Record of the Cardiovascular Advisory Committee Meeting held on 27 June 2025

Cardiovascular Advisory Committee records are published in accordance with the Terms of Reference for the Specialist Advisory Committees 2021.

Note that this document is not necessarily a complete record of the Cardiovascular Advisory Committee meeting; only the relevant portions of the meeting record relating to Cardiovascular Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Cardiovascular Advisory Committee may:

(a) recommend that a pharmaceutical be listed by Pharmac on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that Pharmac decline to list a pharmaceutical on the Pharmaceutical Schedule.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

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1. Attendance

Present
Bruce King (Chair)
Christine Pihema
James Chisnall
Mark Webster
Matthew Dawes
Mayanna Lund
Richard Medlicott

Apologies
Liza Lack
Sam Whittaker

2. Summary of recommendations

Pharmaceutical and Indication	Recommendation
• Empagliflozin for the treatment of chronic heart failure with mildly reduced or preserved ejection fraction, for people with NYHA class II-IV, within the context of cardiovascular disease, subject to eligibility criteria	High Priority

3. The role of Specialist Advisory Committees and records of meetings

3.1. This meeting record of the Cardiovascular Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) 2021 and Specialist Advisory Committees 2021.Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

3.2. Conflicts of Interest are described and managed in accordance with section 6.4 of the SAC Terms of Reference.

3.3. The Cardiovascular Advisory Committee is a Specialist Advisory Committee of Pharmac. The Cardiovascular Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Cardiovascular Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for Cardiovascular that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for Cardiovascular that differ from the Cardiovascular Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

Pharmac considers the recommendations provided by both the Cardiovascular Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for Cardiovascular.

4. Welcome and introduction

4.1. The Chair welcomed the Committee with a karakia followed by whakawhanaungatanga.

4.2. The Chair welcomed Dr Matthew Dawes (PTAC member, Physician and Clinical Pharmacologist) and Dr James Chisnall (General Practitioner), members of Pharmac's expert advisory network who are joining the Committee to support this agenda.

5. Pharmac Update

5.1. The Committee noted the Pharmac Update.

5.2. Members noted the Pharmac is currently seeking expressions of interest for new members to this Cardiovascular Advisory Committee.

6. Empagliflozin for the treatment of chronic heart failure with preserved/mildly reduced ejection fraction for people with NYHA class II-IV heart failure

Application

6.1. The Committee reviewed the application for empagliflozin in the treatment of chronic heart failure with mildly reduced or preserved ejection fraction (HFmrEF/HFpEF), NYHA II-IV and LVEF >40%.

6.2. The Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

6.3. The Committee recommended that empagliflozin for the treatment of chronic heart failure with mildly reduced or preserved ejection fraction, for people with NYHA class

II-IV, be listed with a high priority within the context of cardiovascular disease, subject to the following eligibility criteria:

> **Initial application — Heart failure** Applications from any relevant practitioner on the recommendation of a relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:
>
> 1. Patient has symptomatic left sided heart failure; and
> 2. Patient would benefit from medical therapy that includes the use of empagliflozin; and
> 3. Patient has an elevated age-adjusted NT-BNP result.

6.4. The Committee, in making its recommendation, considered:

6.4.1. the mortality and health-related quality of life impacts associated with HFpEF/HFmrEF, which results in high health need

6.4.2. the disproportionate impact of chronic left-sided heart failure and associated comorbidities among populations with high health needs, including Māori and Pacific peoples

6.4.3. the lack of funded and effective therapies available for the HFpEF/HFmrEF

6.4.4. the strength and quality of evidence to support use of empagliflozin for the treatment of HFpEF/HFmrEF

6.4.5. the applicability of the trial evidence to the New Zealand context

6.4.6. that empagliflozin may provide additional benefit in individuals with comorbidities such as chronic kidney disease and type 2 diabetes mellitus.

6.4.7. that empagliflozin is already funded for chronic heart failure with reduced ejection fraction (HFrEF) and finalising eligibility criteria for the entire chronic heart failure population, regardless of ejection fraction, would be more useful than criteria specifically targeting mildly reduced (HFmrEF) or preserved ejection fraction (HFpEF).

Discussion

Māori impact

6.5. The Committee discussed the impact of funding empagliflozin for the treatment of HFpEF/HFmrEF on Māori health areas of focus and Māori health outcomes. The Committee noted that Māori experience higher rates of heart failure and have more disability and mortality related to heart failure compared to NZ Europeans (Doughty et al. N Z Med J. 2024;137:93-9). The Committee also considered that heart failure with preserved or mildly reduced ejection fraction (HFpEF/HFmrEF) is underdiagnosed in primary care due to the lack of phenotype-specific coding and diagnostic tools, which may contribute to an underdiagnosis of HFpEF/HFmrEF among Māori.

Populations with high health needs

6.6. The Committee noted that Pacific peoples experience higher rates of heart failure and experience higher rates of disability and mortality related to heart failure compared to NZ Europeans (Doughty et al. 2024).

Background

6.7. The Committee noted that this funding application was reviewed by PTAC in May 2023 and recommended for decline. The Committee noted that, at that time, PTAC considered that a reduced frequency of heart failure (HF) related hospitalisations without reductions in all-cause hospitalisations, cardiovascular mortality and all-cause

mortality did not provide sufficient benefit to warrant the funding of empagliflozin in this group.

6.8. The Committee noted that PTAC also considered that if empagliflozin were to be funded for treatment of HF it would be ideal to fund it for both reduced ejection fraction and preserved ejection fraction HF, so that the need for an echocardiogram / Cardiac MRI could be removed from the criteria, which may improve equity of access.

Health need

6.9. The Committee noted that heart failure (HF) with a left ventricular ejection fraction (LVEF) of more than 40% (>40%) includes two categories of heart failure: HF with preserved LVEF of >50% (HFpEF) and HF with mildly reduced LVEF of 41 to 49% (HFmrEF).

6.10. The Committee noted that people with HFpEF/HFmrEF experience high rates of hospitalisation and mortality, although the risk of recurrent admission to hospital among this group, although substantial, is lower than for individuals who have HF with reduced LVEF ≤40% (HFrEF). The Committee also noted that HFpEF/HFmrEF is associated with lower mortality than HFrEF (NHFA CSANZ Heart Failure Guidelines, Heart Lung Circ. 2018;27:1123-208; Lam et al. Eur Heart J. 2018;20:1770-80).

6.11. The Committee noted the impacts of HFpEF/HFmrEF on health-related quality of life (HRQoL), with individuals experiencing symptoms such as breathlessness, exhaustion following exertion, dizziness, fatigue, and palpitations (NHFA CSANZ Heart Failure Guidelines, Heart Lung Circ. 2018;27:1123-208).

6.12. The Committee noted that there is a lack of efficacious funded medicines for people with HFpEF/HFmrEF, which was in contrast to the setting of HFrEF where a range of funded medicines have demonstrated efficacy in randomised controlled trials (eg empagliflozin is funded in New Zealand for HFrEF, efficaciously, but not currently funded for HFpEF/HFmrEF, hence people with HFpEF/HFmrEF cannot benefit incrementally from that specific treatment). The Committee considered that the currently funded treatments for heart failure have a superior efficacy in the HFrEF population in terms of reduction in hospitalisation and mortality, compared to their use in people with HFpEF/HFmrEF. The Committee considered that this means the HFpEF/HFmrEF population experience less health benefit from currently funded treatments in comparison to.

6.13. The Committee noted that people with HFpEF/HFmrEF may receive a range of medicines in the community, but these were mainly used to manage comorbidities rather than impacting outcomes.

6.14. The Committee considered that hospitalisations for HF generally occurred when people experienced clinical deterioration. The Committee considered that the hospital setting was not conducive to respite and was a stressful place for both individuals and their whānau. The Committee noted a New Zealand observational study that reported high rates of recurrent hospitalisation and post-discharge mortality following 'first-ever HF hospitalisation' (Chan et al. Heart Lung Circ. 2024;33:1475-83).

6.15. The Committee was made aware of unpublished data from the national heart failure registry that indicated that fewer than 30% of people with HFrEF are discharged with prescriptions for the four medicines recommended in evidence-based treatment (i.e., angiotensin pathway inhibitors, mineralocorticoid antagonists, beta-blockers, and SGLT2 inhibitors). The Committee considered that this rate is likely similar for people with HFpEF/HFmrEF and suggested that hospitalisation does not necessarily result in improved disease management in the post-discharge period.

6.16. The Committee noted that delineating HFpEF/HFmrEF and HFrEF in the diagnostic process can be difficult given the limited access to diagnostic technology such as ultrasound/Cardiac MRI in New Zealand.

6.17. The Committee noted the high health need of the families, whānau and wider society in people with HFpEF/HFmrEF and considered that it is similar to that of families of people with HFrEF. The Committee considered that people with HFpEF/HFmrEF can have a higher symptomatic burden than people with HFrEF due to the more limited range of treatment options specific to the disease phenotype.

Health benefit

6.18. The Committee considered that the evidence provided during its discussion did not support some of PTAC's comments regarding the clinical meaningfulness of hospitalisation in the May 2023 PTAC record.

6.19. The Committee noted that empagliflozin is funded for HFpEF/HFmrEF in similar countries, including:

- Australia (PBAC) in 2023 recommended to expand the access of empagliflozin to include HF with LVEF >40%.
- Canada (CDEC) in 2022 recommended empagliflozin for HF regardless of the LVEF (i.e., inclusive of HFpEF/HFmrEF and HFrEF).
- Scotland (SMC) in 2023 recommended to expand the access of empagliflozin to include HF with LVEF >40%.
- England/Wales (NICE) in 2023 recommended to expand the access of empagliflozin to include HF with LVEF >40%.

6.20. The Committee noted that SGLT2 inhibitors (empagliflozin and dapagliflozin) are categorised as class 1 in the ESC 2023 focused update of the 2021 Clinical Practice Guidelines and class 2a in the 2023 ACC Clinical Practice guidelines for the treatment of both HFpEF/HFmrEF and HFrEF.

6.21. The Committee was made aware of the 2023 ACC Expert Consensus Decision Pathway on Management of HFpEF that noted that SGLT2 inhibitors may mitigate many of the accompanying comorbidities associated with chronic heart failure, including chronic kidney disease, sleep apnoea, atrial fibrillation, coronary artery disease, obesity, hypertension, and diabetes.

6.22. Regarding the efficacy of empagliflozin, the Committee noted the following evidence:

6.22.1. Anker et al. N Engl J Med. 2021;385: 1451-61 (EMPEROR-preserved): A randomised, double-blind, parallel group, placebo-controlled trial investigating the efficacy of empagliflozin in people with HFmrEF/HFpEF (n = 5988). The co-primary endpoints were cardiovascular death or hospitalization for heart failure. The Committee noted that, regarding all-cause mortality, there has been no evidence of therapeutic benefit in for participants over a two-year follow-up period. The Committee considered that this lack of evidence is an issue of time (i.e., the follow up period has not matured), and not drug efficacy – suggesting that mortality benefit may be established over a longer period. The Committee noted that HF-related hospitalisation was reduced in the treatment group compared to placebo (hazard ratio, 0.71; 95% CI, 0.60 to 0.83).

6.22.2. Butler et al. Circulation. 2022;145:184-93: A secondary publication of the EMPEROR-preserved trial investigating the effects of empagliflozin on health-related quality of life (HRQoL) using Kansas City Cardiomyopathy

Questionnaire (KCCQ) clinical summary scores, total symptom score and overall summary score at 12 weeks, 32 weeks, and 52 weeks. The study reported that empagliflozin treatment was associated with improved KCCQ scores compared to placebo at 52 weeks (mean 1.50 points improvement, 95% CI 0.64 to 2.36).

6.23. Related to the earlier discussion around PTAC's 2023 view of the clinical meaningfulness of hospitalisation for heart failure, the Committee considered the reduced risk of hospitalisation observed in the EMPEROR-Preserved trial to be clinically meaningful and that, in the absence of an evidenced mortality benefit, this was the main benefit of interest in the setting of HFpEF/HFmrEF.

6.24. The Committee considered there was no easily identifiable subgroup in EMPEROR-Preserved that benefitted disproportionately more from treatment with empagliflozin than others, noting that the treatment effect appeared consistent across most subgroups and the primary factor influencing the magnitude of hospitalisation risk reduction was ejection fraction (Anker et al. 2021; Figure 2).

6.25. The Committee considered that the magnitude of mean improvement in the KCCQ scores reported in EMPEROR-Preserved of 1.5 points was relatively small. The Committee noted that the minimally clinically important difference (MCID) for the KCCQ score was typically considered to be 5.0 points but considered that changes smaller than the MCID may be meaningful to patients.

6.26. The Committee considered that empagliflozin would not be associated with a reduction in mortality among people with HFpEF/HFmrEF. The Committee noted that the there was no difference in all-cause mortality between the two arms of EMPEROR-Preserved (HR = 1.00, 95% CI 0.87 to 1.15) at two years of follow-up and there was no significant reduction in cardiovascular mortality. The Committee considered that it would be appropriate to exclude a survival benefit in any economic assessment of empagliflozin for HFpEF/HFmrEF, based on current evidence.

6.27. The Committee considered that some individuals may gain additional benefit from treatment with empagliflozin depending on their comorbidities, including reduced renal function decline, and improved glycaemic control.

6.28. The Committee considered that empagliflozin would provide a health benefit to family, whānau and wider society by reducing hospitalisation and thereby reducing the carer impact of the condition.

6.29. The Committee noted that, in regard to comorbidity with chronic kidney disease, manifesting with an elevated urinary albumin to creatinine ratio, there is strong evidence that empagliflozin reduces the progression of renal disease (Anker et al. 2021). The Committee considered that delay to renal replacement therapy is a highly meaningful clinical benefit.

6.30. The Committee noted the DELIVER trial investigating dapagliflozin in people with HFpEF/HFmrEF with the coprimary endpoints of worsening of heart failure (ie. unplanned hospitalisation for HF or urgent visit for HF) or cardiovascular death (Solomon et al. NEJM 2022;387:1089-98). The Committee considered that the inclusion criteria and endpoints of the DELIVER trial were similar to those of the EMPEROR-preserved trials, and the efficacy and safety results of dapagliflozin and empagliflozin were comparable.

6.31. The Committee considered that there was a class effect of efficacy among the two SGLT2 inhibitors indicated for HFpEF/HFmrEF (empagliflozin and dapagliflozin). The Committee considered that the two treatments would be associated with similar benefits and safety. The Committee noted that the 2023 ACC Expert Consensus

Decision Pathway on Management of HFpEF also considers there to be a class effect present among dapagliflozin and empagliflozin.

6.32. The Committee considered that there is high quality evidence supporting empagliflozin for treatment of HFpEF/HFmrEF, showing a benefit on hospitalisation rates. The Committee noted the classification of evidence for empagliflozin as class one in the ACC clinical practice guidelines and ESC clinical practice guidelines. The Committee considered that the EMPEROR-preserved trial for empagliflozin and DELIVER trial for dapagliflozin were both large, well conducted, randomised controlled trials in HFpEF/HFmrEF with confirmatory outcomes.

Suitability

6.33. The Committee noted that empagliflozin is an oral tablet taken once daily at a single fixed 10mg dose. The Committee considered that the fixed dose of empagliflozin represents a suitability advantage to other treatments, as there would be no need for regular clinic visits to titrate people to a certain target maintenance dose.

6.34. The Committee noted that some people may require dose adjustments to concomitant medicines, such as diabetes medicines and diuretics, following initiation on empagliflozin.

6.35. The Committee considered that there were limited monitoring requirements associated with empagliflozin, though people with HF would continue to receive annual blood tests and monitoring for the management of other medicines and comorbidities.

6.36. The Committee considered that adherence to empagliflozin treatment in the setting of diabetes and HFrEF has generally been high in New Zealand clinical experience, and this was likely to be the case for HFpEF/HFmrEF if it were to be funded for this indication.

Cost and savings

6.37. The Committee considered that some people with HF may already be eligible for empagliflozin via the funding for type 2 diabetes mellitus. The Committee noted that the PEOPLE study suggested there was substantial overlap between the populations in New Zealand with diabetes and HF (Lam et al. 2018).

6.38. The Committee considered that alongside the savings from reduced hospitalisations for HF and delayed progression of renal disease, funding empagliflozin for HF may result in costs to the health sector related to adverse events such as including urinary tract infection, ketoacidosis, skin infections, and other severe complications.

Funding criteria

6.39. The Committee considered that the requirement to receive an echocardiogram / Cardiac MRI to be eligible for funded access to empagliflozin for heart failure could be removed if empagliflozin was funded for HF regardless of LVEF. The Committee considered that retaining the criterion requiring an echocardiogram would create an unnecessary barrier to accessing treatment, especially in areas where access to these tests were limited. The Committee noted again that PTAC had made similar comments during its consideration of empagliflozin for HFpEF/HFmrEF.

6.40. The Committee considered that, if the requirement to receive an echocardiogram/Cardiac MRI was removed from the access criteria for empagliflozin, a requirement for natriuretic peptide testing (NT-BNP) would be reasonable to rule out conditions that can have symptoms in common with HF, such as chronic obstructive pulmonary disease and other lung diseases.

Summary for assessment

6.41. The Committee considered that the below summarises its interpretation of the most appropriate PICO table (population, intervention, comparator, outcomes) information for empagliflozin if it were to be funded in New Zealand for HFmrEF and HFpEF. This PICO table captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO table is based on the Committee's assessment at this time and may differ from that requested by the applicant. The PICO table may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

6.42. The Committee noted that elements of in the PICO (population, intervention, comparator, outcomes) for this application is unclear/uncertain at this time. The PICO may develop based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	People with symptomatic heart failure with LVEF >40%
Intervention	Empagliflozin, 10mg once daily. Taken in addition to optimal standard chronic heart failure treatments.
Comparator(s) (NZ context)	Funded pharmacological treatments, mainly to manage comorbidities, which may include the following: • loop diuretics • angiotensin-converting enzyme inhibitors • angiotensin II receptor blockers • beta blockers • mineralocorticoid receptor antagonists
Outcome(s)	Reduced risk of hospitalisation for heart failure • EMPEROR-Preserved: empagliflozin treatment was associated with a reduced risk of hospitalisation for heart failure compared to placebo (HR=0.71, 95% CI 0.69 to 0.90) (Anker et al. N E J Med. 2021;385:1451-61). Delayed progression of renal disease • EMPEROR-Preserved eGFR (CKD-EPI) mean slope change per year (mean difference 1.36, 95% CI 1.06 to 1.66) (Anker et al. 2021). Improved health-related quality of life • Butler et al. Circulation. 2022;145:184-93: empagliflozin treatment was associated with improved KCCQ scores compared to placebo at 52 weeks (mean 1.50 points, 95% CI 0.64 to 2.36).

Table definitions:

Population: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup)

Intervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).

Comparator: Details the therapy(s) that the patient population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).

Outcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.