PUBLIC SUMMARY DOCUMENT

Product: Saxagliptin with Metformin, tablet, 2.5 mg/500 mg, 2.5 mg/850 mg and 2.5 mg/1000 mg, Kombiglyze®
Sponsor: Bristol-Myers Squibb Australia Pty Ltd and AstraZeneca Pty Ltd
Date of PBAC Consideration: March 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 gliptin, 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.

2. Background

The PBAC had not previously considered this product. Saxagliptin tablets and metformin tablets are both currently TGA registered and PBS listed.

3. Registration Status

The submission was considered under the TGA/PBAC parallel process. At the time of PBAC consideration, the Clinical Evaluation Report and TGA Delegate's overview were available.

Kombiglyze was registered by the TGA on 13 May 2013.

4. Listing Requested and PBAC's View

Authority required (STREAMLINED)
Type 2 diabetes 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.

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

A patient in these circumstances will be eligible for treatment where blood glucose monitoring over a 2 week period shows blood glucose levels greater than 10 mmol per L in more than 20% of tests. 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, a glitazone or a glucagon-like peptide-1, must be documented in the patient's medical records.

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

For PBAC's view, see Recommendations and Reasons.

5. Clinical Place for the Proposed Therapy

Saxagliptin/metformin FDC will provide a treatment alternative to concurrent use of saxagliptin and metformin for T2DM patients with inadequate glycaemic control despite using metformin alone. There are currently three other FDCs involving a dipeptidyl peptidase-4 (DPP-4) inhibitor or a thiazolidinedione in combination with metformin for the treatment of T2DM listed on the PBS:

- rosiglitazone/metformin FDC,
- sitagliptin/metformin FDC, and
- vildagliptin/metformin FDC.

The submission proposed that saxagliptin with metformin would be used as third line treatment. The algorithm indicated that first line pharmacological therapy is metformin or a sulfonylurea. If glycaemic control was not achieved, dual combination therapy should be considered, including metformin+sulfonylurea, metformin/sulfonylurea with either a DPP4-inhibitor, a thiazolidinedione, arcabose, GLP1 agonist, or insulin.

The submission claimed that listing the saxagliptin/metformin FDC on the PBS will not change the current treatment algorithm, as saxagliptin/metformin FDC will be prescribed to patients who would otherwise be prescribed saxagliptin and metformin as separate tablets.

6. Comparator

The submission nominated the individual components, saxagliptin 5 mg and metformin 500 mg, 850 mg and 1000 mg, as the appropriate main comparator. The PBAC accepted this as the appropriate comparator.

For PBAC's view, see Recommendation and Reasons.

7. Clinical Trials

The submission presented four unpublished bioequivalence trials (Studies 081, 092, 120 and 152) in healthy subjects and one unpublished head-to-head randomised controlled trial (RCT) (Study 080) comparing saxagliptin 2.5mg BID in combination with metformin to metformin alone in patients with T2DM.

Details of the studies are presented in the table below.

Course of treatment in clinical trials and economic evaluation

		Drug 1	Drug 2	Subjects
Bioequivalence data	Study 081	Saxagliptin/metformin FDC 2.5 mg/500 mg BID	Saxagliptin 2.5mg BID + metformin 500 mg BID	24 healthy subjects
	Study 092	Saxagliptin/metformin FDC 2.5mg/1000mg BID	Saxagliptin 2.5 mg BID + metformin 1000 mg BID	24 healthy subjects
	Study 120	Diabex metformin (500 mg, 1000mg)	Glucophage metformin (500 mg, 1000 mg)	28 healthy subjects
	Study 152	Saxagliptin 2.5 mg BID	Saxagliptin 5 mg QD	16 healthy subjects

Efficacy and safety data	Study 080	Saxagliptin 2.5 mg BID + metformin BID (1500-3000 mg/day)	Placebo + metformin BID (1500-3000 mg/ day)	160 patients with T2DM

BID: twice daily, QD: once daily.
Source: Compiled during evaluation

The four bioequivalence trials were open-label, cross-over randomised controlled trials (RCTs) with washout periods between treatment arms. The trials were analysed on the basis of treated patients (had received a dose during the treatment period), but this also corresponded with the ITT population in two trials (Study 081 and 152). No adjustments were made for missing data. The efficacy trial was a double-blind, multi-centre RCT. The trial was analysed on an "all randomised patients who took at least 1 dose" basis. Last observation carried forward (LOCF) was used to adjust for missing data.

The clinically relevant outcomes for benefits and harms were overall survival, cardiovascular disease, diabetic retinopathy, kidney failure, amputations etc. The PBAC recalled that it had previously accepted the relevance of the change in HbA1c as a surrogate outcome for assessing efficacy[1].

8. Results of Trials

From the bioequivalence studies, the results showed that the saxagliptin maximum observed plasma concentration (Cmax), metformin Cmax, saxagliptin area under the plasma concentration-time curve from time zero extrapolated to infinite time (AUC(INF)) and metformin AUC(INF) met the criteria for bioequivalence in all trials.

The results of Study 080 showed that there was a statistically significant reduction in the adjusted mean change in HbA1c from baseline to week 12 in the saxagliptin 2.5 mg BID + metformin treatment arm compared to metformin alone. The submission noted that the placebo response in Study 080 was unusually high and may be attributed to biological variability.

Additionally, there was a numerically greater decrease in the adjusted mean change in fasting plasma glucose (FPG, not statistically significant) from baseline to week 12 in the saxagliptin 2.5mg BID + metformin treatment arm compared to metformin alone.

There was a statistically significant greater proportion of patients who achieved an HbA1C less than 7% in the saxagliptin 2.5 mg BID + metformin treatment arm compared to metformin alone. A similar result was also observed for HbA1C less than 6.5 %.

In study 080, the incidence of adverse events (AEs) was lower or comparable with saxagliptin 2.5 mg BID + metformin versus metformin alone with the exception of hypoglycaemic AEs. Patients treated with saxagliptin 2.5 mg BID + metformin experienced more hypoglycaemia than metformin alone (all events were mild or moderate). The incidence of confirmed hypoglycaemia[2] was lower with saxagliptin 2.5 mg BID + metformin but the incidence of hypoglycaemic AEs was higher.

An extended assessment of comparative harms was not presented.

[1] PBAC (March 2009) Sitagliptin with metformin FDC, extract of March 2009 PBAC minutes.
PBAC (Nov 2010) Vildagliptin with metformin FDC, extract of November 2010 PBAC minutes.
[2] Fingerstick glucose value ≤ 50mg/dL with associated hypoglycaemia symptoms.

For PBAC's view, see Recommendations and Reasons.

9. Clinical Claim

The submission described saxagliptin/metformin FDC as bioequivalent in terms of the pharmacodynamics and pharmacokinetics to concomitant administration of the individual tablets of saxagliptin and metformin at the corresponding dose strengths. The PBAC considered the claim was adequately supported, but noted that the final assessment of bioequivalence was a TGA matter.

The submission further described saxagliptin/metformin FDC as safe and effective in the treatment of patients with T2DM, although it did not specify the comparator to which claim this claim related. In terms of reduction of HbA1c, the PBAC considered that Study 080 provided adequate evidence of an additional clinical effect compared to metformin alone.

The PBAC considered that the submission did not provide evidence that at the corresponding dose strengths, that the efficacy and safety of saxagliptin/metformin FDC are the same as concomitant administration of the individual tablets of saxagliptin and metformin. The submission also did not provide adequate evidence that the efficacy and safety of saxagliptin 5 mg QD (once daily) are the same as that of saxagliptin 2.5 mg BID (twice daily). A visual comparison of the efficacy results reported by Study 080 to other studies was presented.

10. Economic Analysis

A cost-minimisation analysis was presented, based on non-inferiority between saxagliptin/metformin FDC and the individual components, on grounds of bioequivalence, and not including any additional costs/offsets. The equi-effective doses were estimated as:

- Saxagliptin/metformin FDC: saxagliptin 2.5 mg BID plus either metformin 500 mg, 850 mg or 1000 mg BID, whichever appropriate.
- Individual components form: saxagliptin 5 mg QD plus either metformin 500 mg, 850 mg or 1000 mg BID, whichever appropriate.

The PBAC accepted the estimated equi-effective doses and considered the cost-minimisation analysis reasonable based on the submission's claim of bioequivalence.

11. Estimated PBS Usage and Financial Implications

The likely number of patients per year was estimated to be between 10,000 and 50,000 in Year 5. The total number of prescriptions supplied was estimated to be more than 200, 000 in Year 5. The submission claimed a nil net cost to the PBS/RPBS, as a result of a directly proportional decrease in the use of the single-drug items.

The PBAC considered that the submission's estimate of usage was uncertain and would likely be an underestimate given the potential for leakage beyond the requested PBS population for the saxagliptin/metformin FDC, to patients without a contraindication or intolerance to sulfonylurea therapy. In addition, the PBAC noted that experience with other PBS listed gliptin/metformin FDCs indicated potential for higher uptake than anticipated, and that a proportional decrease in the proposed substituted therapies may not eventuate in practice.

Therefore, the PBAC did not consider that the listing of saxagliptin/metformin FDC would result in an overall net nil cost to the PBS.

The PBAC also noted the potential for use outside of the PBS subsidy criteria, including as triple oral therapy with sulfonylurea, metformin and a gliptin, and a proportion of patients where a gliptin is added to metformin, where the patient does not have a contraindication or intolerance to a sulfonylurea.

The PBAC also considered the submission's assumption that patient's will switch from other gliptin/metformin FDC combinations uncertain.

The PBAC noted the following concerns with the saxagliptin/metformin FDC with respect to meeting submission guidelines for listing FDCs:

- Criterion (f) requires that the combination not encourage or result in an inappropriate increase in overall utilisation of the components, nor inappropriate use of one or both components in specific patient groups. The PBAC considered that there is a risk that saxagliptin/metformin FDC may be used earlier in the treatment algorithm than specified in the PBS restriction based on sources of information provided by the DUSC relating to predicted versus actual use of combination drugs.
- Criterion (g) requires that the combination product not result in inappropriate dosing of either component, nor contain components that require individual dose titration. The PBAC considered that there was risk of inappropriate dosing with saxagliptin/metformin FDC as the metformin component requires titration.
- Criterion (h) requires that the combination product not result in unnecessary proliferation of product and/or dose forms. The PBAC was not convinced of a pressing clinical need for a saxagliptin/metformin FDC as there are currently two PBS listed gliptin/metformin FDCs.

12. Recommendation and Reasons

The PBAC deferred consideration of this submission pending finalisation of the TGA registration process, particularly the final indication, confirmation of bioequivalence with the single components given concomitantly, and further consideration of predicted utilisation and financial implications based on the Drug Utilisation Sub-Committee (DUSC) utilisation analysis.

The PBAC noted the requested restriction was consistent with current restrictions for other gliptin with metformin FDC products.

The PBAC also noted a PBS post market review (PMR) of products used in the management of diabetes was currently underway. It noted that one of the terms of reference of this review was to describe the utilisation and patterns of treatment of PBS listed drugs for type 2 diabetes mellitus, and to compare these with PBS restrictions. Hence, the findings of this review may impact the PBS restrictions for medicines for the treatment of diabetes mellitus.

The PBAC noted a preliminary report from the Drug Utilisation Sub-Committee (DUSC) from its February 2013 meeting on the utilisation of gliptins and gliptin-metformin FDCs. The DUSC utilisation analysis, which had been provided to sponsors for comment, suggested that at least 30% of current use of gliptins and gliptin-FDCS is not consistent with existing restrictions. The PBAC considered that new products of this class would need to be assessed in this context.

The PBAC considered that it would be essential to consider the final report from DUSC before defining the appropriate restrictions for saxagliptin/metformin as a new FDC. There may also be implications for the current restrictions for existing gliptin/metformin FDCs following consideration of the DUSC report. If there is in fact evidence to support what appears to be the evolving clinical use of gliptins higher up the treatment algorithm, including as alternative to sulfonylureas as second line therapy, then this use is not consistent with the cost-effective use that was previously accepted by the PBAC for gliptins or gliptin/metformin FDCs. The PBAC also considered that the addition of another fixed dose combination of gliptin with metformin could promote the current rapid growth in utilisation of gliptins.

The PBAC further noted that the final report from DUSC would be provided to PBAC for consideration at a PBAC Special meeting in April 2013, and agreed to re-consider this listing at the meeting.

The application was subsequently considered at the April 2013 PBAC Special meeting and the outcome will be published at a later date.

Based on the DUSC utilisation analysis, the PBAC considered that the submission's estimates of utilisation and financial implications were highly uncertain and likely to be significantly underestimated if the saxagliptin/metformin FDC is used in the same way as currently PBS listed dipeptidyl peptidase-4 (DPP-4) inhibitor (gliptin)/metformin FDCs.

If the PBS indication was approved as proposed, the PBAC noted that it would be reasonable to extrapolate the risk of use outside the restriction seen for currently listed gliptin/metformin FDCs, to saxagliptin/metformin FDC.

The PBAC noted that whilst the requested listing of saxagliptin/metformin FDC on the PBS would allow prescribing to patients who would otherwise be prescribed saxagliptin and metformin as separate tablets, preliminary results from the DUSC utilisation review suggest gliptins are being used earlier in the treatment algorithm.

The PBAC considered the submission's cost minimisation approach based on bioequivalence of the FDC against the individual components to be reasonable.

The PBAC considered the nominated comparator was appropriate and consistent with comparators previously accepted for other gliptin/metformin FDCs. However, the PBAC also noted that the two currently PBS-listed gliptin/metformin FDCs may also be replaced in practice.

Recommendation:
Deferred

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 notes that this submission was subsequently considered at the April 2013 PBAC Special meeting.

ADDENDUM – APRIL 2013

Product: Saxagliptin with metformin hydrochloride, tablet, 2.5 mg/500 mg, 2.5mg/850 mg, 2.5 mg/1,000 mg, Kombiglyze®
Sponsor: Bristol-Myers Squibb and AstraZeneca.
Date of PBAC Consideration: April 2013

1. Purpose of Application

To reconsider the submission, deferred at the March 2013 PBAC meeting, requesting an Authority required (STREAMLINED) listing for treatment of type 2 diabetes mellitus (T2DM).

2. Background and Requested listing

Refer to the March 2013 Public Summary Document to which this addendum is appended.

3. Registration status

As at 13 May 2013, saxagliptin with metformin FDC was TGA registered 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. Clinical place for the proposed therapy

Refer to the March 2013 Public Summary Document.

5. Comparator

Refer to the March 2013 Public Summary Document.

6. PBAC consideration of the evidence

Refer to the March 2013 Public Summary Document.

Drug Utilisation sub-Committee (DUSC) Analysis of Medicines for Type 2 diabetes

The PBAC noted that the October 2012 and February 2013 DUSC utilisation analyses hadbeen provided to the sponsor.

The PBAC noted the following findings from the February 2013 DUSC analysis of utilisation of PBS listed medicines for type 2 diabetes:

- There is extensive use of gliptins, glitazones and exenatide beyond the PBS restrictions;
- When considering medicines that can or cannot be prescribed in combination for PBS subsidy, 27.9% of patient medication regimens that include a gliptin, glitazone or exenatide do not meet the restrictions, that is:
    - The combination of a gliptin or rosiglitazone with both metformin and a sulfonylurea accounts for almost half of the patient medication regimens that are beyond the PBS restriction.

    - Monotherapy with a gliptin or a glitazone or exenatide is the next most frequent regimen that is non-compliant with PBS restrictions, accounting for 23%.
    - 34.6% of regimens containing gliptins do not comply with PBS criteria.
- When considering whether prescribing of gliptins, glitazones and exenatide complies with the requirements for patients to be contraindicated or intolerant to either metformin or a sulfonylurea:
    - Overall, 47.7% of patients initiated on a gliptin, glitazone or exenatide had not received a supply of both metformin and a sulfonylurea in the previous two years. A proportion of these patients may have a contraindication to one or both of these agents, but the rate is higher than plausible based on the likely frequency of true contraindication.
    - 4.9% of patients had no evidence of a supply of metformin or a sulfonylurea in the 2 years prior to the index prescription of a gliptin, glitazone, or exenatide. This group may represent patients who have contraindications to both metformin and a sulfonylurea. To comply with the conditions for PBS subsidy, however, the gliptins should be used in combination with either metformin or a sulfonylurea, and exenatide should be used with one or both of metformin and sulfonylurea. This group is unlikely to meet PBS criteria for co-administered therapy.
    - 6.7% of patients had a sulfonylurea supplied, but no metformin, which is consistent with reported rates of metformin contraindication.
    - 36.1% of patients had metformin supplied, but not a sulfonylurea, which is not consistent with the rate of contraindication to sulfonylurea.
    - Of all patient initiations to gliptins, glitazones or exenatide between July-December 2011, 85% were for gliptins. Although it is acknowledged that there are safety concerns with the glitazones, which is probably reducing their use, it is inconsistent that 85% of initiations are for gliptins, which are only subsidised where there is a contraindication or intolerance to metformin of sulfonylurea, whereas pioglitazone has two additional indications covering a larger population.

With specific regard to gliptins, the PBAC noted that for all regimens containing a gliptin the total non-compliance with PBS criteria was 34.6%. 18.5% of use of gliptins was in combination with BOTH metformin and a sulfonylurea. The cost-effectiveness of this treatment regimen has not been established.

With specific regard to gliptin+metformin FDCs, 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 (i.e., they had not been supplied a sulfonylurea). While the PBAC acknowledged that a proportion of these patients may have a true contraindication to sulfonylureas, the PBAC considered that this proportion would be small, and 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 findings of the DUSC review confirmed the PBAC's concerns, expressed during the March 2013 consideration of the submission, that there was significant potential for use of the proposed saxagliptin+metformin FDC outside the requested PBS population.

The PBAC considered that this concern was well supported by observed experience with the currently PBS listed gliptin+metformin FDCs, where the review of utilisation of the products showed that utilisation has been substantially greater than anticipated.

Similarly, the PBAC considered that it was highly likely, that utilisation of saxagliptin+metformin FDC would also be considerably higher than predicted, and therefore the submission's estimated costs to the PBS and Government were underestimated and highly uncertain.

7. Recommendation and Reasons

The PBAC noted that the ACPM had found that saxagliptin+metformin FDC had a favourable risk-benefit profile for the requested indication. Therefore, the PBAC was satisfied that the TGA registration was consistent with the requested PBS listing.

As in March 2013, the PBAC remained concerned regarding saxagliptin+metformin FDC with respect to completely meeting the guidelines for FDCs. (Refer to the March 2013 Public Summary Document).

The PBAC reiterated its position that it considered the submission's estimates of utilisation and financial implications to be highly uncertain and likely to be significantly underestimated should the saxagliptin+metformin FDC be used in the same way as currently PBS listed gliptin+metformin FDCs, based on the DUSC utilisation analysis, and experience with currently listed gliptin+metformin FDCs.

The PBAC remained confident that it was reasonable to extrapolate the risk of use outside the restriction seen for currently listed gliptin+metformin FDCs to saxagliptin+metformin FDC, should the PBS indication be approved as proposed. The PBAC noted that the majority of use outside the requested PBS indication was likely to be use earlier in the treatment algorithm, in place of sulfonylureas, in patients who are not intolerant of sulfonylureas or in whom sulfonylureas are not contraindicated.

The PBAC considered that there was no compelling clinical need for an additional gliptin+metformin FDC on the PBS, and had significant concerns regarding the highly uncertain and underestimated usage and financial implications. The PBAC gave consideration to the following two options that it thought might provide a reasonable basis of approval of the submission, and ensure the cost to the PBS and Government was acceptable.

Option 1

As the PBAC did not have confidence in the predictions of use beyond Year 1, and noting that the gliptin+FDC market is expanding, the PBAC considered that one option was to approve saxagliptin+metformin FDC for listing with the requested restriction, (i.e., limiting use to patients in whom combination treatment with metformin and a sulfonylurea is contraindicated or not tolerated), at the price proposed in the submission, with a risk sharing arrangement involving a hard cap based on Year 1 utilisation estimates beyond which a 100% rebate would apply. However, the PBAC did not have any confidence in the predicted

estimates of use in year 2 and did not consider that it was able to advise the Minister or the Department of what the financial cap should be in year 2 and beyond.

Option 2

Taking into account the findings of the DUSC utilisation analysis with regard to the use of gliptin+FDCs earlier in the treatment algorithm in patients not supplied a sulfonylurea, the PBAC considered it would be reasonable to recommend listing with a restriction more reflective of the likely use of this combination product, (i.e., remove the requirement for patients to have a contraindication or be intolerant of sulfonylureas) but at a reduced price, noting that the Committee had not been provided with any evidence to support cost-effectiveness in this expanded population.

The PBAC noted the DUSC utilisation analysis finding that 46.7% of patients initiating on a gliptin+metformin FDC were not supplied a prior sulfonylurea. 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. While noting prescriber concerns about risk of hypoglycaemia particularly in the elderly with some sulfonylureas, the PBAC considered that the rate of true contraindication or intolerance would be very small, less than 5% of the patient population. With this assumption, it remained that usage in approximately 40% of patients initiated on a gliptin+metformin FDC has not been demonstrated to be cost-effective. Therefore, the PBAC considered that listing under these circumstances would require a price reduction to account for the likely non-cost-effective use, and that approximately 40% of use should be cost-minimised to the price of the average daily dose of a sulfonylurea in combination with metformin.

Overall, given the unknown likely utilisation, the PBAC considered that Option 2 was preferred, and recommended listing of saxagliptin+metformin FDC as an Authority Required (STREAMLINED) benefit in patients 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, at a reduced price which takes into account the proportion of use in patients where the cost-effectiveness of this combination has not been established, as described above.

The PBAC recommended that an amended listing with removal of the requirement for patients to be contraindicated or intolerant of sulfonylureas for single ingredient saxagliptin was appropriate, should a similar price reduction be agreed for the single ingredient formulation.

The PBAC recommended that saxagliptin+metformin FDC is suitable for inclusion in the list of PBS medicines for prescribing by nurse practitioners within collaborative arrangements.

Recommendation:

Recommended

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer	
SAXAGLIPTIN + METFORMIN				
tablet: film-coated, 2.5/500, 56	1	5	Kombiglyze	BQ
tablet: film-coated, 2.5/850, 56	1	5		
tablet: film-coated, 2.5/1000, 56	1	5		

Condition/Indication:	Type 2 diabetes
Treatment phase:	Initial treatment
Restriction:	Authority Required (STREAMLINED)
Clinical criteria:	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 10 mmol per L in more than 20% of blood glucose monitoring tests over a 2-week period despite treatment with metformin in circumstances where assessment of HbA1c is not appropriate.
Prescriber Instructions	The date and level of the qualifying HbA1c must be documented in the patient's medical records at the time treatment with a gliptin, a glitazone or a glucagon-like peptide-1 is initiated. The HbA1c must be no more than 4 months old at the time treatment with a gliptin, a glitazone or a 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, a glitazone or a glucagon-like peptide-1, must be documented in the patient's medical records.
Administrative Advice	Saxagliptin with metformin fixed dose combination tablet is not PBS-subsidised for use in combination with a sulfonylurea (triple oral therapy), as initial therapy or in combination with a thiazolidinedione (glitazone) or a glucagon-like peptide-1.

Condition/Indication:	Type 2 diabetes
Treatment phase:	Continuing treatment
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	Saxagliptin with metformin fixed dose combination tablet is not PBS-subsidised for use in combination with a sulfonylurea (triple oral therapy), as initial therapy or in combination with a thiazolidinedione (glitazone) or a glucagon-like peptide-1.

8. 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.

9. Sponsor's Comment

The sponsor is pleased with the PBAC recommendation and is working towards PBS listing of this FDC option for patients with T2DM.