PUBLIC SUMMARY DOCUMENT
Product: VILDAGLIPTIN, tablet, 50 mg, Galvus®
Sponsor: Novartis Pharmaceuticals Australia Pty Ltd
Date of PBAC Consideration: March 2010

1. Purpose of Application

The submission sought an Authority required (Streamlined) listing for the treatment of type 2 diabetes in combination with metformin or a sulfonylurea in patients who meet certain criteria.

2. Background

This drug had not previously been considered by the PBAC.

3. Registration Status

Vildagliptin was registered with the Therapeutic Goods Administration (TGA) on 2 March 2010. Vildagliptin is indicated for the treatment of diabetes mellitus type 2 in persons 18 years of age and older, as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes with one of metformin, a sulfonylurea or pioglitazone when diet, exercise and the single agent do not result in adequate glycaemic control.

4. Listing Requested and PBAC's View

Authority required (STREAMLINED)
Dual oral combination therapy with metformin or a sulfonylurea.

Type 2 diabetes mellitus, in combination with metformin or a sulfonylurea, in a patient whose HbA1c is greater than 7 % prior to initiation of a DPP-4 inhibitor (gliptin) despite treatment with either metformin or a sulfonylurea and where a combination of metformin and a sulfonylurea is contraindicated or not tolerated.

If it is desirable to transfer from a thiazolidinedione (glitazone) to vildagliptin, the HbA1c must have been greater than 7 % prior to initiation of the glitazone.

The date and level of the qualifying HbA1c must be documented in the patient's medical records at the time gliptin or glitazone treatment is initiated. The HbA1c must be no more than 4 months old at the time gliptin or glitazone treatment 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 gliptin or glitazone initiation therapy, must be documented in the patient's medical records.

Note:

Vildagliptin is not PBS-subsidised for use in combination with metformin and a sulfonylurea (triple oral therapy), as monotherapy or in combination with a thiazolidinedione (glitazone).

The PBAC recommended the restriction wording for vildagliptin and all currently PBS subsidised dipeptidyl peptidase 4 inhibitors (gliptins) and thiazolidinediones (glitazones) be modified to allow patients to switch between agents in these two classes without having to requalify with respect to glycosylated haemoglobin levels (HbA1c). Although the evidence to support switches from a gliptin to a glitazone, and vice versa, is limited, the Committee considered it unreasonable to require a loss of diabetic control prior to switching.

5. Clinical Place for the Proposed Therapy

Type 2 diabetes is a metabolic disorder characterised by hyperglycaemia resulting from resistance to the action of insulin, insufficient insulin secretion or both. Diet and lifestyle modifications are the first steps in managing the disease, followed by the addition of drug therapy with metformin. When diet, lifestyle modifications and metformin monotherapy is inadequate in controlling blood glucose levels, current treatment guidelines recommend adding a sulfonylurea. If dual therapy with metformin and a sulfonylurea is unsuccessful, insulin should preferably be added. Other options include thiazolidinediones, acarbose, incretins, glitinides and gliptins. Vildagliptin would provide another gliptin option.

6. Comparator

The submission nominated sitagliptin as the main comparator. Comparison to pioglitazone and rosiglitazone were presented as supplementary analyses. The PBAC considered the primary and secondary comparators appropriate.

7. Clinical Trials

The basis of the submission was 16 direct randomised comparative trials; 12 trials were placebo-controlled; four were non-inferiority trials, with active treatment comparisons.

There were no head-to-head trials of vildagliptin versus sitagliptin.

A summary of the trials presented in the submission is shown in the table below:

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Vildagliptin vs primary comparator, sitagliptin		
Combination therapy with metformin		
Placebo-controlled vildagliptin trials used in indirect comparisons		
Ahren B et al. (2004)	Twelve- and 52-week efficacy of the dipeptidyl peptidase IV inhibitor LAF237 in metformin-treated patients with type 2 diabetes.	*Diabetes Care* 2004; 27: 2874-80
Bosi E et al. (2007)	Effects of vildagliptin on glucose control over 24 weeks in patients with type 2 diabetes inadequately controlled with metformin.	*Diabetes Care* 2007; 30: 890-895
Active-controlled vildagliptin trials used in indirect comparisons		
Ferrannin E et al. (2009)	Fifty-two-week efficacy and safety of vildagliptin vs. glimepiride in patients with type 2 diabetes mellitus inadequately controlled on metformin monotherapy.	*Diabetes, Obesity and Metabolism* 2009;11:157-66

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Filozof C & Gautier J-F (2010)[a]	A comparison of efficacy and safety of vildagliptin and gliclazide in combination with metformin in patients with Type 2 diabetes inadequately controlled with metformin alone: a 52-week, randomized study.	*Diabetic Medicine 2010; 27: 318-26*
Placebo-controlled sitagliptin trials used in indirect comparisons		
Charbonnel B et al. (2006)	Efficacy and Safety of the dipeptidyl peptidase-4 inhibitor sitagliptin added to ongoing metformin therapy in patients with type 2 diabetes inadequately controlled with metformin alone.	*Diabetes Care* 2006;29(12):2638-43
Scott R et al. (2008)	Efficacy and safety of sitagliptin when added to ongoing metformin therapy in patients with type 2 diabetes.	*Diabetes, Obesity and Metabolism* 2008; 10: 959-69
Raz I et al. (2008)	Efficacy and safety of sitagliptin added to ongoing metformin therapy in patients with type 2 diabetes.	*Current Medical Research and Opinion* 2008; 24(2): 537-550
Active-controlled sitagliptin trial used in indirect comparisons		
Nauck MA et al. (2007)	Efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, compared with the sulfonylurea, glipizide, in patients with type 2 diabetes inadequately controlled on metformin alone: a randomized, double-blind, non-inferiority trial.	*Diabetes, Obesity and Metabolism* 2007; 9:194-205
Combination therapy with a sulfonylurea		
Placebo-controlled vildagliptin trial used in indirect comparisons		
Garber A.J et al. (2008)	Effects on vildagliptin on glucose control in patients with type 2 diabetes inadequately controlled with a sulphonylurea.	*Diabetes, Obesity and Metabolism* 2008;10: 1047-56
Placebo-controlled sitagliptin trial used in indirect comparisons		
Hermansen K et al. (2007)	Efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, in patients with type 2 diabetes mellitus inadequately controlled on glimepiride alone or on glimepiride and metformin.	*Diabetes, Obesity and Metabolism* 2007;9: 733-45
Vildagliptin vs secondary comparators, pioglitazone or rosiglitazone		
Combination therapy with metformin		
Direct head-to-head trial: vildagliptin vs pioglitazone		
Bolli G et al. (2008) Bolli G et al. (2009)	Efficacy and tolerability of vildagliptin vs. pioglitazone when added to metformin: a 24-week, randomized, double-blind study. Comparison of vildagliptin and pioglitazone in patients with type 2 diabetes inadequately controlled with metformin.	*Diabetes, Obesity and Metabolism* 2008; 10: 82-90 *Diabetes, Obesity and Metabolism* 2009;11:589-95
Placebo-controlled glitazone trials used in indirect comparisons		
Einhorn D et al. (2000)	Pioglitazone hydrochloride in combination with metformin in the treatment of type 2 diabetes mellitus: A randomized, placebo-controlled study.	*Clinical Therapeutics* 2000; 22(12): 1395-1409
Kaku K (2009)	Efficacy and safety of therapy with metformin plus pioglitazone in the treatment of patients with type 2 diabetes: a double-blind, placebo-controlled, clinical trial.	*Current Medical Research and Opinion* 2009;25:1111-19
Fonseca V et al. (2000)	Effect of metformin and rosiglitazone combination therapy in patients with type 2 diabetes mellitus.	*JAMA* 2000; 283(13):1695-1702
Lowry (1998)	GSK trial not published but presented in: Lord J, Paisley S, Taylor R. The clinical effectiveness and cost-effectiveness of rosiglitazone for type 2 diabetes mellitus.	May 2000 London: National Institute for Clinical Excellence, 2000.
Gomez-Perez FJ et al. (2002)	Efficacy and safety of rosiglitazone plus metformin in Mexicans with type 2 diabetes.	*Diabetes/Metabolism Research and Reviews* 2002; 18: 127-34

[a] The Clinical Study Report for trial 2338 was included in the submission, and the trial has since been published

8. Results of Trials

The within-trial comparisons demonstrated that vildagliptin plus metformin, sitagliptin plus metformin, pioglitazone or rosiglitazone plus metformin produce similar and statistically significantly larger reductions in mean HbA1c than metformin alone.

In all non-inferiority studies, there were no statistically significant differences between vildagliptin and glimepiride, gliclazide, or pioglitazone (added to background metformin treatment) or between sitagliptin and glipizide (added to background metformin treatment). In each of the non-inferiority trials the upper limit of the 95 % CI for the difference in mean change in HbA1c was below the non-inferiority margin (< 0.3 %).

The results of indirect analysis #1 are in the following table: Mean change in HbA1c: Indirect comparison of vildagliptin 50 mg once daily versus sitagliptin using placebo as common comparator (background metformin therapy).

Trial	Treatment		Control		Mean difference* (95% CI)
	Baseline HbA1c	Change in HbA1c	Baseline HbA1c	Change in HbA1c	
Vildagliptin 50mg daily					
2204 (12wk)	7.7	-0.56	7.8	0.09	-0.69 (-0.89, -0.50) (I^2=0%)
2303 (24wk)	8.4	-0.51	8.3	0.23	
Sitagliptin 100mg daily					
Charbonnel 2006 (24wk)	8.0	-0.67	8.0	-0.02	-0.70 (-0.94, -0.46) (I^2=75%)
Scott 2008 (18wk)	7.8	-0.73	7.7	-0.22	
Raz 2008 (18wk)	9.3	-1.0	9.1	0.0	
Indirect comparison: Indirect mean difference in HbA1c (95% CI)					
Vildagliptin 50mg once daily vs sitagliptin 100mg					0.01 (-0.30, 0.32)

* Weighted estimate using random effects meta-analysis if >1 trial

The results of indirect analysis #2 are in the following table: Mean change in HbA1c: Indirect comparison of vildagliptin 50 mg twice daily versus sitagliptin using placebo as common comparator (background metformin therapy).

Trial	Treatment		Control		Mean difference* (95% CI)
	Baseline HbA1c	Change in HbA1c	Baseline HbA1c	Change in HbA1c	
Vildagliptin 50mg twice daily					
2303 (24wk)	8.4	-0.88	8.3	0.23	-1.11 (-1.37, -0.84)
Sitagliptin 100mg daily					
Charbonnel 2006 (24wk)	8.0	-0.67	8.0	-0.02	-0.70 (-0.94, -0.46) (I^2=75%)
Scott 2008 (18wk)	7.8	-0.73	7.7	-0.22	
Raz 2008 (18wk)	9.3	-1.0	9.1	0.0	
Indirect comparison: Indirect mean difference in HbA1c (95% CI)					
Vildagliptin 50mg twice daily vs sitagliptin 100mg					-0.40 (-0.76, -0.04)

* Weighted estimate using random effects meta-analysis if >1 trial

The results of indirect analysis #3 are in the following table: Mean change in HbA1c: Indirect comparison of vildagliptin 50 mg twice daily versus sitagliptin using a sulfonylurea as common comparator (background metformin therapy).

Trial	Treatment	Control	Mean difference*

	Baseline HbA1c	Change in HbA1c	Baseline HbA1c	Change in HbA1c	(95% CI)
Vildagliptin 50mg twice daily					
2308 (52wk)	7.3	-0.44	7.3	-0.53	0.09 (0.03, 0.14) (I^2=0%)
2338 (52wk)	8.5	-0.81	8.5	-0.85	
Sitagliptin 100mg daily					
Nauck 2007 (52wk)	7.7	-0.67	7.6	-0.67	0.00 (-0.11, 0.11)
Indirect comparison: Indirect mean difference in HbA1c (95% CI)					
Vildagliptin 50mg twice daily vs sitagliptin 100mg					0.09 (-0.04, 0.22)

* Weighted estimate using random effects meta-analysis if >1 trial

The results of indirect analysis #4 are in the following table: Mean change in HbA1c: Indirect comparison of vildagliptin 50 mg twice daily versus pioglitazone using placebo as common comparator (background metformin therapy).

Trial	Treatment		Control		Mean difference* (95% CI)
	Baseline HbA1c	Change in HbA1c	Baseline HbA1c	Change in HbA1c	
Vildagliptin 50mg twice daily					
2303 (24wk)	8.4	-0.88	8.3	0.23	-1.11 (-1.37, -0.84)
Pioglitazone 30mg					
Einhorn 2000 (16wk)	9.9	-0.64	9.8	0.19	-0.88 (-1.08, -0.68) (I^2=0%)
Kaku 2009 (28wk)	7.6	-0.67	7.6	0.25	
Indirect comparison: Indirect analysis in HbA1c (95% CI)					
Vildagliptin 50mg twice daily vs pioglitazone 30mg					-0.22 (-0.56, 0.12)

* Weighted estimate using random effects meta-analysis if >1 trial

The results of indirect analysis #5 are in the following table: Mean change in HbA1c: Indirect comparison of vildagliptin 50 mg twice daily versus rosiglitazone using placebo as common comparator (background metformin therapy).

Trial	Treatment		Control		Mean difference* (95% CI)
	Baseline HbA1c	Change in HbA1c	Baseline HbA1c	Change in HbA1c	
Vildagliptin 50mg twice daily					
2303 (24wk)	8.4	-0.88	8.3	0.23	-1.11 (-1.37, -0.84)
Rosiglitazone 8mg daily					
Fonseca 2000 (26wk)	8.9	-0.78	8.6	0.45	-1.10 (-1.47, -0.73) (I^2=58%)
Lowry 1998 (26wk)	8.7	-0.7	8.8	0.1	
Gomez-Perez 2002 (26wk)	~ 9.7	-1.20	~ 9.8	0.30	
Indirect comparison: Indirect mean difference in HbA1c (95% CI)					
Vildagliptin 50mg twice daily vs rosiglitazone 8mg					0 (-0.46, 0.46)

* Weighted estimate using random effects meta-analysis if >1 trial

The results of indirect analysis #6 are in the following table: Mean change in HbA1c: Indirect comparison of vildagliptin 50 mg once daily versus sitagliptin using placebo as common comparator (background sulfonylurea therapy).

Trial	Treatment		Control		Mean difference (95% CI)
	Baseline HbA1c	Change in HbA1c	Baseline HbA1c	Change in HbA1c	
Vildagliptin 50 mg twice daily					
2305 (24wk)	8.5	-0.58	8.5	0.07	-0.64 (-0.90, -0.39)
Sitagliptin 100mg daily					

Hermansen 2007 (24wk)	8.4	-0.30	8.4	0.27	-0.57 (-0.82, -0.32)
Indirect comparison: Indirect mean difference in HbA1c (95% CI)					
Vildagliptin 50mg twice daily vs sitagliptin 100mg daily					-0.07 (-0.43, 0.29)

The results of the 6 indirect analyses showed:

(i) No difference between vildagliptin 50 mg once daily and sitagliptin 100 mg (added to background metformin treatment) using placebo as common comparator. However, 50 mg twice daily is the recommended dose of vildagliptin in combination with metformin;

(ii) Vildagliptin 50 mg twice daily was superior to sitagliptin 100 mg (added to background metformin treatment) using placebo as common comparator;

(iii) No difference between vildagliptin 50 mg twice daily and sitagliptin 100 mg (added to background metformin treatment) using sulfonylurea as the common comparator;

(iv) No difference between vildagliptin 50 mg twice daily and pioglitazone 30 mg (added to background metformin treatment) using placebo as the common comparator;

(v) No difference between vildagliptin 50 mg twice daily and rosiglitazone 8 mg (added to background metformin treatment) using placebo as the common comparator; and

(vi) No difference between vildagliptin 50 mg once daily and sitagliptin 100 mg (added to background sulfonylurea treatment) using placebo as the common comparator.

There were no statistically significant differences in indirect mean differences in HbA1c in five of six indirect analyses. The comparison of vildagliptin 50 mg twice daily and sitagliptin with placebo as common comparator showed superiority of vildagliptin. Five of the six indirect analyses satisfied the non-inferiority margin of 0.3 % - 0.4 %, the exception being the vildagliptin 50 mg twice daily and rosiglitazone 8 mg comparison using placebo as the common comparator, where the upper bound of the 95 % CI for the mean difference was 0.46 %.

The indirect comparisons using the outcome proportions of HbA1c responders (achieving HbA1c less than 7 %) similarly demonstrated no statistically significant differences in responder rates between vildagliptin and sitagliptin or rosiglitazone.

The submission presented analyses of change in HbA1c stratified by baseline HbA1c levels, comparing subjects with baseline HbA1c less than or equal to 8 % and those greater than 8 % and comparing subjects with baseline HbA1c less than or equal to 9 % and those greater than 9 %. The submission suggested that patients with a higher baseline HbA1c had a higher mean reduction in HbA1c at study endpoint. A published meta-regression (Bloomgarden 2006) provided some support for a larger treatment response with higher baseline HbA1c. However, a test of interaction of treatment with baseline HbA1c conducted during the evaluation using five placebo-controlled trials showed no statistically significant treatment interaction effect.

In addition, the submission presented results for changes in fasting plasma glucose (FPG), changes in prandial blood glucose, blood pressure, weight and lipids. These analyses suggested that vildagliptin is superior to placebo and similar to active treatment controls in reducing FPG. There were no statistically significant differences between vildagliptin and placebo in changes in weight; changes in weight were similar to sitagliptin and weight gain was statistically significantly lower with vildagliptin than with glimepiride, gliclazide and pioglitazone.

The submission concluded that vildagliptin is equivalent to sitagliptin regarding safety including risk of hypoglycaemia. Liver enzyme abnormalities were noted with vildagliptin, mainly in the 100 mg once daily dose that was not a part of the requested registration or PBS restriction. The product information recommends liver enzyme monitoring in the first year. Cases of pancreatitis have been reported with sitagliptin.

The submission noted studies suggesting increased risk of cardiovascular events and fractures with thiazolidinediones. The submission stated that vildagliptin is superior to pioglitazone and rosiglitazone because of the potential effects of pioglitazone and rosiglitazone on weight and bone density/fracture, and superior to rosiglitazone because of the effect of rosiglitazone on cardiovascular events. These arguments were used in the submission to support switching from thiazolidinedione to vildagliptin for patients "experiencing or are at risk of side-effects". There was no comparative safety data for vildagliptin versus glitazones presented in the submission to support a listing for switching from a thiazolidinedione beyond the results showing less weight gain in vildagliptin treated patients compared to pioglitazone in the head-to-head trial (Bolli et al 2008; Bolli et al 2009).

9. Clinical Claim

The submission concluded that vildagliptin 50 mg twice daily, sitagliptin 100 mg/day, pioglitazone 30 mg/day and rosiglitazone 8 mg/day are equi-effective in the context of combination usage with metformin, and that vildagliptin 50 mg once daily, sitagliptin 100 mg/day, pioglitazone 30 mg, and rosiglitazone 8 mg/day are equi-effective in the context of combination usage with sulfonylurea.

The PBAC accepted this claim.

10. Economic Analysis

The submission presented a cost-minimisation analysis. The submission's proposed equi-effective doses in the setting of combination usage with metformin were vildagliptin 50 mg twice daily, sitagliptin 100 mg, pioglitazone 30 mg, and rosiglitazone 8 mg. The equi-effective doses in the combination usage with sulfonylurea were vildagliptin 50 mg once daily, sitagliptin 100 mg, pioglitazone 30 mg, and rosiglitazone 8 mg.

Although the evidentiary basis for the submission's claim that vildagliptin is non-inferior to the primary comparator, sitagliptin, relies entirely on indirect comparisons with their attendant uncertainties, the PBAC was satisfied that the criteria for a cost-minimisation recommendation had been met.

The PBAC considered the submission's base case cost-minimisation analysis which assumed 50 % of vildagliptin would be used with metformin and 50 % with a sulfonylurea to be highly uncertain. This was because the sample of Medicare concession patient data used by the sponsor to support this assumption had a number of selection and treatment allocation biases that affected the applicability of the result to the whole market. Additionally, prescription data indicated that the use of sulfonylureas is declining overall. The PBAC considered 60:40 a more reasonable estimate of metformin versus sulfonylurea use for inclusion in the base case at this point in time.

The PBAC however agreed with the submission's proposal to base the price of vildagliptin on the conclusion that vildagliptin 50 mg twice daily is equivalent to sitagliptin 100 mg once daily only. The PBAC considered that there are additional costs associated with liver function tests required for patients receiving vildagliptin compared to those receiving sitagliptin, but these extra costs are offset by the lower dose and subsequent cost of vildagliptin per day compared to sitagliptin per day when either agent is used in combination with a sulfonylurea, when at least 40 % of vildagliptin is used in combination with a sulphonylurea. The PBAC requested that the Drug Utilisation Sub-Committee monitor the utilisation of vildagliptin going forward.

11. Estimated PBS Usage and Financial Implications

The likely number of patients/year was estimated by the submission to be in the range of 10,000 – 50,000 in Year 5 for a metformin to sulfonylurea usage ratio of 50 % to 50 %.

The financial consequences/year to government health budgets was estimated by the submission to be less than $5 million in savings in Year 5 based on a 50:50 split between combination therapy with metformin and combination therapy with sulphonylurea and taking into account the cost of monitoring liver enzymes, and an increase in cost to government of less than $5 million in Year 5 if combination usage is with metformin only.

12. Recommendation and Reasons

The PBAC recommended the listing of vildagliptin as an Authority required (Streamlined) benefit for the treatment of Type 2 diabetes mellitus, in combination with metformin or a sulfonylurea, in a patient whose HbA1c is greater than 7 % despite treatment with either metformin or a sulfonylurea and where a combination of metformin and a sulfonylurea is contraindicated or not tolerated. Listing was recommended on a cost-minimisation basis with sitagliptin. The equi-effective doses in the setting of combination usage with metformin are vildagliptin 50 mg twice daily, sitagliptin 100 mg daily, pioglitazone 30 mg daily, and rosiglitazone 8 mg daily. The equi-effective doses in the combination usage with sulfonylurea are vildagliptin 50 mg once daily, sitagliptin 100 mg daily, pioglitazone 30 mg daily, and rosiglitazone 8 mg daily.

Although the evidentiary basis for the submission's claim that vildagliptin is non-inferior to the primary comparator, sitagliptin, relies entirely on indirect comparisons with their attendant uncertainties, the PBAC was satisfied that the criteria for a cost-minimisation recommendation had been met.

The PBAC considered the submission's base case cost-minimisation analysis which assumed 50 % of vildagliptin would be used with metformin and 50 % with a sulfonylurea to be highly uncertain. This is because the sample of Medicare concession patient data used by the sponsor to support this assumption has a number of selection and treatment allocation biases that affect the applicability of the result to the whole market. Additionally, prescription data indicate that the use of sulfonylureas is declining overall. The PBAC considered 60:40 a more reasonable estimate of metformin versus sulfonylurea use for inclusion in the base case at this point in time.

The PBAC however agreed with the submission's proposal to base the price of vildagliptin on the conclusion that vildagliptin 50 mg twice daily is equivalent to sitagliptin 100 mg once daily only. The PBAC considered that there are additional costs

associated with liver function tests required for patients receiving vildagliptin compared to those receiving sitagliptin, but these extra costs are offset by the lower dose and subsequent cost of vildagliptin per day compared to sitagliptin per day when either agent is used in combination with a sulfonylurea, when at least 40 % of vildagliptin is used in combination with a sulphonylurea. The PBAC requested that the DUSC monitor the utilisation of vildagliptin going forward.

Although the PBAC accepted the proposed price of vildagliptin in this submission, any applications to subsidise new vildagliptin monotherapy or combination products may need to be priced differently to take into account the additional costs associated with liver function tests for vildagliptin compared to sitagliptin.

The PBAC recommended the restriction wording for vildagliptin and all currently PBS subsidised dipeptidyl peptidase 4 inhibitors (gliptins) and thiazolidinediones (glitazones) be modified to allow patients to switch between agents in these two classes without having to requalify with respect to glycosylated haemoglobin levels (HbA1c). Although the evidence to support switches from a gliptin to a glitazone, and vice versa, is limited, the Committee considered it unreasonable to require a loss of diabetic control prior to switching. Comment should be sought from the relevant sponsors prior to this change being implemented.

Recommendation:
VILDAGLIPTIN, tablet, 50 mg

Restriction:

Note:
Vildagliptin is not PBS-subsidised for use in combination with metformin and a sulfonylurea (triple oral therapy), as monotherapy or in combination with a thiazolidinedione (glitazone).

Authority required (STREAMLINED)
Dual oral combination therapy with metformin or a sulfonylurea.

Type 2 diabetes mellitus, in combination with metformin or a sulfonylurea, in a patient whose HbA1c is greater than 7 % prior to initiation of a dipeptidyl peptidase 4 inhibitor (gliptin) or a thiozolidinedione (glitazone) despite treatment with either metformin or a sulfonylurea 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 or glitazone is initiated. The HbA1c must be no more than 4 months old at the time treatment with a gliptin or glitazone 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 or glitazone, must be documented in the patient's medical records.

Maximum quantity: 60
Repeats: 5

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

Novartis welcomes the PBAC's decision to recommend the PBS listing of vildagliptin for patients with type 2 diabetes.