PUBLIC SUMMARY DOCUMENT

Product: Metformin and Saxagliptin, tablet, 1,000mg/2.5mg, 1,000mg/5mg, 500mg/5mg, Kombiglyze® XR
Sponsor: Bristol-Myers Squibb Australia
Date of PBAC Consideration: November 2013

1. Purpose of Application

The submission requested an Authority required (STREAMLINED) listing for treatment of type 2 diabetes mellitus (T2DM) in a patient whose HbA1c is greater than 7% prior to initiation of a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone) or a glucagon-like peptide-1 despite treatment with metformin and where a combination of metformin and a sulfonylurea is contraindicated or not tolerated.

This application was made under the TGA/PBAC parallel process. Subsequently, this product was included on the Australian Register of Therapeutic Goods in October 2013, prior to PBAC consisderation.

2. Background

The PBAC recommended the PBS listing of metformin immediate release (IR)/saxagliptin fixed dose combination (FDC) at its April 2013 special meeting as an Authority Required (STREAMLINED) benefit in patients whose HbA1c is greater than 7% prior to initiation of a gliptin, glitazone, or a glucagon-like peptide-1 despite treatment with metformin (i.e., without the requirement for patients to be contraindicated or intolerant of sulfonylureas). Listing was recommended at a lower price and with a different restriction than the currently PBS subsidised metformin/gliptin FDCs to take into account the likely proportion of non-cost-effective use of the gliptins as identified by the Drug Utilisation Sub-Committee (DUSC) Analysis of Medicines for Type 2 Diabetes (see also PBAC Recommendation and Reasons).

3. Registration Status

Metformin extended release (XR)/saxagliptin FDC was TGA registered on 10 October 2013 and is indicated as an adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate.

4. Listing Requested and PBAC's View

Authority required (STREAMLINED)
Type 2 diabetes.

Patient must have an HbA1c greater than 7% prior to initiation of a dipeptidyl peptidase 4 inhibitor (gliptin), a thiazolidinedione (glitazone) or a glucagon-like peptide-1 despite treatment with metformin; OR

The patient must show blood glucose levels greater than 10mmol per L in more than 20% of blood glucose monitoring tests over a 2 week period in circumstances where assessment of HbA1c is not appropriate.

The patient must be unable to use metformin in combination with a sulfonylurea due to a contraindication or intolerance.

The date and level of the qualifying HbA1c must be documented in the patient's medical records at the time treatment with a gliptin, glitazone or glucagon-like peptide-1 is initiated. The HbA1c must be no more than 4 months old at the time treatment with a gliptin, glitazone, or glucagon-like peptide-1 is initiated.

Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances:

a) Clinical conditions with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or
b) Red cell transfusion within the previous 3 months.

The results of this blood glucose monitoring, which must be no more than 4 months old at the time of initiation of treatment with a gliptin, glitazone, or glucagon-like peptide-1, must be documented in the patient's medical records.

Continuing treatment

The patient must have previously received and been stabilised on a PBS-subsidised regimen or oral diabetic medicines which includes metformin and saxagliptin.

Administrative advice

Saxagliptin with metformin XR in fixed dose combination is not PBS-subsidised for use as initial combination therapy or in combination with a sulfonylurea (triple oral therapy), combination with a thiazolidinedione (glitazone), combination with a glucagon-like peptide-1 or combination with insulin.

The requested prices were based on the June 2013 PBS Schedule and did not include the 1 August 2013 price reductions for all metformin forms.

The requested ex-manufacturer prices were based on the sum of the PBS ex-manufacturer prices of the components in the fixed dose combination (FDC). For PBAC's view of this approach, see Recommendation and Reasons.

5. Clinical Place for the Proposed Therapy

Metformin XR/saxagliptin FDC will provide a treatment alternative for patients with T2DM with inadequate glycaemic control despite treatment with metformin alone, or patients with T2DM currently treated with concurrent metformin XR and saxagliptin (or other DPP4 inhibitors) in dual oral therapy.

The submission acknowledged that metformin IR/saxagliptin FDC (500mg/2.5mg; 850mg/2.5mg; 1000mg/2.5mg) was recommended for listing at the April 2013 PBAC Special

Meeting, but stated that should metformin XR/saxagliptin FDC receive a positive recommendation, the metformin IR/saxagliptin FDC product will not be marketed in Australia.

6. Comparator

The submission nominated the corresponding doses of the individual components of metformin XR and saxagliptin as the appropriate comparator, on the basis that these are the therapies most likely to be substituted in practice. The PBAC considered that this FDC would also replace other metformin/gliptin FDCs and that these other FDCs were also appropriate comparators.

7. Clinical Trials

The submission was based on three bioequivalence studies (Studies 111, 112 and 004) comparing metformin XR/saxagliptin FDC with its constituent agents, and one supportive randomised controlled trial (Trial 086) comparing saxagliptin + concomitant metformin XR 1,500mg to metformin XR 2000mg (administered as metformin XR 500mg + concomitant metformin XR 1,500mg). Details of the trials are presented in the table below.

Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Bioequivalence studies		
Study 111	Bioequivalence study of the fixed-dose combination of 5mg saxagliptin and 500mg metformin XR tablet (manufactured in Mt Vernon, IN) relative to 5mg saxagliptin tablet and 500mg metformin XR tablet (manufactured in Evansville, IN) coadministered to healthy subjects in a fed condition.	11 October 2010.
Study 112	Bioequivalence study of the fixed-dose combination of 5mg saxagliptin/1000mg metformin XR (manufactured in Mt Vernon, IN) relative to 5mg of Onglyza and 2 × 500mg Glucophage XR coadministered to healthy subjects in the fed state and steady-state pharmacokinetic assessment of the fixed-dose combination of 5mg saxagliptin/1000mg metformin XR.	11 October 2010.
Study 004	Bioequivalence study of the fixed-dose combination of metformin XR/saxagliptin tablets relative to saxagliptin (Onglyza™) tablets and Australia sourced Diabex® XR tablets coadministered to healthy subjects in the fed state during steady-state administration.	12 May 2012.
Supplementary trial		
Trial 086	An 18-week, multicenter, randomized, double-blind phase 3b trial to evaluate the efficacy and safety of saxagliptin in combination with extended release metformin, 1500mg versus metformin uptitrated to 2000mg in subjects with type 2 diabetes who have inadequate glycaemic control after diet and exercise and a stable dose of metformin XR 1500mg. Fonseca, V., T. Zhu, et al. (2011). Adding saxagliptin (SAXA) 5 mg is superior to uptitrating metformin extended release (MET XR) in type 2 diabetes mellitus (T2DM)	*Diabetes 60: A279.*

	patients with inadequate glycaemic control on a stable dose of MET XR 1500mg.	

8. Results of Trials

With regard to comparative effectiveness. the geometric mean ratios (FDC/components) and 90% confidence intervals for the pairwise pharmacokinetic outcomes (AUC, Cmax) of metformin XR and saxagliptin were within the pre-specified bounds of 0.80 - 1.25 in Studies 111 and 112.

The geometric mean ratios (FDC/components) and 90% confidence intervals for the pairwise pharmacokinetic outcomes AUC and Cmax (at steady state) in Study 004 were generally within the pre-specified bounds of 0.8 - 1.25. However, the saxagliptin Cmax.ss upper confidence interval exceeded the pre-specified bounds for both the metformin XR/saxagliptin 500mg/5mg and 1000mg/5mg combinations.

The supportive Trial 086 showed that saxagliptin 5mg in addition to metformin XR 1500mg resulted in statistically significantly larger reductions in HbA1c from baseline compared to metformin XR 2000mg (mean difference in change from baseline HbA1c -0.52, 96% CI [-0.73, -0.31]).

The PBAC noted that the TGA had completed its evaluation of the bioequivalence data for the metformin XR/saxaglitpin FDC and that the FDC was registered.

With regard to comparative harms, the submission suggested that the listing of a metformin XR/saxagliptin FDC will not expose Australian patients with T2DM to any additional harms over those already identified for metformin XR and saxagliptin in dual therapy, and previously considered by the PBAC.

The proportions of patients reporting one or more adverse events were small, and vary within and across the bioequivalence studies, consistent with the short study duration and small sample sizes. The most frequently reported adverse events (in ≥2% of any treatment group) in all studies were mild, and included headache, nasopharyngitis, gastrointestinal disorders (e.g. diarrhoea), back pain and pain in the extremities, anaemia, rash and proteinuria. No additional data were presented on potential safety concerns beyond those identified in the trials.

Patient relevant outcome study

The PBAC noted the advice from its Economic Sub-Committee (ESC) that the only outcome data that had previously been presented for gliptins has been based on surrogate endpoints (in particular HbA1c), and agreed that patient relevant outcomes would be more informative.

The PBAC further noted that a recent study of the cardiovascular safety of saxagliptin found that saxagliptin did not increase or decrease the rate of ischaemic events, though the rate of hospitalisation for heart failure was increased. Patients enrolled in the trial had a history of, or were at risk for, cardiovascular events. The comparator was a variety of other antiglycaemic therapy (excluding DPP-4 inhibitors or GLP-1) and changes in therapy were

permitted in the control group (most frequently titration of insulin dose) to maintain appropriate HbA1c levels. Even given this, the proportions of patients achieving appropriate HbA1c (<7%) was higher in saxagliptin patients (35%) compared to placebo (28%). (Scirica, B et al. Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes mellitus. N Engl J Med 2013;369:1317-26). A summary of benefits/harms based on Scirica et al is presented in the table below. The PBAC requested it be provided with updates relating to the cardiovascular safety of saxagliptin as they become available.

Benefit/harms summary based on Scirica et al (SAVOR-TIMI)

Outcome[1]	Number of participants (studies)	Relative effect from trial(s)	Control event rate per 100 patients over trial duration (2 years)	Intervention event rate per 100 patients over trial duration (2 years)	Increment
Efficacy and safety					
Composite of cardiovascular death, myocardial infarction or ischaemic stroke[a]	16,492 (1)	HR: 1.00 (0.89-1.12)	3.71	3.70	NS
Cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, heart failure, or coronary revascularization	16,492 (1)	HR: 1.02 (0.94-1.11)	6.30	6.39	NS
Death from any cause	16,492 (1)	HR: 1.11 (0.96-1.27)	2.30	2.54	NS
Death from cardiovascular causes	16,492 (1)	HR: 1.03 (0.87-1.22)	1.58	1.62	NS
Hospitalisation from heart failure	16,492 (1)	HR: 1.27 (1.07-1.51)	1.39	1.75	0.36

[1] SAVOR-TIMI 54. Scirica, B et al. N Engl J Med 2013;369:1317-26
NS = Not significant

In addition the PBAC noted that an increase in the rate of pancreatitis, albeit non-significant, had been observed in clinical trials with alogliptin and saxagliptin. The PBAC considered this an important safety signal which requires ongoing monitoring and review.

9. Clinical Claim

The submission described metformin XR/saxagliptin FDC 500mg/5mg, 1000mg/5mg and 1000mg/2.5mg as similar in efficacy and safety to the co-administration of the same doses of the individual components.

The PBAC considered this claim reasonable, but noted that a comparison with other metformin/gliptin FDCs was also appropriate and that no evidence was provided that this FDC is associated with an improvement in efficacy or a reduction in toxicity compared to other metformin/gliptin FDCs.

The PBAC noted that the sponsor's Pre Sub Committee Response (PSCR) stated, 'the sponsor believes that the FDC containing saxagliptin and XR metformin should not be considered interchangeable with FDCs containing other gliptins and metformin'. The reasons outlined in the PSCR were:

- because the transition between XR and IR metformin forms requires specific management, particularly in circumstances where renal function may be compromised; and
- in patients already using an IR form of metformin, and FDC containing IR metformin would be 'a clear choice' for transition.

For PBAC's view, see Recommendation and Reasons.

10. Economic Analysis

The submission presented a cost-minimisation analysis of metformin XR/saxagliptin FDC compared to its component products (metformin XR and saxagliptin) taken concomitantly.

The equi-effective doses based on the total daily dose of the metformin XR/saxagliptin FDCs and the equivalent strengths of metformin XR and saxagliptin component products were estimated as:

- Metformin XR/saxagliptin FDC 500mg/5mg = metformin XR 500mg + saxagliptin 5mg;
- Metformin XR/saxagliptin FDC 1000mg/5mg = metformin XR 1000mg + saxagliptin 5mg; and
- Metformin XR/saxagliptin FDC 1000mg/2.5mg (BD) = metformin XR 1000mg ×2 + saxagliptin 5mg.

For the reasons outlined in the Recommendation and Reasons below, the PBAC considered that the cost-effectiveness of the metformin XR/saxagliptin FDC would be acceptable if it were cost-minimised against the alogliptin/metformin FDC. The equi-effective doses were considered to be 5 mg of saxagliptin is equivalent to 25 mg of alogliptin and to 100 mg of sitagliptin. The PBAC further considered that the ex-manufacturer price of the metformin XR component should be equivalent to the ex-manufacturer price of the corresponding amount of metformin IR in the other gliptin/metformin FDCs.

11. Estimated PBS Usage and Financial Implications

The submission estimated the likely number of patients treated with the metformin XR/saxagliptin FDC to be between 50,000 – 100,000 in Year 5, and a total of between 100,000 and 200,000 patients in the first 5 years of listing. The estimate of patient numbers was based on estimated script numbers assuming 13 scripts per year/patient.

The submission estimated the likely number of prescriptions with the listing of metformin XR/saxagliptin FDC was greater than 200,000 in Year 5, and a total of less than 10 million scripts over the first 5 years of listing.

The submission used a market share approach relying on pharmacy claim data collected by Medicare Australia to establish the number of scripts for all gliptins in dual oral therapy with metformin and gliptin/metformin FDCs.

The submission assumed that the current rapid market growth observed in the data for gliptin + metformin dual oral therapy market (38% per annum) and the gliptin/metformin FDC market (40% per annum) was not sustainable, and will plateau at approximately 20% per annum by Year 4. Uptake of metformin XR/saxagliptin FDC from each market was estimated separately.

The PBAC recalled that in its April 2013 consideration of the DUSC Analysis of Medicines for Type 2 Diabetes, it had noted that the use of gliptin FDC products substantially exceeds the expected utilisation. The PBAC considered that the listing of the metformin/saxagliptin FDC as recommended would not be expected to increase the rate of growth of the metformin/gliptin FDCs but rather take a share of the existing metformin/gliptin FDC market. Thus, any financial impact would be limited and result from substitution of gliptin FDCs in packs containing 28 days of supply with those containing 30 days of supply and vice versa.

12. Recommendation and Reasons

The PBAC considered the sponsor's submission, the Commentary and ESC advice for the submission and the sponsor's responses to the Commentary and ESC advice.

The PBAC recommended the fixed dose combination (FDC) metformin XR/saxagliptin for listing on the PBS for the treatment of Type 2 diabetes in a patient whose HbA1c is greater than 7% despite treatment with metformin. For the reasons outlined below, the PBAC considered that the cost-effectiveness of the metformin XR/saxagliptin FDC would be acceptable if it were cost-minimised against the alogliptin/metformin FDC. The equi-effective doses of the gliptin component were considered to be 5 mg of saxagliptin is equivalent to 25 mg of alogliptin and to 100 mg of sitagliptin. The ex-manufacturer price of the metformin XR component should be equivalent to the ex-manufacturer price of the corresponding amount of metformin IR in the other gliptin/metformin FDCs.

In making this recommendation, the PBAC agreed that the appropriate comparators were the individual components, metformin and saxaglipin as well as other metformin/gliptin FDCs.

The PBAC also recalled its April 2013 consideration of the DUSC Analysis of Medicines for Type 2 Diabetes. At that time, the PBAC *"noted that 46.7% of patients initiated on a regimen containing a gliptin+metformin FDC had been supplied only metformin as pre-initiation treatment. The PBAC considered whether it could estimate the likely true frequency of patients who are intolerant to sulfonylureas, or in whom the class of drugs is contraindicated. No precise estimates were identified in the review, and the product information documents for existing sulfonylureas include only general warning statements without quantification. The PBAC considered that 'intolerance' to sulfonylurea is being interpreted more liberally in practice than was anticipated. While noting prescriber concerns about risk of hypoglycaemia particularly in the elderly with some sulfonylureas the PBAC considered that the true rate of contraindication or intolerance would be very small, less than 5% of the patient population. The PBAC considered that the majority of the 46.7% were probably supplied gliptin+metformin FDCs under circumstances that were non-compliant with PBS criteria. Again, the PBAC noted that the cost-effectiveness of this treatment*

regimen (i.e. dual therapy as an alternative to sulfonylureas in a population WITHOUT contraindications) has not been established."

The PBAC further recalled that it had recommended FDCs of metformin/linagliptin and metformin/saxagliptin immediate release at its April 2013 meeting and the single ingredient drug, alogliptin, at its July 2013 meeting. The listings of these two FDCs and alogliptin were recommended at a lower price and with a different restriction than the currently PBS subsidised gliptin FDCs or single agents to take into account the likely proportion of non-cost-effective use of the gliptins as identified by the DUSC analysis.

The PBAC also noted that the Department's advice at the meeting that the Minister (through his Delegate) intends to declare alogliptin as a pharmaceutical benefit under section 85(2) of the *National Health Act 1953* (the Act) and that the PBS listing will proceed with a price and restriction consistent with the PBAC recommendation of July 2013.

As the PBAC considered that saxagliptin offers no improvement in efficacy or reduction in toxicity over alogliptin, and noting that saxagliptin may be associated with increased cardiac failure hospitalisations, the PBAC considered it is therefore appropriate for the subsidy price for the saxagliptin component of the FDC, to be cost minimised against alogliptin.

The PBAC also requested it be provided with updates relating to the cardiovascular safety of saxagliptin as they become available.

With respect to the price of the metformin component of the FDC, the PBAC acknowledged that the sponsor had followed the sum of components method suggested in the PBAC Guidelines, but noted that the Guidelines acknowledge this is not the only method for pricing FDCs. The PBAC considered that a price for the metformin component that is equal to the corresponding amount of metformin IR in the other gliptin/metformin FDCs would be consistent with its recommendation for the metformin XR/sitagliptin FDC. Additionally this approach to pricing the metformin XR component is appropriate in the absence of any evidence that this FDC is associated with an improvement in efficacy or a reduction in toxicity compared to other FDCs of a gliptin and metformin.

The PBAC re-confirmed its April 2013 recommendation that an amended listing with removal of the requirement for patients to be contraindicated or intolerant of sulfonylureas was appropriate for this FDC and would also be appropriate for single ingredient saxagliptin benefits, should a new lower price be agreed.

The PBAC considered the proliferation of metformin/gliptin FDCs and range of doses of both the gliptin and metformin components available creates the potential for prescriber and patient confusion. The Committee noted the sponsor's advice that it does not intend to pursue the PBS listing of its metformin immediate release/saxagliptin FDC (recommended by PBAC in April 2013) in the event PBAC recommends the metformin XR/saxagliptin FDC for subsidy, and agreed this approach goes some way to addressing this concern, particularly with respect to FDCs containing saxagliptin. However, the Committee remained concerned with the potential for Quality Use of Medicines issues arising from number and variety of gliptin FDCs that will likely be available through the PBS in the future.

The PBAC recalled that in its April 2013 consideration of the DUSC Analysis of Medicines for Type 2 Diabetes, it had noted that the use of gliptin FDC products substantially exceeds the expected utilisation. The PBAC considered that the listing of the metformin/saxagliptin FDC as recommended would not be expected to increase the rate of growth of the metformin/gliptin FDCs but rather take a share of the existing metformin/gliptin FDC market. Thus, any financial impact would be limited and result from substitution of gliptin FDCs in packs containing 28 days of supply with those containing 30 days of supply and vice versa.

The PBAC re-confirmed its earlier recommendation that the metformin/saxagliptin FDC is suitable for inclusion in the list of PBS medicines for prescribing by nurse practitioners within collaborative arrangements.

The PBAC advised the Minister that under Section 101(3BA) of the National Health Act, saxagliptin with metformin fixed dose combination should be treated as interchangeable on an individual patient basis with:

i) alogliptin with metformin fixed dose combination; and
ii) linagliptin with metformin fixed dose combination; and
iii) vildagliptin with metformin fixed dose combination; and
iv) sitagliptin with metformin fixed dose combination.

In providing this advice the PBAC noted that in the 2011 AstraZeneca case ([2011] FCA 487) the court said (at [19]):

Contrary to the submissions of the applicant in the present case, neither the PBAC nor the Minister was obliged, in my view, to consider whether particular doses of rosuvastatin or atorvastatin were interchangeable on an individual patient basis. An assessment of interchangeability, where necessary, must consider the interchangeability of drugs, not particular doses of drugs or of individual pharmaceutical items. … it was open to the PBAC to recommend the exclusion of a particular dose of a particular drug from a therapeutic group by way of specifying the circumstances in which a listed drug is, or is not, in a therapeutic group.

The PBAC considered that a gliptin and metformin FDC was the same drug, for the purposes of considerations of interchangeability, regardless of whether the metformin component was immediate release or extended release. If that were not the case, while the PBAC acknowledged that for the metformin/gliptin FDCs there are differences in the release properties of the pharmaceutical items that contain metformin extended release (XR) versus those containing metformin immediate release (IR), it considered that there is no evidence of a difference in therapeutic outcomes, at comparable doses, between these different forms. And so the PBAC would still consider them to be interchangeable with one another on an individual patient basis if they were different drugs.

Outcome:

Recommended

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
METFORMIN HYDROCHLORIDE EXTENDED RELEASE/SAXAGLIPTIN Tablet, 500mg/5mg	28	5	Kombiglyze XR	Bristol Myers Squibb

METFORMIN HYDROCHLORIDE EXTENDED RELEASE/SAXAGLIPTIN 1000mg/5mg	28	5
METFORMIN HYDROCHLORIDE EXTENDED RELEASE/SAXAGLIPTIN 1000mg/2.5mg	56	5

Condition/Indication:	Diabetes mellitus type 2
Restriction:	Authority required (STREAMLINED)
Clinical criteria:	Patient must have, or have had, a HbA1c measurement greater than 7% despite treatment with metformin; OR 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.
Prescriber Instructions	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 gliptin, a glitazone, a glucagon-like peptide-1 or an SGLT2 inhibitor is initiated. 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. Blood glucose monitoring may be used as an alternative assessment to HbA1c levels in the following circumstances: (a) A clinical condition with reduced red blood cell survival, including haemolytic anaemias and haemoglobinopathies; and/or (b) Had red cell transfusion within the previous 3 months. The results 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 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.
Administrative Advice	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 a thiazolidinedione (glitazone), a glucagon-like peptide-1 or an SGLT2 inhibitor.

Condition/Indication:	Diabetes mellitus type 2
Treatment Phase	Continuing
Restriction:	Authority required (STREAMLINED)
Clinical criteria:	Patient must have previously received and been stabilised on a PBS-subsidised regimen of oral diabetic medicines which includes metformin and saxagliptin

Administrative Advice	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 a thiazolidinedione (glitazone), a glucagon-like peptide-1 or an SGLT2 inhibitor.

13. 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.

14. Sponsor's Comment

The sponsor had no comment.