5%	13.1%	14.1%
GLP-1	20.7%	2.7%	20.1%	19.5%	2.6%	2.9%

*Wu et al. (2025) baseline characteristics presented for full analysis set i.e. HFpEF and HFrEF. Baseline characteristics were not available for the HFpEF subgroup

Link back to key issue slides

Abbreviations: ACE; angiotensin-converting enzyme; ARB, angiotensin receptor blocker; GLP-1, glucagon-like peptide-1 receptor agonist; ICER, incremental cost-effectiveness ratio; nsMRA, non-steroidal mineralocorticoid receptor antagonist; RWE, real-world evidence; sMRA, steroidal mineralocorticoid receptor antagonist; SGLT2, sodium-glucose co-transporter-2; TE, technical engagement

Key issues 1b: Evidence for comparison (7): summary of results

Company response to TE: ITC and RWE results comparing finerenone vs spironolactone

Outcome	TOPCAT	TOPCAT Americas	Almas et al. 2026	Wu et al. 2025
All-cause mortality (HR)	1.022 (95% CI 0.829, 1.259)	1.120 (95% CI 0.884, 1.420)	0.38 (95% CI 0.23, 0.64)	0.51 (95% CI 0.32, 0.81)
CV mortality (HR)	1.033 (95% CI 0.783, 1.364)	1.257 (95% CI 0.913, 1.729)	-	-
Hospitalisation due to HF (HR)	1.036 (95% CI 0.833, 1.288)	1.049 (95% CI 0.833, 1.320)	-	-
All-cause hospitalisation (HR)	-	-	-	0.83 (95% CI 0.67, 1.02)
Worsening HF/HF exacerbation* (HR)	-	-	0.63 (95% CI 0.54, 0.74)	0.6 (95% CI 0.45, 0.79)
Hyperkalaemia	OR: 0.979 (95% CI 0.820, 1.169)	OR: 0.649 (95% CI 0.467, 0.902)	HR: 0.96 (95% CI 0.69, 1.33)	HR: 0.89 (95% CI 0.68, 1.17)**
Serious adverse events (OR)	0.968 (95% CI 0.817, 1.146)	-	-	-
Treatment discontinuation (IRR)	0.923 (95% CI 0.792, 1.074)	-	-	-

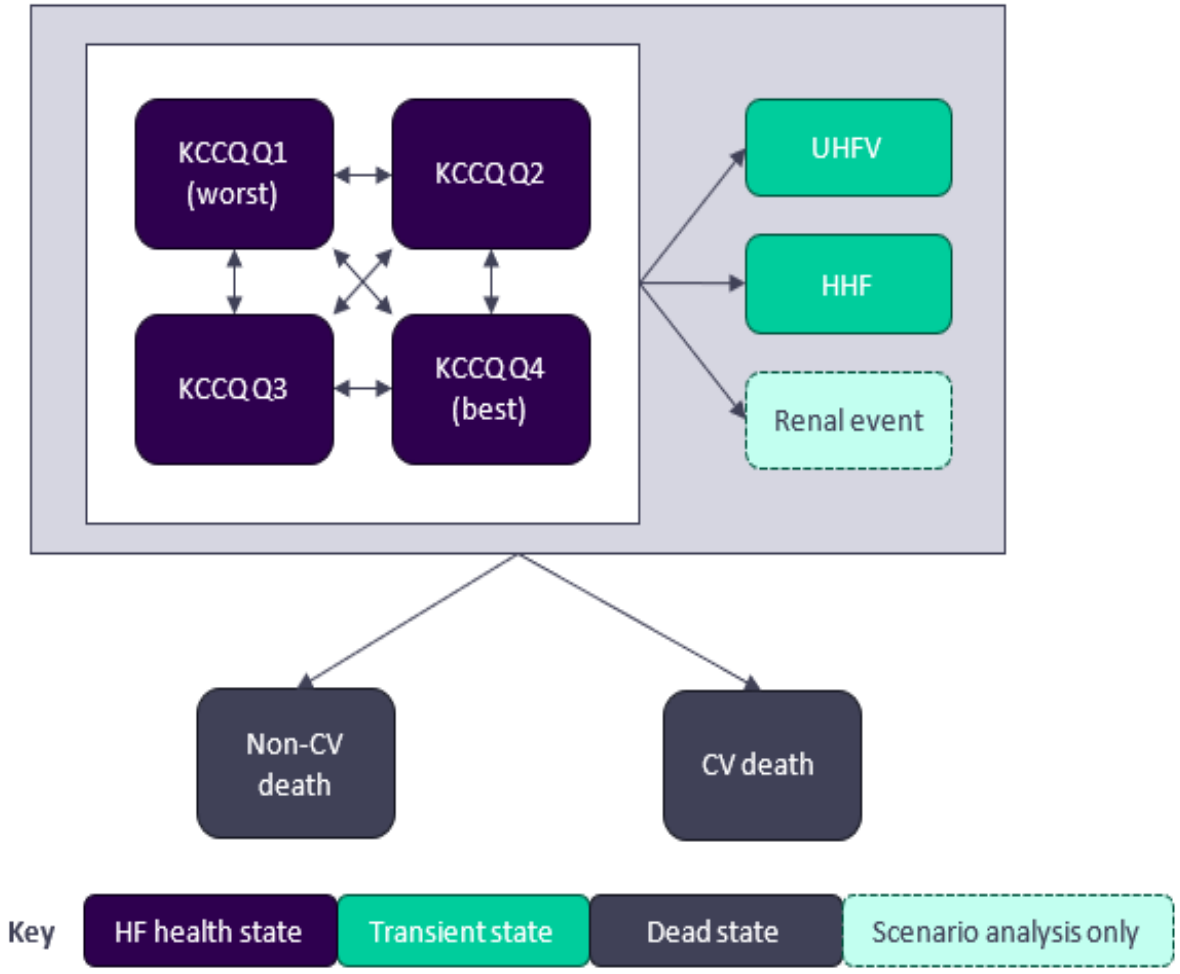
Values <1 indicate lower risk/odds/rate with finerenone versus spironolactone, values >1 indicate higher risk/odds/rate with finerenone versus spironolactone

*Reported as “HF exacerbation” in Almas et al 2026, reported as “worsening HF” in Wu et al 2025 **Reported for full HFpEF and HFrEF population only

Link back to key issue slides

Abbreviations: CI, confidence interval; HF, heart failure; HR, hazard ratio; ICER, incremental cost-effectiveness ratio; IRR, incidence rate ratio; OR, odds ratio; TE, technical engagement

Company's model overview



State transition model

- 6 main health states: KCCQ-TSS* quartiles 1 (worst) to 4 (best), CV death* and non-CV death
- 2 transient health states: hospitalisation due to HF (HHF) and urgent heart failure visits (UHFV)
- Cycle length: 28 days with half-cycle correction
- Lifetime horizon: 28 years
- Population: aligned with FINEARTS-HF
- Intervention: finerenone + SoC
- Comparator: SoC (based on FINEARTS-HF, limited steroidal MRA use – see supplementary slide)

Heath state	Mean utility value
KCCQ-TSS Q1: [redacted]	0.58
KCCQ-TSS Q2: [redacted]	0.69
KCCQ-TSS Q3: [redacted]	0.75
KCCQ-TSS Q4: [redacted]	0.79

- *Total symptom score (TSS) on the Kansas City Cardiomyopathy Questionnaire (KCCQ) used to define HF severity
  - KCCQ scores range from 0 to 100, lower scores indicate worse symptoms and/or more severe limitations
    - Minimal clinically important difference is indicated by a 5-point change

*Fatal MI; fatal HF; sudden death; presumed sudden death; presumed CV death; fatal stroke; fatal pulmonary embolism; CV procedure related death; other CV death

NICE

Abbreviations: CV, cardiovascular; HF, heart failure; HHF, hospitalisation for heart failure; KCCQ-TSS; Kansas City Cardiomyopathy Questionnaire total symptom score; MRA, mineralocorticoid receptor antagonist; Q, quartile; SoC, standard of care; UHFV, urgent heart failure visit

How company incorporated evidence into model

Company updated model after technical engagement

Input	Assumption and evidence source
Baseline characteristics	FINEARTS-HF (mean age 72 years, 45.5% female)
Finerenone and placebo arms (SoC) efficacy	Per-cycle probabilities: • KCCQ-TSS transitions: estimated from FINEARTS-HF KCCQ-TSS responses* • CV and all-cause mortality: independently fitted Weibull models using FINEARTS-HF • Non-CV mortality: all-cause mortality minus CV mortality, capped by probability of non-CV mortality in general population • HHF and UHFV by treatment and health state: GEE based on FINEARTS-HF
Health state utilities	• Regression model using FINEARTS-HF data (EQ-5D-5L mapped to EQ-5D-3L) ○ KCCQ-TSS quartile 4 capped by general population norms ○ utilities were age-adjusted using age–sex population EQ-5D norms ○ AE disutilities applied separately**
Costs and resource use	Treatment costs, health-state costs, HF event costs, AE costs, CV mortality costs Sources: BNF, eMIT, CE, literature, NICE TAs, NHS Cost Collection 23/24, PSSRU

*KCCQ data was collected at baseline and at approximately at 6 months, 9 months and 12 months post-randomisation

**AEs that could not be estimated directly from the FINEARTS-HF study regressions were taken from the literature or previous NICE submissions

Abbreviations: AE, adverse event; BNF, British National Formulary; CE, clinical expert opinion; CV, cardiovascular; eMIT, drugs and pharmaceutical electronic market information tool; EQ-5D, EuroQol Group 5-dimension; GEE, generalised estimating equations; HF, heart failure; HHF, hospitalisation for heart failure; KCCQ-TSS; Kansas City Cardiomyopathy Questionnaire total symptom score; PSSRU, Personal Social Services Research Unit; SoC, standard of care; UHFV, urgent heart failure visit

Different assumptions used in modelling of spironolactone

Assumptions are required to fill data gaps for both approaches

<table>
<tr><th>Parameter</th><th>TOPCAT ITCs</th><th>RWE studies</th></tr>
<tr><td>Data source</td><td>• ITT population
• Americas only subgroup</td><td>• Almas et al. 2026
• Wu et al. 2025 → HFpEF subgroup used to generate model inputs, FAS population used for baseline characteristics</td></tr>
<tr><td>Transition probabilities</td><td colspan="2">• Assumed same as finerenone + SoC
• Additional scenarios: assume same as SoC, use worsening HF HR (RWE only), use worsening and improving HF HRs (RWE only)</td></tr>
<tr><td>All-cause mortality, hyperkalaemia rates</td><td rowspan="4">• Direct from ITC
• Americas only subgroup: assumed HRs from ITT population for serious AEs and discontinuation
• Additional scenario for discontinuation: used data directly from TOPCAT</td><td>Direct from RWE studies</td></tr>
<tr><td>CV mortality, serious AEs</td><td>• Assumed same as finerenone + SoC
• Additional scenarios: assume same as SoC</td></tr>
<tr><td>HF event rates</td><td>• Wu et al: all-cause hospitalisation used as a proxy for HF events
• Almas et al: assumed same as finerenone + SoC, additional scenario: assumed same HR as Wu et al</td></tr>
<tr><td>Discontinuation</td><td>Used data directly from TOPCAT</td></tr>
</table>

Company tested assumptions in a range of scenario analyses → no material impact on CE results

Abbreviations: AE, adverse events; CE, cost-effectiveness, HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; ITC, indirect treatment comparison; ITT: intention-to-treat; RWE, real-world evidence; SoC, standard of care

SoC treatments included in the model

Analysis of baseline FINEARTS-HF data

Drug class	Treatment	Proportion of patients
SGLT2 inhibitor*	Dapagliflozin (50%), Empagliflozin (50%)	13.6%
ARN inhibitors	Sacubitril valsartan	[redacted]
ACE inhibitors and ARBs	Valsartan	[redacted]
Beta blockers	Bisoprolol fumarate	[redacted]
Loop diuretics	Furosemide	[redacted]
Thiazide diuretics	Irbesartan/ Hydrochlorothiazide	[redacted]
Digoxin	Digoxin	[redacted]
Nitrates	Isosorbide dinitrate	[redacted]
Potassium supplements	Potassium chloride	[redacted]
Potassium lowering agents	Calcium polystyrene sulfonate	[redacted]
Alpha blocking agents	Carvedilol	[redacted]
Calcium channel blockers	Amlodipine	[redacted]
Aspirin	Aspirin (enteric-coated tablet)	[redacted]
Statins	Atorvastatin	[redacted]
Steroidal MRAs	Spironolactone	[redacted]
Insulins and analogues	Insulin aspart	[redacted]
Other anti-diabetic drugs	Metformin hydrochloride	[redacted]

*In the economic model, it was assumed that the SGLT2 inhibitor distribution is split equally between empagliflozin and dapagliflozin

NICE

Abbreviations: ACE; angiotensin-converting enzyme; ARB, angiotensin receptor blocker; ARN, angiotensin receptor/neprilysin; SGLT2, sodium-glucose co-transporter-2; SoC, standard of care