CHANGES TO PRESENT (OR RECOMMENDED) PBS AVAILABILITY

When the PBAC makes a recommendation under section 101(3) of the *National Health Act 1953* ("the Act") in relation to a drug/medicinal preparation which it considers should be made available as a pharmaceutical benefit under Part VII of the Act, it is also required to consider whether the drug/medicinal preparation should be made available only in certain circumstances (see section 101(3C) of the Act). Where the PBAC considers that the drug/medicinal preparation should be made available only in certain circumstances, it specifies the circumstances in its recommendation under section 101(3).

At its meeting on **13 December 2024**, the PBAC in making its recommendation under section 101(3) of the Act, decided to recommend a change to the circumstances under which the following drugs are made available as pharmaceutical benefits under Part VII of the Act:

- Amlodipine + valsartan
- Candesartan cilexetil + hydrochlorothiazide
- Enalapril maleate + hydrochlorothiazide
- Eprosartan + hydrochlorothiazide
- Irbesartan + hydrochlorothiazide
- Lercanidipine hydrochloride + enalapril maleate
- Olmesartan medoxomil + amlodipine
- Olmesartan medoxomil + hydrochlorothiazide
- Perindopril arginine + amlodipine
- Perindopril arginine + indapamide hemihydrate
- Perindopril erbutamine + indapamide hemihydrate
- Quinapril + hydrochlorothiazide
- Ramipril + felodipine
- Telmisartan + amlodipine
- Telmisartan + hydrochlorothiazide
- Trandolapril + verapamil hydrochloride
- Valsartan + hydrochlorothiazide.

A note of the PBAC's decision follows.

9.01 PBS restrictions for antihypertensive fixed dose combinations (FDCs)

1 Purpose of item

To request that the PBAC:

1.1 **NOTE** the draft report on antihypertensive utilisation through the PBS, which includes a costing analysis and literature review.

1.2 **PROVIDE ADVICE** regarding proposed changes to simplify the PBS restrictions for antihypertensive FDCs, including any preferred option.

1.3 **NOTE** that the Department will prepare financial estimates of any proposed restriction changes for PBAC consideration at a future meeting.

1.4 **PROVIDE ADVICE** on the need to consult relevant prescriber and consumer groups regarding the proposed restriction changes.

1.5 **PROVIDE ADVICE** on whether the antihypertensive report should be provided to the Drug Utilisation Sub-Committee (DUSC) for noting or advice.

1.6 **NOTE** any pre-PBAC responses from sponsors of PBS-listed antihypertensive FDCs.

2 Background

2.1 In September 2023, the PBAC supported a proposal to undertake a research project on antihypertensives as part of the Post-market Review workplan. The PBAC noted that this project would involve:

- A patient-level analysis of the utilisation of antihypertensives, focusing on quantifying the potential underuse of FDCs, and initiation of antihypertensive therapy with two or more medicines (including initiation with FDCs versus single drug products).
- Reviewing the appropriateness of the PBS restrictions for antihypertensives by comparison with current Australian and international clinical guidelines.
- Quantification of the potential savings to the PBS and consumers from addressing any underuse of antihypertensive FDCs and outlining potential options to increase use.
- Stakeholder consultation with relevant peak bodies and consumer organisations.
- An optional literature review of the evidence for commencing antihypertensive therapy with two medications compared to one medication.

2.2 In February 2024, the Department contracted the University the of South Australia to provide a report on antihypertensive utilisation. The report would quantify the potential underuse of FDCs and aimed to provide an estimate of the potential savings to the PBS and consumers that could occur through addressing any FDC underuse. The report would also document a narrative literature review of the comparative effectiveness of commencing antihypertensive therapy with 'standard care' (i.e. low dose monotherapy, followed by the addition of a second low dose therapy, then titrating up the doses) versus commencing low-dose dual FDC therapy.

PBS listings

Restrictions

2.3 A summary of the PBS restrictions as at 1 November 2024 for antihypertensives that were made available through the PBS between 2013-2023 (the period of the utilisation analysis) was presented.

2.4 Of the PBS-listed antihypertensives available in an FDC form (which includes combinations of angiotensin-converting enzyme inhibitors – ACEs; angiotensin II receptor agonists – ATRAs; calcium-channel blockers – CCBs; and thiazide diuretics), all are unrestricted listings on the PBS in the monotherapy form. Most of these monotherapy antihypertensives also have 60-day dispensing items that are Restricted Benefit listings with the standard clinical criteria "The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient". An exception to this is eprosartan monotherapy, which has Authority Required (telephone) listings for patients who are unable to initiate or continue other base-priced drugs under the 30-day and 60-day PBS item codes. These listings are in addition to a 30-day PBS item code (inclusive of a brand price premium) that is currently listed as an unrestricted listing, and a 60-day PBS item code (inclusive of a brand price premium), currently listed as a Restricted Benefit with the aforementioned standard clinical criteria.

2.5 All dual therapy FDCs of ACEs, ATRAs, CCBs and thiazide diuretics have Restricted Benefit PBS listings for the treatment of hypertension that require patients to be inadequately controlled on one of the classes of medicines in the combination. The only exception is perindopril 2.5 mg + indapamide 625 µg, which has an unrestricted listing to align with the TGA indication for this strength and an Authority required (Restricted Benefit) listing for the 60-day prescriptions. For triple therapy antihypertensive FDCs, patients must be inadequately controlled on two classes. The listings specifically state that the FDCs may not be used for initiation of therapy.

Available strengths

2.6 Table 1 shows the PBS-listed antihypertensive FDCs with the number of available strengths as at 1 November 2024. As shown, the number of strengths available for most FDCs is more limited than if the agents are prescribed individually. There are two triple therapy FDCs available on the PBS. These combinations consist of either valsartan or olmesartan, in combination with amlodipine and hydrochlorothiazide (HCTZ). There are 5 strength combinations available of each.

2.7 For some antihypertensive FDCs, the available combinations may be limited to moderate to higher strengths of the ACE or ATRA. For example, candesartan is available in 4 mg, 8 mg, 16 mg, and 32 mg strengths, but is only available in 16 mg or 32 mg strengths when in an FDC with hydrochlorothiazide (HCTZ).

2.8 For FDCs with diuretics, the diuretic component is often available in a strength lower than that available with the monotherapy form. For example, indapamide is available in 1.5 mg and 2.5 mg strengths, but in the FDC with perindopril, it is available in only lower strengths of 1.25 mg or 625 µg. HCTZ alone is only available in a 25 mg strength, whereas in FDC form it is available in 12.5 mg and 6 mg strengths. Pill cutting of monotherapy drugs would be required to achieve the strengths available in some FDCs and may not be feasible for some strengths.

2.9 The strength combinations available for antihypertensive FDCs on the PBS may pose limitations for prescribers in up- or down-titrating patients using an FDC. This may potentially discourage use of FDCs or lead to increased medication switches.

2.10 Not all the strength combinations registered in Australia are listed on the PBS. For example, there are multiple brands of olmesartan 20 mg + amlodipine 10 mg registered with the Therapeutic Goods Administration (TGA), but this dose FDC is not listed on the PBS. The PBAC considered this combination previously through a PBAC submission requesting the PBS listing of olmesartan and amlodipine. The Public Summary Document (PSD) stated that 'The PBAC noted with some concern that the sponsor had advised in the pre-subcommittee response that it will not proceed with the listing of the olmesartan 20 mg – amlodipine 10 mg combination tablet. This means that a patient whose hypertension is uncontrolled with the 20 mg – 5 mg tablet who wishes to continue to use the dual combination only has the option of increasing the olmesartan dose by moving to the 40 mg - 5 mg strength…The PBAC noted that the sponsor had provided no explanation for its decision not to proceed with the 20 mg – 10 mg product…'.[1]

2.11 The availability of antihypertensive FDC strengths varies between countries. For example, enalapril + HCTZ is PBS-listed for only the 20 mg-6 mg strength, while in the UK it is available as 20 mg-12.5 mg, and in the US as 5 mg-12.5 mg or 10 mg-25 mg.

[1] Department of Health and Aged Care, PBAC PSD Olmesartan medoxomil with amlodipine, Sevikar®, July 2010.

Table 1. Antihypertensive FDCs on the PBS showing the number of strengths available for each combination as at 1 November 2024

	HCTZ (Diuretic)	Indapamide (Diuretic)	Amlodipine (CCB)	Lercanidipine (CCB)	Felodipine (CCB)	Verapamil (CCB)
Enalapril (ACE)	1	NA	NA	2	NA	NA
Perindopril (ACE)	NA	3	4	NA	NA	NA
Quinapril (ACE)	2	NA	NA	NA	NA	NA
Ramipril (ACE)	NA	NA	NA	NA	2	NA
Trandolapril (ACE)	NA	NA	NA	NA	NA	2
Eprosartan (ATRA)	1	NA	NA	NA	NA	NA
Valsartan[1] (ATRA)	5	NA	5	NA	NA	NA
Irbesartan (ATRA)	3	NA	NA	NA	NA	NA
Candesartan (ATRA)	3	NA	NA	NA	NA	NA
Telmisartan (ATRA)	3	NA	4	NA	NA	NA
Olmesartan[1] (ATRA)	3	NA	3	NA	NA	NA

Abbreviations: ACE - Angiotensin converting enzyme inhibitor; ATRA - Angiotensin II receptor antagonist; CCB – calcium-channel blocker; HCTZ –Hydrochlorothiazide; NA – Not available.

Key: Shaded cells - No FDC available through the PBS; Numbered cells – Number of strengths available in FDC.

Notes:

1. Triple therapy FDCs available on the PBS: Amlodipine + valsartan + HCTZ (5 strengths) and Olmesartan + amlodipine + HCTZ (5 strengths)

Cost comparison between FDCs and component medicines

2.12 Antihypertensive FDCs are lower in cost than the combined cost of the component medicines at the same strength. For combinations of CCBs with ACE or ATRA, savings are usually around $12-$16 for 30-day prescription items. Savings are lowest for FDCs containing diuretics at around $2-$5 per month, as the PBS listings provide 90-100 tablets (around 3 months therapy).

Therapeutic Goods Administration (TGA) indication

2.13 The TGA indications for antihypertensive FDCs generally align with the PBS restrictions, with most specifying that they are not to be used for therapy initiation, except for perindopril 2.5 mg + indapamide 625 µg which is PBS listed and TGA indicated for hypertension with no additional requirements (refer to Appendix 1, Table 1A).

2.14 The TGA indications for two FDCs further specify that they are to be used in substitution therapy in patients adequately controlled with separate doses of the component drugs at the same dose (amlodipine + perindopril FDC; and amlodipine + valsartan + HCTZ FDC).

Australian guidelines

2.15 Australian clinical guidelines (Heart Foundation guidelines,[2] Therapeutic Guidelines[3]) generally recommend that patients commence antihypertensive treatment with a single drug at a low dose and then add a second drug at a low dose before titrating up the doses. The Heart Foundation guidelines recommend, based on weak evidence, that combination therapy at commencement may be considered for patients with very high baseline blood pressure (BP) (>20/10 mmHg above target). Potential benefits of commencing therapy with two drugs are cited as more rapid reduction in BP, reduced clinical inertia, and less drug and dose changes, while limitations include difficulties in assessing efficacy of the individual drugs and attributing any adverse events. The Therapeutic Guidelines state that antihypertensive treatment can be started with two drugs at a low dose, and that this approach is reasonable in all patients, especially those at high cardiovascular (CV) risk or particularly elevated BP.

2.16 The Heart Foundation guidelines note that 50-70% of patients will require treatment with more than one antihypertensive. Further, cumulative data from clinical trials indicates that around 25% of patients will require triple therapy to achieve BP control.[4]

2.17 The Heart Foundation and Stroke Foundation announced in August 2024 the development of new guidelines for managing and treating hypertension that are anticipated to be released in 2025.[5]

2.18 The National Hypertension Taskforce was established in 2022, a collaboration between the Australian Cardiovascular Alliance and Hypertension Australia, with the aim of increasing BP control (defined as <140/90 mmHg) from 32% to 80% by 2030 in Australia. The Taskforce notes that in 2022, an estimated 6.8 million Australians had hypertension, with 1.2 million (18%) having diagnosed but uncontrolled hypertension and 2.2 million (32%) having diagnosed and effectively treated hypertension.[6,7]

[2] National Heart Foundation of Australia, Guideline for the diagnosis and management of hypertension in adults – 2016, accessed 4 August 2023.
[3] Therapeutic Guidelines, Hypertension and Blood Pressure Reduction, published June 2023, accessed 4 August 2023.
[4] Epstein BJ, Shah NK, and Borja-Hart NL (2013), 'Management of Hypertension with fixed-dose triple-combination treatments', *Therapeutic Advances in Cardiovascular Disease*, 7(5):246-59.
[5] Heart Foundation, New guidelines for managing and treating hypertension and lipids, accessed 15 November 2024.
[6] National Hypertension Taskforce, Goal, accessed 15 November 2024.
[7] Carnagarin R et al (2023), 'Stagnating rates of blood pressure control in Australia: insights from the opportunistic screening of 10046 participants of the May Measurement Month campaigns', *J Hypertension*, 41(4):632-637.

International guidelines

2.19 International guidelines for the treatment of hypertension, such as the 2020 International Society of Hypertension (ISH) guideline[8] and the 2024 European Society of Cardiology (ESC) guideline[9] recommend starting antihypertensive treatment with a two-component low dose FDC for most patients, except in frail or very old patients, or low risk grade 1 hypertension, for whom low dose monotherapy is recommended. Guidelines suggest that starting two drugs at low dose is a reasonable approach in most patients but especially those with high CV risk or particularly elevated BP.

2.20 The World Health Organization guideline[10] includes a conditional recommendation based on moderate-certainty evidence for combination therapy as an initial treatment, preferably as an FDC to improve therapy adherence and persistence. Combination therapy is considered particularly useful for patients with baseline BP ≥20/10 mm Hg over target.

Sponsor consultation

2.21 All sponsors of PBS-listed antihypertensive FDCs were consulted on this item in line with standard PBAC processes and timelines.

Consumer comments

2.22 The PBAC noted that no consumer comments were received for this item.

3 Antihypertensives report key findings

3.1 The PBAC noted the key findings from the report, including:

- In 2023, there were almost 59 million antihypertensive prescriptions dispensed through the PBS to 5.0 million people (around 19% of the Australian population).
- In July 2023, around half of the antihypertensive prevalent population were dispensed multiple classes of antihypertensives; 35% were supplied two concurrent antihypertensive classes, and 15% were supplied three or more concurrent classes. Of those supplied multiple antihypertensive classes, around 60% were dispensed at least one FDC.

[8] Unger T et al. (2020) '2020 International Society of Hypertension Global Hypertension Practice Guidelines', *Hypertension*, 75(6): 1334-54.
[9] McEvoy JW et al. (2024) '2024 ESC Guidelines for the management of elevated blood pressure and hypertension: Developed by the task force on the management of elevated blood pressure and hypertension of the European Society of Cardiology (ESC) and endorsed by the European Society of Endocrinology (ESE) and the European Stroke Organisation (ESO)', *European Heart Journal*, 45(38): 3912-4018.
[10] World Health Organization (2021), Guideline for the pharmacological treatment of hypertension in adults, Geneva.

- In 2023, an estimated 378,000 Australians were using multiple antihypertensive classes that could have been using at least one FDC (i.e. the classes being used were available in an FDC).
- In 2023, around 400,000 patients initiated antihypertensive therapy, of which approximately 90% started with monotherapy, 6% commenced multiple therapies (not as an FDC) and 4% commenced an FDC. Within 12 weeks of commencing antihypertensive monotherapy, around 8% of patients were being supplied multiple therapies and 17% had ceased all antihypertensive treatment. At 12-months follow-up, around 19% were supplied multiple antihypertensive therapies, while 54% had ceased all antihypertensive treatment.
- Between 2013 and 2023, the proportion of individuals dispensed FDCs containing a CCB with either an ACE or ATRA increased, while the proportion dispensed FDCs containing thiazides with either ACE or ATRA decreased. In 2023, of patients supplied an FDC, around 48% of patients were supplied an ACE or ARB in combination with a CCB, while 38% were dispensed an ARB in combination with a thiazide.
- Four-year persistence to any antihypertensive therapy based on patients initiating therapy between 2015-2019 was similar between those initiated on combination treatment (FDC or multiple single-drug products) or monotherapy. For patients commencing therapy with ACE or ATRA, persistence to index therapy was slightly better for those commencing an FDC than for those who commenced multiple single-drug therapies. Patients who commenced therapy with an ATRA generally had greater persistence to the index therapy than those who commenced therapy with an ACE, CCB or thiazide, although the differences were small.
- Overall, it was estimated that allowing use of FDCs at antihypertensive treatment commencement would save consumers $20.5 million over 6 years (weighted by general and safety net prescriptions) and the PBS would save $17.9 million over 6 years, based on the proportion of patients who added another monotherapy product or switched to an FDC by 12 weeks. The PBAC noted that these estimates had not been validated by the Department and should be considered indicative only.
- A literature review found no systematic reviews of studies specifically comparing the safety and effectiveness of commencing antihypertensive treatment with standard care (monotherapy followed by add-on therapy) versus low dose dual FDC. Individual RCTs (N=2) found that initiating antihypertensive treatment with a low dose dual FDC was associated with a more rapid reduction in BP in the short term, but at an increased risk of hypotension.

4 Proposed PBS listing changes

4.1 The PBAC was requested to provide advice on whether to simplify the PBS restrictions for antihypertensive FDCs. Three options for proposed changes were provided as shown below. The PBAC noted that a fourth option would be to maintain the current restrictions for antihypertensive FDCs and reconsider potential changes to the restrictions following the release of the updated Heart Foundation guidelines in 2025.

4.2 Option 1: Unrestricted listings for all antihypertensive FDCs

Option 1 proposed allowing the use of any antihypertensive FDC at therapy initiation by changing the restriction level from Restricted Benefit to unrestricted. All current restriction wording would therefore be removed from these listings. The 60-day prescription items would remain Authority Required (Restricted Benefit) listings, however all clinical criteria would be removed except for the following clinical criteria:

The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient.

Any cautionary notes would also remain on these listings. This change could apply to only dual therapy FDCs or could also be applied to triple therapy FDCs, noting that clinical guidelines have not recommended commencing antihypertensive therapy with triple therapy.

4.3 Option 2: Unrestricted listings for selected low-moderate dose dual therapy FDCs

Option 2 proposed changing the restriction level for only selected low-moderate dose dual therapy antihypertensive FDCs to unrestricted listings. The 60-day prescription items would remain Restricted Benefit items, with only the standard clinical criterion requiring the patient's condition to be stable.

4.4 Option 3: Unrestricted listings for selected low-moderate dose dual therapy FDCs with sufficient available strength combinations

Option 3 proposed changing the restriction level for selected low-moderate dose dual therapy antihypertensive FDCs to unrestricted listings, but only for combinations where the PBAC considered that the strengths available provided sufficient dose titration options. For example, the changes could be limited to low-moderate strengths of the following drug combinations that have 4-5 strengths available on the PBS (see also Table 1):

- valsartan + HCTZ (5 strengths)
- valsartan + amlodipine (5 strengths)
- telmisartan + amlodipine (4 strengths)
- perindopril + amlodipine (4 strengths).

This option may encourage prescribers to commence their patients on antihypertensive therapy with FDCs where sufficient strength combinations are available for adequate dose titration, reducing the need for medication switches or the addition of a monotherapy drug to achieve the appropriate dose.

If olmesartan 20 mg + amlodipine 10 mg were listed on the PBS, the restriction level could also be changed for low-moderate dose dual therapy listings of olmesartan + amlodipine. Unrestricted listings for valsartan/olmesartan + amlodipine may have the benefit of increasing use of triple therapy antihypertensive FDCs, as these drugs are the only drugs available in triple therapy combination with HCTZ through the PBS.

4.5 The PBAC noted the potential quality use of medicines issues with commencing patients on dual therapy, such as the inability to determine efficacy of the individual drugs, or to reliably attribute adverse events.

4.6 The antihypertensives report estimated savings to the PBS from allowing patients to commence therapy with FDCs. The PBAC noted that these estimates included only drug costs and did not include any health system impacts associated with either reduced CV events or increased adverse events. The estimated savings did not include any potential increase in costs to the PBS from patients initiating FDCs, who would otherwise have commenced and continued monotherapy. The PBAC noted that the estimates in the report had not been validated by the Department and should be considered indicative only. The PBAC noted that the Department would develop revised financial estimates to reflect any restriction changes recommended by the PBAC.

4.7 The PBAC noted that changing antihypertensive FDCs to unrestricted listings would be consistent with the PBAC's May 2024 recommendation to change the restriction level for ezetimibe + statin (HMG-CoA reductase inhibitor) FDCs from Authority Required (Streamlined) to unrestricted listings. These changes were implemented on 1 November 2024. Like antihypertensive FDCs, in the case of ezetimibe + statin FDCs there was misalignment between the TGA indication/PBS restrictions and the place of ezetimibe + statin combination therapy in clinical guidelines.

4.8 The PBAC noted that if changes to the PBS restrictions for antihypertensive FDCs were recommended and implemented, that the Department intended to work with the Australian Commission on Safety and Quality in Health Care (ACSQHC) to communicate these changes to prescribers.

5 PBAC Outcome

5.1 The PBAC noted the report on antihypertensive utilisation through the PBS, which included a costing analysis and literature review. The PBAC noted the key findings from the report detailed above, and considered that the report illustrated the following additional utilisation trends:

- That the proportion of patients initiating antihypertensive therapy with an FDC had trended down over the ten years between 2013-2023 but the proportion of the prevalent patient population on an FDC had remained relatively stable over this time.
- That patients on antihypertensive triple therapy were more likely to be on an FDC than patients on dual therapy, which demonstrated that prescribers were attempting to reduce pill burden for patients as therapy is escalated. However, the PBAC noted that in 2023 there were around 378,000 patients who could potentially benefit from being switched to an FDC.
- That for patients who initiated antihypertensive therapy between 2015 to 2019, the median time to discontinuation of index therapy due to switch or cessation was significantly higher for patients initiated on monotherapy than those on an ACE/ATRA FDC (10 months vs 4 months; HR 0.71 95% CI 0.69-0.72). However, overall persistence to any antihypertensive therapy at 4 years was similar between patients who started monotherapy and those who started an FDC, with a slightly lower persistence occurring in the first few months following initiation for patients using an FDC.
- That adherence rates were high for all antihypertensive classes.
- That female patients, and older patients, generally had lower antihypertensive FDC use.
- That the analysis of comorbid conditions and use of antihypertensives concordant with current clinical guidelines indicated that use of an ACE/ATRA in patients with chronic kidney disease, guideline recommended, was only 53%. Use of BBs or thiazides in patients with diabetes, where caution is advised due to potential adverse effects on glucose metabolism and hypoglycaemic awareness, was 32% and 20%, respectively. The PBAC considered these important quality use of medicines findings that should be communicated to prescribers.

5.2 The PBAC noted that interpretation of the utilisation analysis findings was complicated for those antihypertensives, e.g. BBs, which are also indicated for the treatment of conditions other than hypertension.

5.3 The PBAC considered the three proposed options for changes to simplify the PBS restrictions for antihypertensive FDCs. The PBAC considered an additional option of maintaining the current PBS restrictions and reconsidering any changes following release of the updated Heart Foundation guidelines for hypertension. The PBAC recommended Option 1, changing all antihypertensive dual therapy FDCs to unrestricted benefit listings. The dual therapy FDC 60-day prescription items will remain Restricted Benefit listings with the standard clinical criterion requiring the patient's condition to be stable to be retained. The PBAC considered that the restrictions for antihypertensive triple therapy FDCs should remain Restricted Benefit listings with the current criteria.

5.4 The PBAC considered that Option 2 (Unrestricted listings for selected low-moderate dose dual therapy FDCs) and Option 3 (Unrestricted listings for selected low-moderate dose dual therapy FDCs with sufficient available strength combinations) would add unnecessary complexity to the PBS restrictions for antihypertensives. The PBAC considered that clinicians were experienced in navigating antihypertensive dose titration within the available PBS-listed strengths, and in managing medicine supply shortages, making it unnecessary to limit the restriction changes to FDCs with sufficient available strengths (Option 3).

5.5 The PBAC noted that there was limited evidence to support initiation of antihypertensive therapy with low dose dual FDC therapy over standard care. The literature review in the report identified no systematic reviews or meta-analyses and only two relevant RCTs. The PBAC noted that the RCTs demonstrated a more rapid improvement in BP for patients who initiated low dose dual FDC therapy versus standard care, and that a more rapid reduction in BP was associated with reductions in CV events.[11]

5.6 The PBAC noted the increased risk of hypotension associated with initiating antihypertensive therapy with low dose dual FDC therapy versus standard care in the PATHWAY trial (25% versus 14%; p <0.001).[12] The PBAC considered that the increased risk of falls associated with hypotension could be managed through appropriate patient selection and noted that clinical guidelines generally recommended initiation of low dose monotherapy for elderly and frail patients.

5.7 The PBAC noted that clinical guidelines cited difficulty in accurately attributing side effects as a reason against initiation of FDCs but considered that common side effects were often readily attributable to a specific antihypertensive on the basis of expected pharmacological actions.

5.8 The PBAC noted that the potential cost savings estimated in the report assumed that all patients who initiated antihypertensive treatment with dual (not FDC) therapy or who initiated monotherapy but were on dual (not FDC) therapy by 12 weeks post initiation, would be initiated on an FDC. The PBAC considered this scenario unlikely in the current Australian clinical context, where most patients are initiated on monotherapy, resulting in an overestimate of the potential savings. The PBAC considered that a significant or rapid change in prescribing patterns to increase initiations with dual therapy was unlikely.

[11] Volpe M, Gallo G, Tocci G. (2018), 'Is early and fast blood pressure control important in hypertension management?', *International Journal of Cardiology*, 254:328-332.

[12] MacDonald TM, Williams B, Webb DJ, et al. (2107), 'Combination therapy is superior to sequential monotherapy for the initial treatment of hypertension: a double-blind randomized controlled trial', *Journal of the American Heart Association*, 6(11):e006986.

5.9 The PBAC noted that the costings did not account for patients who may initiate a dual therapy FDC if the PBS restrictions allowed this, who would previously have been initiated on monotherapy and not required escalation to dual therapy. This population may partially offset any potential savings to the PBS and consumers.

5.10 The PBAC considered that the recommended restriction changes would have minor impact on utilisation and that a greater impact would be expected to come from any changes to Australian clinical guidelines and subsequent prescriber educational activities. The PBAC considered that rates of initiation of antihypertensive therapy with an FDC *may* increase following release of the new Heart Foundation guidelines, if these guidelines recommended that most patients should be initiated on low dose dual FDC therapy. The PBAC considered that consumer education on the utilisation analysis results may encourage consumers to discuss with their prescriber the most appropriate treatment options and potential cost savings.

5.11 The PBAC noted the two sponsor pre-PBAC responses that were received, which generally supported changing the PBS restrictions to allow patients to initiate antihypertensive therapy with a low dose dual therapy FDC. Sponsors considered that these changes would align with international clinical guidelines and provide CV benefits to patients.

5.12 The PBAC advised that consultation on the recommended restriction changes with relevant prescriber and consumer groups was unnecessary given that the changes were likely to be welcomed by stakeholders and that the restrictions would be broadened to align with current international clinical guidelines.

5.13 The PBAC considered that overall, the recommended restriction changes were likely to result in cost savings for the PBS and consumers, but of a smaller magnitude than estimated in the report. The PBAC noted that the Department intended to revise the financial estimates and that these would be brought back to the PBAC for consideration if a cost to the PBS was estimated.

5.14 The PBAC advised that Drug Utilisation Sub-Committee (DUSC) advice on the draft report was unnecessary to inform its recommendation.

5.15 The PBAC considered that it was important to communicate the findings of the report, particularly on quality use of medicines issues. The PBAC advised that the Department disseminate the report's findings by contacting relevant prescriber and consumer representative groups, the Therapeutic Guidelines (publisher of Australian Prescriber) and the ACSQHC (publisher of RADAR).

Outcome:
Recommended

6 Recommended listing

6.1 Amend existing listings as follows:

30-day PBS item codes

Drug, form, and strength	Item	Max quant	Rpts	Pack size
amlodipine 10 mg + valsartan 160 mg tablet, 28	9377M	28	5	28
amlodipine 10 mg + valsartan 320 mg tablet, 28	5460J	28	5	28
amlodipine 5 mg + valsartan 160 mg tablet, 28	9376L	28	5	28
amlodipine 5 mg + valsartan 320 mg tablet, 28	5459H	28	5	28
amlodipine 5 mg + valsartan 80 mg tablet, 28	9375K	28	5	28
candesartan cilexetil 16 mg + hydrochlorothiazide 12.5 mg tablet, 30	8504N	30	5	30
candesartan cilexetil 32 mg + hydrochlorothiazide 12.5 mg tablet, 30	9314F	30	5	30
candesartan cilexetil 32 mg + hydrochlorothiazide 25 mg tablet, 30	9315G	30	5	30
enalapril maleate 20 mg + hydrochlorothiazide 6 mg tablet, 30	8477E	30	5	30
eprosartan 600 mg + hydrochlorothiazide 12.5 mg tablet, 28	8624X	28	5	28
irbesartan 150 mg + hydrochlorothiazide 12.5 mg tablet, 30	8404H	30	5	30
irbesartan 300 mg + hydrochlorothiazide 12.5 mg tablet, 30	8405J	30	5	30
irbesartan 300 mg + hydrochlorothiazide 25 mg tablet, 30	2136K	30	5	30
lercanidipine hydrochloride 10 mg + enalapril maleate 10 mg tablet, 28	9144G	28	5	28
lercanidipine hydrochloride 10 mg + enalapril maleate 20 mg tablet, 28	9145H	28	5	28
olmesartan medoxomil 20 mg + amlodipine 5 mg tablet, 30	5292M	30	5	30
olmesartan medoxomil 40 mg + amlodipine 10 mg tablet, 30	5294P	30	5	30
olmesartan medoxomil 40 mg + amlodipine 5 mg tablet, 30	5293N	30	5	30
olmesartan medoxomil 20 mg + hydrochlorothiazide 12.5 mg tablet, 30	2161R	30	5	30
olmesartan medoxomil 40 mg + hydrochlorothiazide 12.5 mg tablet, 30	2166B	30	5	30
olmesartan medoxomil 40 mg + hydrochlorothiazide 25 mg tablet, 30	2170F	30	5	30
perindopril arginine 10 mg + amlodipine 10 mg tablet, 30	9349C	30	5	30
perindopril arginine 10 mg + amlodipine 5 mg tablet, 30	9348B	30	5	30
perindopril arginine 5 mg + amlodipine 10 mg tablet, 30	9347Y	30	5	30
perindopril arginine 5 mg + amlodipine 5 mg tablet, 30	9346X	30	5	30
perindopril arginine 5 mg + indapamide hemihydrate 1.25 mg tablet, 30	2845R	30	5	30
perindopril erbumine 4 mg + indapamide hemihydrate 1.25 mg tablet, 30	8449Q	30	5	30
quinapril 10 mg + hydrochlorothiazide 12.5 mg tablet, 30	8589C	30	5	30
quinapril 20 mg + hydrochlorothiazide 12.5 mg tablet, 30	8590D	30	5	30
ramipril 2.5 mg + felodipine 2.5 mg modified release tablet, 30	2626F	30	5	30
ramipril 5 mg + felodipine 5 mg modified release tablet, 30	2629J	30	5	30
telmisartan 40 mg + amlodipine 10 mg tablet, 28	8979N	28	5	28
telmisartan 40 mg + amlodipine 5 mg tablet, 28	8978M	28	5	28
telmisartan 80 mg + amlodipine 10 mg tablet, 28	8981Q	28	5	28
telmisartan 80 mg + amlodipine 5 mg tablet, 28	8980P	28	5	28
telmisartan 40 mg + hydrochlorothiazide 12.5 mg tablet, 28	8622T	28	5	28

Drug, form, and strength	Item	Max quant	Rpts	Pack size
telmisartan 80 mg + hydrochlorothiazide 12.5 mg tablet, 28	8623W	28	5	28
telmisartan 80 mg + hydrochlorothiazide 25 mg tablet, 28	9381R	28	5	28
trandolapril 2 mg + verapamil hydrochloride 180 mg modified release tablet, 28	9387C	28	5	28
trandolapril 4 mg + verapamil hydrochloride 240 mg modified release tablet, 28	2857J	28	5	28
valsartan 160 mg + hydrochlorothiazide 12.5 mg tablet, 28	9373H	28	5	28
valsartan 160 mg + hydrochlorothiazide 25 mg tablet, 28	9374J	28	5	28
valsartan 320 mg + hydrochlorothiazide 12.5 mg tablet, 28	9481B	28	5	28
valsartan 320 mg + hydrochlorothiazide 25 mg tablet, 28	9482C	28	5	28
valsartan 80 mg + hydrochlorothiazide 12.5 mg tablet, 28	9372G	28	5	28

Restriction Summary

Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners
	Restriction type: ☒Unrestricted benefit

- Change the Authority level from Authority Required (Restricted Benefit) to Unrestricted Benefit
- All restriction wording currently included in the PBS item codes to be removed.

60-day prescription items

- All clinical criteria to be removed from the PBS item codes below, except for:

  The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient.

- All other cautions and/or notes to remain, where applicable.

A. ATRA (angiotensin II receptor agonist) and calcium channel blocker (CCB) PBS item codes

Drug, form, and strength	Item	Max quant	Rpts	Pack size
amlodipine 10 mg + valsartan 160 mg tablet, 28	13454D	56	5	28
amlodipine 10 mg + valsartan 320 mg tablet, 28	13389Q	56	5	28
amlodipine 5 mg + valsartan 160 mg tablet, 28	13516J	56	5	28
amlodipine 5 mg + valsartan 320 mg tablet, 28	13604B	56	5	28
amlodipine 5 mg + valsartan 80 mg tablet, 28	13421J	56	5	28
olmesartan medoxomil 40 mg + amlodipine 10 mg tablet, 30	13943	60	5	30
olmesartan medoxomil 40 mg + amlodipine 5 mg tablet, 30	13964Y	60	5	30
telmisartan 40 mg + amlodipine 10 mg tablet, 28	13515H	56	5	28
telmisartan 40 mg + amlodipine 5 mg tablet, 28	13483P	56	5	28
telmisartan 80 mg + amlodipine 10 mg tablet, 28	13451Y	56	5	28

Drug, form, and strength	Item	Max quant	Rpts	Pack size
telmisartan 80 mg + amlodipine 5 mg tablet, 28	13450X	56	5	28

Restriction Summary

Concept ID (for internal Dept. use)	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners ☒ Nurse practitioners
	Restriction Type: ☒ Restricted Benefit
30503	**Clinical criteria:**
30502	The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The treatment must not be for the initiation of anti-hypertensive therapy~~
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The condition must be inadequately controlled with an angiotensin II antagonist~~
	~~OR~~
	~~The condition must be inadequately controlled with a dihydropyridine calcium channel blocker~~

B. ATRA and hydrochlorothiazide (HCTZ) PBS item codes

Drug, form, and strength	Item	Max quant	Rpts	Pack size
candesartan cilexetil 16 mg + hydrochlorothiazide 12.5 mg tablet, 30	13391T	60	5	30
candesartan cilexetil 32 mg + hydrochlorothiazide 12.5 mg tablet, 30	13452B	60	5	30
candesartan cilexetil 32 mg + hydrochlorothiazide 25 mg tablet, 30	13392Q	60	5	30
eprosartan 600 mg + hydrochlorothiazide 12.5 mg tablet, 28	14337N	56	5	28
irbesartan 150 mg + hydrochlorothiazide 12.5 mg tablet, 30	13572H	60	5	30
irbesartan 300 mg + hydrochlorothiazide 12.5 mg tablet, 30	13545X	60	5	30
irbesartan 300 mg + hydrochlorothiazide 25 mg tablet, 30	13446Q	60	5	30
telmisartan 40 mg + hydrochlorothiazide 12.5 mg tablet, 28	13546Y	56	5	28
telmisartan 80 mg + hydrochlorothiazide 12.5 mg tablet, 28	13574K	56	5	28
telmisartan 80 mg + hydrochlorothiazide 25 mg tablet, 28	13607E	56	5	28
valsartan 160 mg + hydrochlorothiazide 12.5 mg tablet, 28	13606D	56	5	28
valsartan 160 mg + hydrochlorothiazide 25 mg tablet, 28	13453C	56	5	28
valsartan 320 mg + hydrochlorothiazide 12.5 mg tablet, 28	13517K	56	5	28
valsartan 320 mg + hydrochlorothiazide 25 mg tablet, 28	13455E	56	5	28
valsartan 80 mg + hydrochlorothiazide 12.5 mg tablet, 28	13393X	56	5	28
olmesartan medoxomil 20 mg + hydrochlorothiazide 12.5 mg tablet, 30	13447R	60	5	30
olmesartan medoxomil 40 mg + hydrochlorothiazide 12.5 mg tablet, 30	13601W	60	5	30
olmesartan medoxomil 40 mg + hydrochlorothiazide 25 mg tablet, 30	13602X	60	5	30

Restriction Summary

Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners
	Restriction Type: ☒ Restricted Benefit
30503	**Clinical criteria:**
30502	The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The treatment must not be for the initiation of anti-hypertensive therapy~~
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The condition must be inadequately controlled with an angiotensin II antagonist~~
	~~OR~~
	~~The condition must be inadequately controlled with a thiazide diuretic.~~

C. ACE (angiotensin converting enzyme inhibitor) and HCTZ PBS item code

Drug, form, and strength	Item	Max quant	Rpts	Pack size
enalapril maleate 20 mg + hydrochlorothiazide 6 mg tablet, 30	13439H	60	5	30

Restriction Summary

Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners
	Restriction Type: ☒ Restricted Benefit
30503	**Clinical criteria:**
30502	The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The treatment must not be for the initiation of anti-hypertensive therapy~~
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The condition must be inadequately controlled with an ACE inhibitor~~
	~~OR~~
	~~The condition must be inadequately controlled with a thiazide diuretic.~~

D. ACE and CCB PBS item codes

Drug, form, and strength	Item	Max quant	Rpts	Pack size
lercanidipine hydrochloride 10 mg + enalapril maleate 10 mg tablet, 28	13507X	56	5	28
lercanidipine hydrochloride 10 mg + enalapril maleate 20 mg tablet, 28	13477H	56	5	28
perindopril arginine 10 mg + amlodipine 10 mg tablet, 30	13382H	60	5	30
perindopril arginine 10 mg + amlodipine 5 mg tablet, 30	13478J	60	5	30
perindopril arginine 5 mg + amlodipine 10 mg tablet, 30	13381G	60	5	30
perindopril arginine 5 mg + amlodipine 5 mg tablet, 30	13508Y	60	5	30
ramipril 2.5 mg + felodipine 2.5 mg modified release tablet, 30	13563W	60	5	30
ramipril 5 mg + felodipine 5 mg modified release tablet, 30	13534H	60	5	30

Restriction Summary

Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒ Medical Practitioners ☒ Nurse practitioners
	Restriction Type: ☒ Restricted Benefit
30503	**Clinical criteria:**
30502	The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The treatment must not be for the initiation of anti-hypertensive therapy~~
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The condition must be inadequately controlled with an ACE inhibitor~~
	~~OR~~
	~~The condition must be inadequately controlled with a dihydropyridine calcium channel blocker.~~

E. ACE and indapamide PBS item codes

Drug, form, and strength	Item	Max quant	Rpts	Pack size
perindopril arginine 5 mg + indapamide hemihydrate 1.25 mg tablet, 30	13506W	60	5	30
perindopril erbumine 4 mg + indapamide hemihydrate 1.25 mg tablet, 30	13476G	60	5	30

Restriction Summary

Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners
	Restriction Type: ☒ Restricted Benefit
30503	**Clinical criteria:**
30502	The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The treatment must not be for the initiation of anti-hypertensive therapy~~
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The condition must be inadequately controlled with an ACE inhibitor~~
	~~OR~~
	~~The condition must be inadequately controlled with a thiazide-like diuretic.~~

F. ACE and verapamil PBS item codes

Drug, form, and strength	Item	Max quant	Rpts	Pack size
trandolapril 2 mg + verapamil hydrochloride 180 mg modified release tablet, 28	13594L	56	5	28
trandolapril 4 mg + verapamil hydrochloride 240 mg modified release tablet, 28	13591H	56	5	28

Restriction Summary

Concept ID (for internal Dept. use)	**Category / Program:** GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners
	Restriction Type: ☒ Restricted Benefit
30503	**Clinical criteria:**
30502	The condition must be stable for the prescriber to consider the listed maximum quantity of this medicine suitable for this patient
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The treatment must not be for the initiation of anti-hypertensive therapy~~
	~~**AND**~~
	~~**Clinical criteria:**~~
	~~The condition must be inadequately controlled with an ACE inhibitor~~
	~~OR~~
	~~The condition must be inadequately controlled with verapamil~~