

**5.3 DAPAGLIFLOZIN AND METFORMIN XR (FDC), modified release tablets, 10 mg/500 mg, 10 mg/1000 mg, 5 mg/1000 mg, Xigduo XR<sup>®</sup>, AstraZeneca Pty Ltd**

**1 Purpose of Application**

1.1 The submission requested an Authority Required listing for dapagliflozin/metformin XR fixed dose combination (FDC) for treatment of type 2 diabetes.

**2 Requested listing**

2.1 The submission sought the following listing:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
DAPAGLIFLOZIN / METFORMIN HYDROCHLORIDE EXTENDED RELEASE Tablet, 10mg/500mg	28	5	Xigduo® XR	AstraZeneca
DAPAGLIFLOZIN / METFORMIN HYDROCHLORIDE EXTENDED RELEASE Tablet, 10mg/1000mg	28	5		
DAPAGLIFLOZIN / METFORMIN HYDROCHLORIDE EXTENDED RELEASE Tablet, 5mg/1000mg	56	5		
<b>Authority required</b>				
Clinical criteria: The condition must not be able to be adequately controlled by treatment with metformin and a sulfonylurea AND Patient must have, or have had, a HbA1c measurement greater than 7% prior to the initiation of a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), a glucagon-like peptide-1 (GLP1) or a sodium-glucose co-transporter-2 (SGLT2) inhibitor; OR Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10mmol per L in more than 20% of tests over a 2 week period prior to initiation with a gliptin, glitazone, glucagon-like peptide-1 or an SGLT2 inhibitor.				
Administrative advice: Dapagliflozin/metformin XR FDC is not subsidised for use in combination with a sulfonylurea, insulin, a glitazone, a gliptin, a GLP1 or another SGLT2 inhibitor.				

2.2 The evaluation noted the submission’s requested listing is consistent with the current restriction for dapagliflozin, which is as a third-line treatment. The PBAC recently made a recommendation to amend the PBS restrictions of dipeptidyl peptidase 4 inhibitors (gliptins) for the treatment of type 2 diabetes mellitus. The change to listings took effect on 1 April 2014. The change positions gliptins earlier in the PBS-subsidised treatment algorithm as second-line treatment options rather than third-line treatment options. The Department has reviewed the current restrictions for PBS-subsidised third-line treatment options for type 2 diabetes mellitus to reflect the change in the PBS availability of the gliptins. Drafts of the revised restrictions were provided to the relevant sponsors for consideration and comment, including sponsors who have applications for a PBS-subsidised third-line treatment for type 2 diabetes currently before the PBAC.

- 2.3 The PBAC noted the sponsor's request, in its pre-PBAC response, for a listing for dapagliflozin and dapagliflozin/metformin XR that is consistent with the current second-line gliptin listing at a price also consistent with the current gliptin price (and taking into account the current offsets of dapagliflozin).
- 2.4 The Department's proposed amendments to the restrictions for PBS-subsidised third-line treatments for type 2 diabetes and sponsor responses to consultation on the proposed changes were considered by PBAC in a separate item on this agenda.
- 2.5 The requested basis for listing is a cost minimisation with the individual components of the fixed dose combination (FDC).

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

### **3 Background**

- 3.1 The submission was made under TGA/PBAC Parallel Process. At the time of PBAC consideration, the TGA Delegates Overview and the ACPM minutes were available.
- 3.2 In March 2012, the PBAC rejected a submission for dapagliflozin in dual oral therapy with metformin or a sulfonylurea on the basis of uncertain comparative effectiveness and uncertain cost-effectiveness. In July 2013, the PBAC recommended listing of dapagliflozin and canagliflozin on a cost minimisation basis with sitagliptin; with an Authority Required restriction for use in combination with metformin or a sulfonylurea, where the patient is unable to be controlled by treatment with metformin and a sulfonylurea. The PBAC recommended cost-offsets for dapagliflozin and canagliflozin to account for an increased rate of adverse events (compared to sitagliptin). The PBAC considered that the risk of use of the gliflozins outside of the restriction could be managed through a risk share agreement.
- 3.3 In July 2013, the PBAC recommended listing of alogliptin for treatment in combination with metformin or a sulfonylurea, without the requirement for patients to have contraindications to, or be intolerant of a combination of metformin and a sulfonylurea. The PBAC stated that the listing should be at a reduced price, which takes into account the likely proportion of use in patients who have not trialled a sulfonylurea and where cost-effectiveness has not been established. On 1 April 2014, the PBS listings for all other gliptins (sitagliptin, saxagliptin, linagliptin, vildagliptin), including fixed dose combinations of gliptins and metformin, were amended in line with the restriction and price for alogliptin.
- 3.4 A submission for another gliflozin, empagliflozin for dual therapy with metformin or a sulfonylurea, was also considered at the July 2014 PBAC Meeting.

### **4 Clinical place for the proposed therapy**

- 4.1 Dapagliflozin/metformin XR fixed dose combination (FDC) will provide a treatment alternative for patients taking concomitant dapagliflozin and either metformin extended release (XR) or metformin immediate release (IR) for the treatment of type 2 diabetes.

*For PBAC's view, see section 7 "PBAC outcome"*

### **5 Comparator**

- 5.1 The submission nominated the corresponding doses of the individual components of dapagliflozin and metformin XR as the comparator. The submission also suggested that co-administered dapagliflozin and metformin IR would be an appropriate comparator. The ESC agreed that these were both relevant comparators.

*For PBAC’s view, see section 7 “PBAC outcome”*

## 6 PBAC consideration of the evidence

### **Sponsor hearing**

- 6.1 There was no hearing for this item.

### **Consumer comments**

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

### **Clinical trials**

- 6.3 The submission presented data from three bioequivalence trials (CT-092, CT-100, CT-125) comparing dapagliflozin/metformin XR with concomitant treatment using individual components. Details of the trials presented in the submission are below.
- 6.4 The submission also presented data from Trial CT-014 to support a claim of additive efficacy when dapagliflozin is added to metformin. This trial was previously assessed by the PBAC as part of the dapagliflozin submission that received a positive recommendation for dual oral therapy with metformin or a sulfonylurea at the July 2013 PBAC meeting.

#### **Trials and associated reports presented in the submission**

<b>Trial ID</b>	<b>Protocol title/ Publication title</b>	<b>Publication citation</b>
<b>Bioequivalence trials</b>		
CT-065	Bioavailability study of two prototype fixed dose combination (FDC) formulations of 10mg dapagliflozin and 1000mg metformin extended release (XR) tablet relative to dapagliflozin 10mg tablet and Glucophage® XR x 2 500mg tablets co-administered to healthy subjects in a fasted state.	Internal study report
CT-071	Bioavailability study of two prototype fixed dose combination (FDC) formulations of 10mg dapagliflozin and 500mg metformin extended release (XR) tablet relative to dapagliflozin 10mg tablet and a 500mg Glucophage® XR tablet, in healthy subjects in a fasted state.	Internal study report
CT-092	Bioequivalence study of a fixed-dose combination tablet of 10mg dapagliflozin/1000mg metformin XR relative to a single 10mg dapagliflozin tablet and two 500mg Glucophage® XR tablets co-administered to healthy subjects in the fed and fasted states and steady-state pharmacokinetic assessment of the fixed-dose combination of 10mg dapagliflozin /1000mg metformin XR.	Internal study report
CT-100	Bioequivalence study of a fixed-dose combination tablet of 5mg dapagliflozin/500mg metformin XR relative to a single 5mg dapagliflozin tablet and a single 500mg Glucophage® XR tablet co-administered to health subjects in the fed and fasted states and steady-state pharmacokinetic assessment of the fixed dose combination of 5mg dapagliflozin/500mg metformin XR.	Internal study report
CT-125	Bioequivalence study of a dapagliflozin/metformin XR fixed-dose combination tablet relative to a single dapagliflozin and a single Diabex® XR tablet at 2 dose strengths co-administered to healthy subjects under fed conditions.	Internal study report
CT-691	A two part, open label, randomized, Phase I bioequivalence study comparing	Internal study report

Trial ID	Protocol title/ Publication title	Publication citation
	the fixed dose combination dapagliflozin/metformin IR tablet (2.5mg/850mg or 5mg/1000mg) vs. the free combination of dapagliflozin and metformin IR tablets, in healthy volunteers, in the fed state.	
<b>Randomised trials assessing additive efficacy</b>		
CT-014  Bailey 2010  Bailey 2011  Bailey 2013  Bastien 2009a  Bastien 2009b	A multicenter, randomized, double-blind, placebo-controlled, parallel group, phase 3 trial to evaluate the safety and efficacy of dapagliflozin in combination with metformin in subjects with type 2 diabetes who have inadequate glycemic control on metformin alone. (NCT00528879) Bailey, C. J., et al. Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin: a randomised, double-blind, placebo-controlled trial. Bailey, C. J., et al. Long-term efficacy of dapagliflozin as add-on to metformin (MET) in T2DM inadequately controlled with MET alone. Bailey, C. J. et al. Dapagliflozin add-on to metformin in type 2 diabetes inadequately controlled with metformin: A randomized, double-blind, placebo-controlled 102-week trial. Bastien, A., et al. Incidence of urinary tract infections and of genital infections in two T2DM populations cotreated with dapagliflozin and oral antidiabetics +/- insulin. Bastien, A., et al. Efficacy of dapagliflozin in three populations of patients on different treatment regimens for various stages of T2DM.	Internal study report  <i>The Lancet</i> 2010; 375(9733): 2223-2233. <i>Diabetes</i> 2011; (60): A271 <i>BMC Medicine</i> 2013; (11): 43  <i>Canadian Journal of Diabetes</i> 2009; 33(3): 233-234. Canadian Journal of Diabetes 2009; 33(3): 233.
CT-012  Bolinder 2014  Bolinder 2012a  Bolinder 2012b  Grandy 2014  Grandy 2013 Ingelganullrd 2012 Ljunggren 2012a Ljunggren 2012b	A 24-week, Multi-centre, International, Double-blind, Randomized, Parallel-group, Placebo-controlled, Phase III Study with a 78-week Extension Period to Evaluate the Effect of Dapagliflozin in Combination with Metformin on Body Weight in Subjects with Type 2 Diabetes Mellitus Who Have Inadequate Glycaemic Control on Metformin Alone. Clinicaltrials.gov ID NCT00855166 Bolinder, J., et al. Dapagliflozin maintains glycaemic control while reducing weight and body fat mass over 2 years in patients with type 2 diabetes mellitus inadequately controlled on metformin. Bolinder, J., et al. Dapagliflozin produces long-term reductions in body weight, waist circumference and total fat mass in patients with type 2 diabetes inadequately controlled on metformin. Bolinder, J., et al. Effects of dapagliflozin on body weight, total fat mass, and regional adipose tissue distribution in patients with type 2 diabetes mellitus with inadequate glycemic control on metformin. Grandy, S., et al. Changes in weight loss-related quality of life among type 2 diabetes mellitus patients treated with dapagliflozin. Grandy, S., et al. Weight loss-related quality of life among type 2 diabetes mellitus (T2DM) patients treated with dapagliflozin. Ingelganullrd, A., et al. Health-related quality of life (EQ-5D) among type 2 diabetes mellitus patients treated with dapagliflozin for 24 weeks. Ljunggren, O., et al. Dapagliflozin has no effect on markers of bone formation and resorption or bone mineral density in patients with inadequately controlled type 2 diabetes mellitus on metformin. Ljunggren, O., et al. Dapagliflozin has no long-term effect on markers of bone turnover or bone mineral density in patients with inadequately controlled type 2 diabetes on metformin.	Internal study report  <i>Diabetes, Obesity and Metabolism</i> 2014; 16(2): 159-169. <i>Diabetologia</i> 2012; 55: S308.  <i>Journal of Clinical Endocrinology and Metabolism</i> 2012; 97(3): 1020-1031. <i>Diabetes, Obesity and Metabolism</i> 2014; Epublication ahead of print <i>Diabetes</i> 2013; 62: A667-A668. <i>Diabetologia</i> 2012; 55: S320. <i>Diabetes, Obesity and Metabolism</i> 2012; 14(11): 990-999. <i>Diabetologia</i> 2012; 55: S306-S307.
CT-003	A 16-week, Multicentre, Randomised, Double-Blind, Placebo-Controlled Phase III Study to Evaluate the Safety and Efficacy of Dapagliflozin 2.5 mg BID, 5 mg BID and 10 mg QD Versus Placebo in Patients with Type 2 Diabetes Who Are Inadequately Controlled on Metformin-IR Monotherapy. Clinicaltrials.gov ID NCT01217892	Internal study report

**Key features of the included evidence**

Trial	N	Design/ duration	Risk of bias	Patient population	Outcome(s)
<b>Dapagliflozin/metformin XR FDC vs individual components</b>					
CT-092	36	BE Up to 7 days	Low	Healthy adults	PK
CT-100	36	BE Up to 7 days	Low	Healthy adults	PK
CT-125	72	BE 10 days	Low	Healthy adults	PK
<b>Dapagliflozin 10mg + metformin vs placebo + metformin</b>					
CT-014	272 <sup>a</sup>	R, DB 24 wks, 102 wks	Low	Type 2 diabetes not controlled on metformin alone	Mean change in HbA1c; responder rate

<sup>a</sup> dapagliflozin 10mg + metformin and placebo + metformin arms only.

Abbreviations: BE, bioequivalence; DB, double blind; PK, pharmacokinetic measures; R, randomised.

Source: compiled during the evaluation

*For PBAC's view, see section 7 "PBAC outcome"*

### **Comparative effectiveness**

- 6.5 The PBAC noted that the TGA delegate concluded that bioequivalence has been established, with the fixed dose combinations in Trials CT-092, CT-100 and CT-125 meeting the pre-specified bioequivalence margins against the individual components.

*For more detail on PBAC's view, see section 7 "PBAC outcome"*

### **Comparative harms**

- 6.6 The submission claimed that the safety profile of the FDC is consistent with that of the individual components. No deaths or serious adverse events were reported in any of the three bioequivalence trials.

*For PBAC's view, see section 7 "PBAC outcome"*

### **Clinical claim**

- 6.7 The submission described dapagliflozin/metformin XR FDC as bioequivalent to the individual components administered concomitantly. The submission makes no claims with regard to comparative safety. The PBAC noted that the claim of bioequivalence has been accepted by the TGA.
- 6.8 The PBAC considered that a conclusion of comparative effectiveness was reasonable.
- 6.9 The PBAC considered that a conclusion of non-inferior comparative safety was reasonable.

### **Economic analysis**

- 6.10 Based on the results of the three bioequivalence trials, the submission claimed that dapagliflozin/metformin XR FDC is equivalent on a milligram per milligram basis to corresponding doses of the individual components. The submission noted that metformin XR and metformin IR are considered therapeutically equivalent on a milligram per milligram basis and thus dapagliflozin/metformin XR FDC is also equivalent to corresponding doses of concomitant dapagliflozin and metformin IR. Equi-effective doses are:
- Dapagliflozin/metformin XR FDC 10mg/500mg and dapagliflozin 10mg with

- metformin XR 500mg (or metformin IR 500mg);
- Dapagliflozin/metformin XR FDC 10mg/1000mg and dapagliflozin 10mg with metformin XR 1000mg (or metformin IR 1000mg);
- Dapagliflozin/metformin XR FDC 2 x 5mg/1000mg and dapagliflozin 10mg with 2 x metformin XR 1000mg (or 2 x metformin IR 1000mg).

The ESC advised that this is reasonable.

- 6.11 The submission priced dapagliflozin and metformin FDC based on the component products. The submission recognised that the FDC will not only replace the individual components, dapagliflozin and metformin XR, it may also replace metformin IR formulations. Because of the price difference between the single-agent metformin IR and metformin XR formulations, the submission proposed a weighted price for the metformin component based on the utilisation of metformin XR and IR (XR:IR ratio of 52:48 and 32:68 for the 500 mg and 1000 mg strengths, respectively). The Pre-Sub-Committee Response (PSCR, p2) and the pre-PBAC response argue that this is justified because weighted prices are often used for ‘monocomponent’ products.
- 6.12 The ESC noted that the prices for dapagliflozin/metformin XR FDC proposed by the submission are higher than the prices that would result from pricing the metformin component based on the IR formulation only (refer to table below).

**Dapagliflozin/metformin XR FDC price using metformin IR costs only**

Product	Pricing based on weighted price of metformin (XR & IR)		Pricing based on IR metformin		Difference in DPMQ compared to pricing proposed in the submission
	Ex-man metformin component price (weighted between XR & IR)	DPMQ	Ex-man price of metformin component (IR only)	DPMQ	
Dapagliflozin/metformin XR 10mg/500mg FDC	\$1.12	\$91.59	\$0.8848	\$91.3184	\$0.27
Dapagliflozin/metformin XR 10mg/1000mg FDC	\$1.96	\$92.60	\$1.7696	\$92.3649	\$0.24
Dapagliflozin/metformin XR 5mg/1000mg FDC	\$3.92	\$94.91	\$3.4284	\$94.3268	\$0.58

Note: the dapagliflozin/metformin XR 5mg/1000mg FDC is dosed as two tablets twice daily which corresponds to a daily dose of 10mg of dapagliflozin and 2000mg of metformin XR

Abbreviations: DPMQ, dispensed price per maximum quantity; ex-man, ex-manufacturer; FDC, fixed dose combination; IR, immediate release; XR, extended release

Source: compiled during the evaluation

- 6.13 The ESC further noted that the PBAC has previously considered FDCs containing metformin XR and FDCs containing metformin IR to be interchangeable. In its consideration of FDCs of metformin XR with saxagliptin and sitagliptin in November 2013, the PBAC recommended that the ex-manufacturer price of the metformin XR component should be equivalent to the ex-manufacturer price of the corresponding amount of IR in other gliptin/metformin FDCs. (November 2013 Public Summary Documents, Metformin XR + Saxagliptin, Metformin XR + Sitagliptin). A consistent pricing approach would be appropriate for dapagliflozin/metformin XR FDC.
- 6.14 The ESC noted that there may be incremental benefits of metformin XR compared to the metformin IR formulation, such as potentially higher tolerability or a perceived compliance advantage. However, evidence to support superiority of the XR formulation and a valuation of any potential benefits was not provided in the submission.
- 6.15 The PBAC noted that it could only recommend listing the dapagliflozin/metformin XR FDC at a higher price than the alternative therapy or therapies if it is satisfied that the



- 6.19 The ESC considered these risks could be mitigated through a risk share arrangement that reflects estimated utilisation based on the current treatment algorithm for type 2 diabetes agents.
- 6.20 The PBAC agreed that if listing proceeded with the second-line listing and lower price, there would no longer be a need for a risk share arrangement to mitigate the risk of usage outside the third-line setting
- 6.21 The evaluation noted that the availability of an FDC containing dapagliflozin may reduce the market share for canagliflozin, given there is no FDC currently available that includes canagliflozin. The ESC agreed that there may be some substitution between concomitant canagliflozin plus metformin and dapagliflozin/metformin XR FDC. The PSCR (p1) claimed that if such substitution were to occur it would not represent a clinical or financial issue. The difference in price between canagliflozin and dapagliflozin relates to the cost of management of adverse events.
- 6.22 The PBAC noted that, at the lower price offered for dapagliflozin in the pre-PBAC response, any substitution of dapagliflozin for canagliflozin would be cost-saving to the PBS/RPBS.

*For PBAC's view, see section 7 "PBAC outcome"*

## **7 PBAC Outcome**

- 7.1 The PBAC recommended an Authority required (STREAMLINED) listing of dapagliflozin/metformin XR FDC for the treatment of Type II diabetes. The equi-effective doses of dapagliflozin/metformin XR FDC are the corresponding doses of dapagliflozin and metformin IR.
- 7.2 The PBAC acknowledged that the TGA has accepted the bioequivalence of dapagliflozin/metformin XR to dapagliflozin and metformin.
- 7.3 The PBAC recommended, as proposed by the sponsor in its pre-PBAC response, that the PBS restrictions for dapagliflozin and dapagliflozin/metformin XR be aligned with the dipeptidyl peptidase-4 inhibitors (gliptins). In making this recommendation the PBAC recalled that it had previously concluded dapagliflozin to be non-inferior to sitagliptin in terms of comparative effectiveness, but to be associated with higher rates of genital mycotic infections and osmotic diuresis associated events compared with sitagliptin. The PBAC considered that with such an alignment of restrictions that dapagliflozin and dapagliflozin/metformin XR would be cost effective if their prices were also aligned with the gliptins and gliptin/metformin FDC respectively, but noting the dapagliflozin price would require adjustment to take into account the current cost offset for adverse events.
- 7.4 For the reasons provided in Section 6, the PBAC considered that the price of the metformin component should be based on metformin IR.
- 7.5 For the reasons provided in Section 6, the PBAC considered that a RSA was not required for dapagliflozin and dapagliflozin/metformin XR if listed with a second-line restriction and price.

- 7.6 The PBAC advised that dapagliflozin/metformin XR FDC is suitable for prescribing by nurse practitioners for continuing therapy only where a patient has been initiated by a medical practitioner.
- 7.7 The PBAC recommended that the Safety Net 20 Day Rule should apply.

**Outcome:**  
Recommended

## 8 Recommended listing

8.1 Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Manufacturer	Name and
DAPAGLIFLOZIN/METFORMIN Dapagliflozin 10 mg/metformin XR 500 mg	28	5	Xigduo XR	AP
Dapagliflozin 10 mg/metformin XR 1000 mg	28	5		
Dapagliflozin 5 mg/metformin XR 1000mg	56	5		

<b>Condition/Indication:</b>	Diabetes mellitus type 2
<b>Restriction:</b>	Authority required ( <i>STREAMLINED</i> )
<b>Clinical criteria</b>	<p>Patient must have, or have had, a HbA1c measurement greater than 7% despite treatment with metformin; OR</p> <p>Patient must have, or have had, where HbA1c measurement is clinically inappropriate, blood glucose levels greater than 10 mmol per L in more than 20% of tests over a 2 week period despite treatment with metformin.</p>

<b>Prescriber Instructions</b>	<p>The date and level of the qualifying HbA1c measurement must be, or must have been, documented in the patient's medical records at the time treatment with a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone), a glucagon-like peptide-1 or a sodium-glucose co-transporter 2 (SGLT2) inhibitor is initiated.</p> <p>The HbA1c must be no more than 4 months old at the time treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor was initiated.</p> <p>Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances:</p>
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	<p>(a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or</p> <p>(b) Had red cell transfusion within the previous 3 months</p> <p>The result of the blood glucose monitoring, which must be no more than 4 months old at the time of initiation of treatment with a gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor, must be documented in the patient's medical records.</p> <p>A patient whose diabetes was previously demonstrated unable to be controlled with metformin does not need to requalify on this criterion before being eligible for PBS-subsidised treatment with this fixed dose combination.</p>
<b>Administrative advice</b>	<p>This fixed dose combination is not PBS-subsidised for use in combination with a sulfonylurea (triple oral therapy), as initial therapy or in combination with an insulin, a thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin) or a glucagon-like peptide-1.</p>

<b>Condition/Indication:</b>	Diabetes mellitus type 2
<b>Treatment Phase</b>	Continuing
<b>Restriction:</b>	Authority required ( <i>STREAMLINED</i> )
<b>Clinical criteria:</b>	Patient must have previously received and been stabilised on a PBS-subsidised regimen of oral diabetic medicines which includes metformin and dapagliflozin.
<b>Administrative Advice</b>	<p><b>Note:</b>  <b>Continuing Therapy Only:</b>                      For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p> <p>This fixed dose combination is not PBS-subsidised for use in combination with a sulfonylurea (triple oral therapy), as initial therapy or in combination with an insulin, thiazolidinedione (glitazone), a dipeptidyl peptidase 4 inhibitor (gliptin) or a glucagon-like peptide-1.</p>

## 9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

## 10 Sponsor's Comment

The sponsor had no comment.