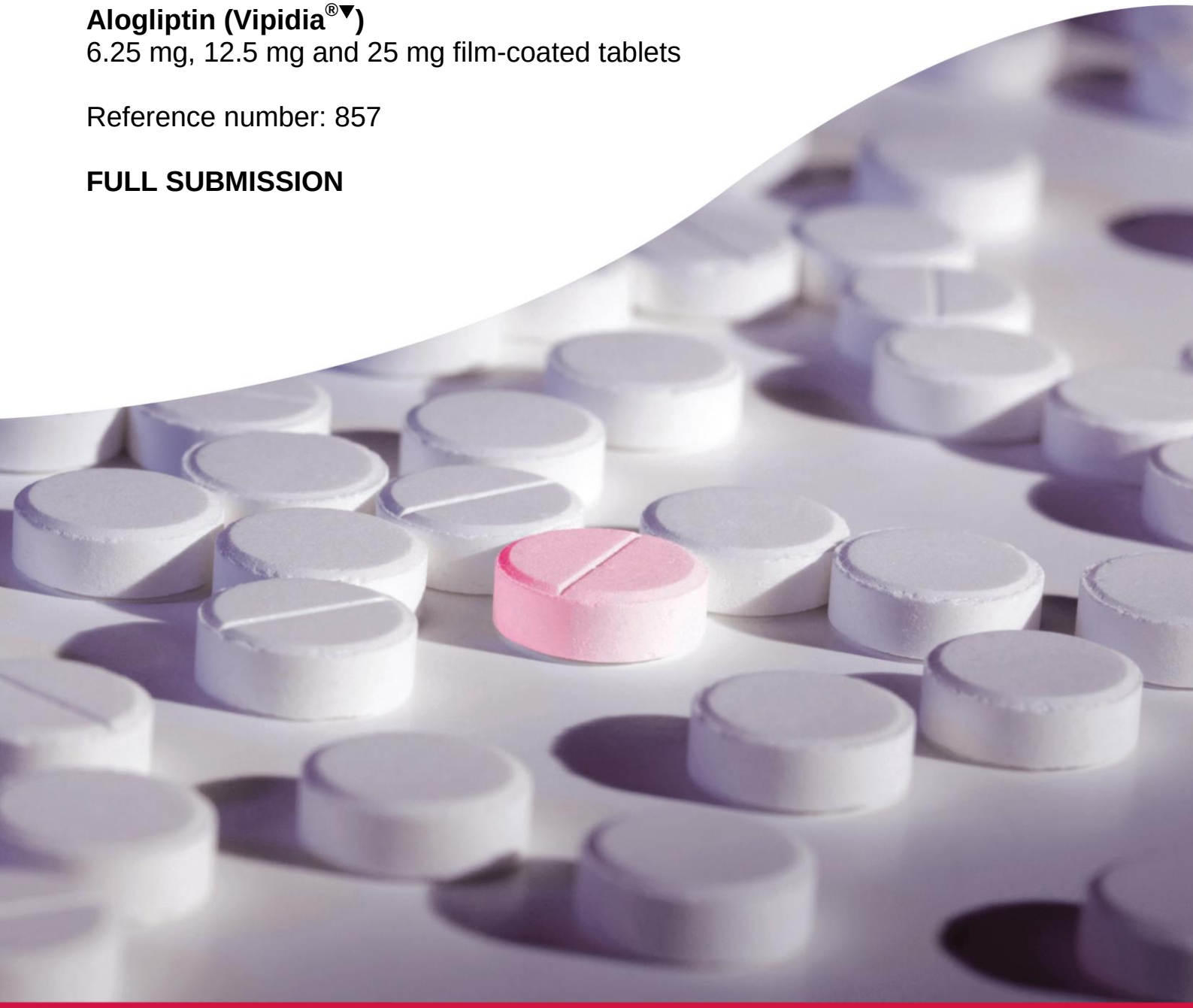
All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG SECRETARIAT ASSESSMENT REPORT

Alogliptin (Vipidia®▼)
6.25 mg, 12.5 mg and 25 mg film-coated tablets

Reference number: 857

FULL SUBMISSION



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AWMSG Secretariat Assessment Report
Alogliptin (Vipidia®▼) 6.25 mg, 12.5 mg and 25 mg film-coated tablets

This assessment report is based on evidence submitted by Takeda UK Ltd on 12 February 2014[1].

1.0 PRODUCT DETAILS

Licensed indication under consideration	Alogliptin (Vipidia®▼) for the treatment of adults aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control in combination with other glucose lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control[1].
Dosing	The recommended dose of alogliptin is one tablet of 25 mg once-daily as add-on therapy to metformin, a thiazolidinedione, a sulphonylurea, or insulin or as triple therapy with metformin and a thiazolidinedione or insulin. Refer to the Summary of Product Characteristics (SPC) for further dosing information[2].
Marketing authorisation date	19 September 2013[3]
UK launch date	27 January 2014[1]

2.0 DECISION CONTEXT

2.1 Background

Type 2 diabetes mellitus (T2DM) is associated with increased macrovascular risk including cardiovascular disease and stroke, and microvascular complications such as retinopathy, neuropathy and nephropathy[4,5]. Alogliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor. These are a class of oral anti-diabetic agents that increase incretin hormone concentrations in the blood, which enhance insulin and reduce glucagon secretions, thereby reducing blood glucose levels[6]. National Institute for Health and Care Excellence (NICE) clinical guidelines recommend DPP-4 inhibitors as a second-line treatment option in combination with metformin or a sulfonylurea (after first-line metformin or sulfonylurea monotherapy) and as a third-line treatment option (after metformin and a sulfonylurea)[5,6].

The applicant company has suggested alogliptin should be considered within its licensed indication for the treatment of T2DM only where a DPP-4 inhibitor is considered appropriate for use in the following settings:

- Dual therapy in combination with metformin;
- Dual therapy in combination with a sulphonylurea[1].

The applicant company has not provided any evidence outside of these settings.

2.2 Comparators

The comparators included in the company submission were:

- Sitagliptin (Januvia®)
- Saxagliptin (Onglyza®)
- Linagliptin (Trajenta®▼)

2.3 Guidance and related advice

- Scottish Intercollegiate Guidelines Network (SIGN). Management of diabetes. Guideline 116 (2010)[7].
- NICE. Clinical guideline (CG) 87. Type 2 diabetes: the management of type 2 diabetes (partial update of CG66 [2009])[5].
- NICE. CG66. Type 2 diabetes: National clinical guideline for management in primary and secondary care (partially updated by CG87 [2008])[8].

The All Wales Medicines Strategy Group (AWMSG) has previously issued recommendations for linagliptin (Trajenta®▼)[9], saxagliptin (Onglyza®)[10–12], vildagliptin (Galvus®)[13] and sitagliptin (Januvia®)[14].

3.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

In support of the use of alogliptin as dual therapy in combination with metformin or a sulphonylurea, the company submission included three pivotal randomised, double-blind, phase III studies. In the absence of head-to-head studies the company submission included a systematic review and mixed treatment comparison (MTC) comparing the efficacy of alogliptin with other DPP-4 inhibitors. The company submission provided results for the 25 mg dose of alogliptin as this is the usual recommended dose as per the licensed indication[1].

3.1 Alogliptin in combination with metformin

3.1.1 Study SYR-322_305 (ENDURE)

This was a randomised, phase III, international, multi-centre, double-blind, active-controlled study designed to investigate the efficacy and safety of alogliptin plus metformin compared to glipizide plus metformin in adult patients with T2DM experiencing inadequate glycaemic control despite treatment with a stable daily dose of metformin[1,15]. Patients with inadequate glycaemic control (defined as HbA_{1c} 7.0-9.0%) whilst receiving a daily metformin dose of ≥ 1,500 mg (or maximum tolerated dose [MTD]) were eligible for study inclusion. Patients (n = 2,639) were randomised to receive either alogliptin 12.5 mg (n = 880) or 25 mg (n = 885) once daily, or glipizide (5-20 mg; n = 874) in a 1:1:1 ratio, all in combination with metformin for a period of 104 weeks[1,15]. The primary efficacy endpoints were changes in HbA_{1c} from baseline at 52 and 104 weeks (see Table 1)[1,4,15]. The primary analyses were conducted in the per protocol set (PPS) while secondary analyses were conducted in the full analysis set (FAS) (see Glossary); however, results were consistent across all analysis sets[1,4]. The study demonstrated statistical non-inferiority of alogliptin 25 mg and metformin compared with glipizide and metformin for the primary endpoint at weeks 52 and 104. In addition, statistical superiority of alogliptin 25 mg in combination with metformin compared with metformin and glipizide was demonstrated at week 104[4,16].

In this study, the mean dosage of the active comparator, glipizide, was lower than expected (5.2 mg daily). The Committee for Medicinal Products for Human Use (CHMP) highlighted that this dose may be a reflection of the low baseline HbA_{1c} and fasting plasma glucose values; however, based on this low dose the non-inferiority of alogliptin compared to glipizide as add-on therapy to metformin has not been established[4].

3.1.2 Study SYR-322-MET-008

This was a randomised, phase III, international, multi-centre, double-blind, placebo-controlled study designed to assess the efficacy and safety of alogliptin plus metformin compared with placebo in combination with metformin in adult patients with T2DM experiencing inadequate glycaemic control with metformin monotherapy[1,17]. Patients (n = 527) with T2DM and experiencing inadequate glycaemic control (defined as HbA_{1c} 7.0-10.0%) continued to receive a stable daily metformin dose of ≥ 1,500 mg or their MTD and were randomised to receive the addition of either placebo (n = 104), alogliptin 12.5 mg (n = 213) or 25 mg (n = 210) once-daily for a duration of 26 weeks[1,17]. The primary efficacy endpoint was the change in HbA_{1c} from baseline to week 26 performed for the FAS using the last observation carried forward (LOCF) method. Statistically significant ($p < 0.001$) reductions in HbA_{1c} were observed in the alogliptin 25 mg treatment arm when compared with placebo (see Table 1). This was supported by secondary endpoints and subgroup analyses[1,17].

3.2 Alogliptin in combination with a sulphonylurea

3.2.1 Study SYR-322-SULF-007

This study was designed to assess the efficacy and safety of alogliptin compared with placebo in combination with a sulphonylurea in patients with T2DM experiencing inadequate glycaemic control with sulphonylurea monotherapy[1]. This study was similar to that of study SYR-322-MET-008 in terms of design, methodology and endpoints (see above); however, instead of using metformin as an add-on to alogliptin or placebo, patients received glibenclamide ≥ 10 mg/day or MTD[1,4]. Statistically significant reductions in HbA_{1c} were observed in the alogliptin 25 mg treatment arm when compared with placebo (see Table 1). This was supported by secondary endpoints and subgroup analyses[1].

3.3 Systematic review and mixed treatment comparison

In the absence of head-to-head evidence for the efficacy and safety of alogliptin versus the other available DPP-4 inhibitors in the treatment of adult patients with T2DM who are receiving dual therapy (i.e. in combination with metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control; or in combination with a sulphonylurea when diet and exercise plus a sulphonylurea alone do not provide adequate glycaemic control), a systematic literature review and mixed treatment comparison (MTC) utilising Bayesian network analysis methods were conducted to estimate the relative efficacy and safety of these treatments. The MTCs were performed using a fixed effects approach, or random effects approach where possible, with model fit statistics presented.

The systematic literature review was conducted to identify published papers of randomised controlled trials (RCTs), systematic reviews and meta-analyses in order to compare alogliptin 25 mg versus the other available DDP-4 inhibitors at their recommended daily doses[1]. The review identified 1435 unique articles; after de-duplication and abstract screening, 155 articles were assessed for eligibility in the MTC. To reduce heterogeneity 25 studies (n = 20: add-on to metformin; n = 5: add-on to sulphonylurea) were selected for inclusion in the MTC. Separate 24 week (± 6 weeks; n = 14) and 52 week (± 6 weeks; n = 6) networks of selected RCTs were created for the add-on to metformin population; in the add-on to sulphonylurea population, only 24 week data were available for inclusion in the MTC.

The primary efficacy measure was mean change in HbA_{1c} from baseline and this formed the base case analyses for add-on to metformin and add-on to sulphonylurea populations. For the add-on to metformin population, the base case only included 24 week studies and a further two were excluded as the intention to treat (ITT) population data were not available. In the add-on to sulphonylurea patient population, all five

RCTs were included. The results for base case analyses (fixed effect model) are presented in Table 2. The company conclude that alogliptin is non-inferior to the other DPP-4 inhibitors. In addition, the random effects model (add-on to metformin only), secondary outcomes (including proportion of patients achieving HbA_{1c} < 7.0%, mean change in weight from baseline and proportion of subjects with at least one hypoglycaemic episode) and several MTC sensitivity analyses supported the applicant company's conclusion that there were no comparisons in which alogliptin 25 mg was found to be significantly less effective than any of the DPP-4 comparators[1].

Table 1. Overview of primary and secondary efficacy endpoints from the ENDURE, SYR-322-MET-008 and SYR-322-SULF-007 studies[1,16,18].

	Dual therapy with Metformin						Dual therapy with a sulphonylurea		
	Study SYR-322_305 (ENDURE)*			Study SYR-322-MET-008**			Study SYR-322-SULF-007**		
	Alogliptin 25 mg	Glipizide	Treatment difference	Alogliptin 25 mg	Placebo	Treatment difference	Alogliptin 25 mg	Placebo	Treatment difference
Primary efficacy endpoint:									
LS mean change (SE) in HbA_{1c} from baseline	−0.72% (0.037)	−0.59% (0.039)	−0.13% (1-sided 98.75% CI: −infinity to −0.006)	−0.6% (0.054)	−0.1% (0.076)	−0.48% (95% CI: -0.67 to −0.30) p < 0.001	−0.52% (0.058)	0.01% (0.0840	−0.53% (95% CI: −0.73 to −0.33) p < 0.001
Key secondary efficacy endpoints:									
LS mean change (SE) in FPG from baseline	−3.2 (1.28)	5.4 (1.29)	−8.6 (95% CI: −12.14 to −5.02) p < 0.001	−17.4 (2.53)	0.0 (3.55)	−17.4 (95% CI: −25.9 to −8.8) p < 0.001	−8.4 (3.36)	2.2 (4.77)	−10.5 (95% CI: −22.0 to 0.9) p = 0.072
Proportion of patients achieving $HbA_{1c} \leq 7.0\%$	420/878 (48.5%)	366/869 (42.8%)	OR: 1.361 (95% CI: 1.1035 to 1.6793) p = 0.004	92/207 (44.4%)	19/104 (18.3%)	p < 0.001	69 (34.8%)	18 (18.2%)	p = 0.002
LS mean change (SE) in body weight (kg) from baseline	−0.89 kg	+0.95 kg	-1.84 kg (95% CI: -2.191 to -1.486) p < 0.001	−0.67 kg	−0.39 kg	-0.28kg (95% CI: -0.94 to 0.38) p = 0.407	0.68 kg	−0.20 kg	0.88 (95% CI: 0.21 to 1.54) p = 0.01

* Changes from baseline to week 104
** Changes from baseline to week 26
CI: confidence interval; FPG: fasting plasma glucose; HbA_{1c}: glycosylated haemoglobin; LS: least squares; OR: odds ratio; SE: standard error.

Table 2. Mixed treatment comparison for the base case analyses of the primary endpoint, adjusted mean change in HbA_{1c}, at 24 weeks[1].

Comparator	DPP-4 comparator vs. alogliptin – fixed effects model add-on to metformin		DPP-4 comparator vs. alogliptin – fixed effects model add-on to sulphonylurea	
	Mean difference % comparator – alogliptin (95% CrI)*	Probability of alogliptin being non-inferior to comparator – fixed effects†§	Mean difference % comparator – alogliptin (95% CrI)*	Probability of alogliptin being non-inferior to comparator – fixed effects†§
Sitagliptin 100 mg	−0.11 (−0.33 to 0.11)	0.96	−0.04 (−0.36 to 0.28)	0.94
Saxagliptin 5 mg	0.11 (−0.11 to 0.32)	1.00	−0.19 (−0.44 to 0.06)	0.80
Linagliptin 5 mg	−0.10 (−0.34 to 0.14)	0.95	0.06 (−0.25 to 0.37)	0.99
Vildagliptin 100 mg	0.22 (0.02 to 0.42)	1.00	−0.17 (−0.48 to 0.14)	0.99

* A positive mean difference indicates a favourable outcome for alogliptin.
† At a margin of 0.3%. § The probability that alogliptin is non-inferior to at least one DPP-4 inhibitor is 1.00 (add-on to metformin) or 0.998 (add-on to sulphonylurea) with fixed effects model.

CrI: credible interval; DPP-4: dipeptidyl peptidase-4 inhibitor; mg: milligrams; vs: versus.

3.4 Comparative safety

At the time of licensing, CHMP concluded that the safety profile of alogliptin was similar to other DPP-4 inhibitors with no potential new safety adverse events identified[4].

Across the clinical study programme the most common treatment-emergent adverse events (TEAEs) reported in ≥ 5% of subjects treated with alogliptin 25 mg and more frequently than in subjects who received placebo or the active comparator, were headache, nasopharyngitis and upper respiratory tract infection[1,4]. Overall, a low and similar percentage of subjects across treatment groups experienced at least one severe adverse event (SAE)[4]. The most frequent SAE were reported in the cardiac disorder system organ class (SOC), followed by the infections and infestations SOC[4]. The administration of alogliptin 25 mg alone, as an add-on to a sulphonylurea, or as an add-on to metformin did not increase hypoglycaemia rate when compared to placebo[4]. Given the increased risk of pancreatitis reported with other DPP-4 inhibitors, pancreatitis is an identified risk in the Risk Management Plan[4].

The company submission also provided data from a cardiovascular safety outcomes study (EXAMINE). The company conclude that the 18 month study showed that treatment with alogliptin resulted in rates of major cardiovascular events that were similar to rates with placebo among patients with T2DM and substantial cardiovascular disease[1].

3.5 AWTTC critique

- The company suggest alogliptin should be considered for dual therapy (in combination with either metformin or a sulphonylurea) for the indication under consideration and in line with current clinical guidelines. The company has not provided any evidence outside of these settings.
- All of the available DPP-4 inhibitors have a marketing authorisation for use in dual therapy (with metformin or sulphonylurea), with the exception of linagliptin which is not licensed for use as dual therapy in combination with a sulphonylurea[2,19–22]. The applicant company state that the leading DDP-4 inhibitors in terms of use in dual therapy is sitagliptin, with around 80% of prescriptions in the UK[1]. They highlight there is very little use of vildagliptin in UK clinical practice, representing only about 1% of prescriptions[1]; vildagliptin is not endorsed for use in Wales for the indication under consideration[13].
- In the absence of any direct comparative data for alogliptin versus other DPP-4 inhibitors the company conducted a systematic literature review and MTC of DPP-4 inhibitors when used in combination with either metformin or a sulphonylurea. While a common approach to the lack of direct head-to-head comparison data, an indirect comparison has inherent limitations. However, the applicant company has taken steps to address these limitations and has outlined the advantages and disadvantages of their approach. The company recognised high between study heterogeneity particularly in the add-on to metformin patient population; however, sensitivity analyses supported the base case results that alogliptin is non-inferior to the other DPP-4 inhibitors in dual therapy.

4.0 SUMMARY OF THE EVIDENCE ON COST-EFFECTIVENESS

4.1 Cost-effectiveness evidence

4.1.1 Context

The company submission describes a cost-minimisation analysis (CMA) of alogliptin versus comparator DPP-4 inhibitors for the treatment of adult patients with T2DM over a 12-month treatment period from the perspective of NHS Wales for:

- Dual therapy in combination with metformin;
- Dual therapy in combination with a sulphonylurea.

The company compared the use of alogliptin in combination with metformin versus sitagliptin, saxagliptin and linagliptin in combination with metformin. The company also compared the use of alogliptin in combination with a sulphonylurea versus sitagliptin in combination with a sulphonylurea. Medication doses and costs are taken from the British National Formulary (BNF)[23].

The CMA was restricted for the use of alogliptin as dual therapy with metformin or a sulphonylurea. The use of alogliptin in combination with metformin and a sulphonylurea (i.e. triple therapy) or insulin was not included in the analysis.

The company justified use of the cost-minimisation approach on the assumption of equal efficacy and safety. These assumptions were based on indirect comparisons between alogliptin and the other DPP-4 inhibitors in combination with metformin or a sulphonylurea. The company claimed that the MTC showed non-inferiority between alogliptin and the other DPP-4 inhibitors for the outcomes of change in HbA_{1c} from baseline, proportion of patients achieving HbA_{1c} < 7.0%, change in body weight and incidence of hypoglycaemic events.

Only the medicine costs of the DPP-4 inhibitors, metformin and sulphonylurea were included in the economic analysis. The company claimed that resource use associated with patient management was not expected to differ significantly between the DPP-4 inhibitors and hence were not included.

4.1.2 Results

Results of the base case analysis suggest that alogliptin in combination with metformin is associated with lower costs compared to the combination of other DPP-4 inhibitors with metformin. Using alogliptin in combination with metformin instead of sitagliptin (or linagliptin) is estimated to result in savings of £87 per patient over a 12-month period. Using alogliptin in combination with metformin instead of saxagliptin would result in savings of £65 per patient over a 12-month period. Similarly, alogliptin in combination with a sulphonylurea is estimated to be associated with lower costs than sitagliptin in combination with a sulphonylurea and would result in a saving of £87 per patient over a 12-month period.

Table 3. Company reported results of the base case analysis.

	Total annual cost
Dual therapy with metformin:	
Alogliptin	£353.79
Sitagliptin	£440.61
Saxagliptin	£418.97
Linagliptin	£440.61
Dual therapy with a sulphonylurea:	
Alogliptin	£356.54
Sitagliptin	£443.36

The applicant company did not conduct any sensitivity analyses and claimed that this was not applicable as the model only included medicine costs.

4.1.3 AWTTC critique

The applicant company's justification for use of the cost-minimisation approach is based on assumptions of equal efficacy and safety. These assumptions were based on indirect comparisons between alogliptin and the other DPP-4 inhibitors in combination with metformin or a sulphonylurea. The MTC suggested non-inferiority between alogliptin and the other DPP-4 inhibitors for the outcomes of change in HbA_{1c} from baseline, proportion of patients achieving HbA_{1c} < 7.0%, change in body weight and incidence of hypoglycaemic events. However, non-inferiority in surrogate outcomes, such as HbA_{1c}, does not necessarily equate to equivalence in health outcomes associated with complications from T2DM and patient preferences in relation to medicine therapy. Furthermore, whilst the MTC suggested non-inferiority between the different DPP-4 inhibitors for the outcomes compared, there are some numerical differences, which whilst not all statistically significant, may suggest actual differences in efficacy.

Other limitations of the economic evidence include:

- The population included in the economic analysis did not include the full licensed indication i.e. the company did not submit economic evidence for the use of alogliptin in combination with metformin and a sulphonylurea (triple therapy) or the use of alogliptin in combination with insulin.
- The applicant company limited the number of comparators included in the economic analysis. Linagliptin is not licensed for dual therapy in combination with a sulphonylurea[19] and vildagliptin is not endorsed for use in Wales for the indication under consideration[13]; therefore, these were not included as comparators. However, saxagliptin in combination with a sulphonylurea could have been included as a comparator[20].
- The applicant company did not include the impact of drop outs in the economic analysis despite drop-out rates being high (44%) in the alogliptin 25 mg treatment arm of the ENDURE study.

5.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

5.1 Budget impact evidence

5.1.1 Context and methods

The company estimates the total number of adult patients with T2DM in Wales to be 155,969[24,25]. This is based on a prevalence of diabetes in Wales of 6.7%[26] and T2DM accounting for 90% of cases[25]. Based on 7,000 new diabetes cases in Wales each

year[25], the company assume an annual number of incident cases of T2DM of 6,650. Using a mortality rate of 3.6% in the diabetes population[27], they thus assume that there would be 156,765 patients with T2DM in year one increasing to 182,407 patients in year five. Based on estimates from NICE, they assume that 90% of patients with T2DM receive treatment, with 4.5% of these treated patients receiving dual therapy with a DPP-4 inhibitor[27]. The company assumes that 10% of those receiving dual therapy with a DPP-4 inhibitor will receive alogliptin in year one, increasing to 50% in year five.

The company has based its budget impact analysis on the costs of DPP-4 inhibitors only and estimates the proportion of patients on each DPP-4 inhibitor therapy that alogliptin will replace.

5.1.2 Results

The applicant company estimates the acquisition costs of treatment with alogliptin to be £346.75 per patient per year, compared with £433.57 for sitagliptin, £411.93 for saxagliptin and £433.57 for linagliptin. The estimated number of patients and the associated costs based on BNF list prices as described by the applicant company in their budget impact analysis are summarised in Table 4. This is based on each of the existing DPP-4 inhibitors being displaced in proportion to its current market share in Wales – sitigliptin 75%, saxagliptin 21%, linagliptin 4%.

Table 4. Company-reported net costs associated with the use of alogliptin as dual therapy for the treatment of adult patients with T2DM.

	Year 1	Year 2	Year 3	Year 4	Year 5
Number of DPP-4 treated patients	6,349	6,609	6,868	7,128	7,387
Alogliptin uptake	10%	20%	30%	40%	50%
Treated patients	635	1,322	2,060	2,851	3,694
Net costs					
Overall net cost	**-£52,239**	**-£108,751**	**-£169,535**	**-234,592**	**-£303,921**

5.1.3 AWTTC critique

The company estimated the eligible patient numbers based on prevalence and incidence rates for diabetes in Wales.

- The applicant company only included drug costs in its estimation of the net costs.
- The applicant company did not include the impact of drop-outs in its analysis of the budget impact.
- The applicant company did not conduct sensitivity analyses.

5.2 Comparative unit costs

Table 5 includes acquisition costs of DPP-4 inhibitors for the treatment of adult patients with T2DM. The example acquisition costs are based on a 28-day treatment period.

Table 5. Examples of acquisition costs per patient of DPP-4 inhibitors for the treatment of adult patients with T2DM.

Regimens	Example maintenance dose*	Cost per 28 days†
Alogliptin (Vipidia®▼) 6.25 mg, 12.5 mg and 25 mg film-coated tablets	25 mg once daily	£26.60
Sitagliptin (Januvia®) 25 mg, 50 mg and 100 mg film-coated tablets	100 mg once daily	£33.26
Saxagliptin (Onglyza®) 2.5 mg and 5 mg film-coated tablets	5 mg once daily	£31.60
Linagliptin (Trajenta®▼) 5 mg film-coated tablets	5 mg once daily	£33.26
Vildagliptin (Galvus®) 50 mg tablets	50 mg once daily (dual therapy with a sulphonylurea) 50 mg twice daily (dual therapy with metformin)	£15.88 £31.76

* Regimen based on SPC dosing instructions[2,19–22].
† Costs based on Monthly Index of Medical Specialities (MIMS) list prices as of July 2014[28].

This table does not imply therapeutic equivalence of medicines or the stated doses.
Refer to the SPCs for full dosing details[2,19–22].

6.0 ADDITIONAL INFORMATION

6.1 Prescribing and supply

AWTTC is of the opinion that, if recommended, alogliptin (Vipidia®▼) may be appropriate for prescribing by all prescribers within NHS Wales for the indication under consideration.

The company do not anticipate that alogliptin (Vipidia®▼) will be supplied by a home healthcare provider.

6.2 Ongoing studies

The company submission states that there are no ongoing studies from which additional evidence is likely to be available within the next 6–12 months.

6.3 AWMSG review

This assessment report will be considered for review three years from the date of the Final Appraisal Recommendation.

6.4 Evidence search

Date of evidence search: 12-13 June 2014
Date range of evidence search: No date limits were applied to database searches.

GLOSSARY

Glycosylated haemoglobin (HbA_{1c})
This is a measure of the average blood glucose level of a patient in the previous 2-3 months, where a higher HbA_{1c} level means that more glucose has been present in the blood. Previously, HbA_{1c} results were reported as a percentage; however, from October 2011, laboratories in the UK switched to reporting results using new HbA_{1c} units, mmol/mol[29] (see Table 7).

Table 6. Comparison of HbA_{1c} results[29].

HbA_{1c} (%)	HbA_{1c} (mmol/mol)
6.0	42
6.5	48
7.0	53
7.5	59
8.0	64
9.0	75

Full analysis set (FAS)
All randomised patients in the safety set. For a particular outcome, the FAS analysis set consisted of all patients who had a baseline assessment and at least one post-baseline assessment for that outcome. In FAS efficacy analyses, patients were analysed by their randomised treatment assignment.

Per protocol set (PPS)
All FAS patients who had no major protocol violations. In PPS analyses, patients were analysed by their randomised treatment assignment.

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