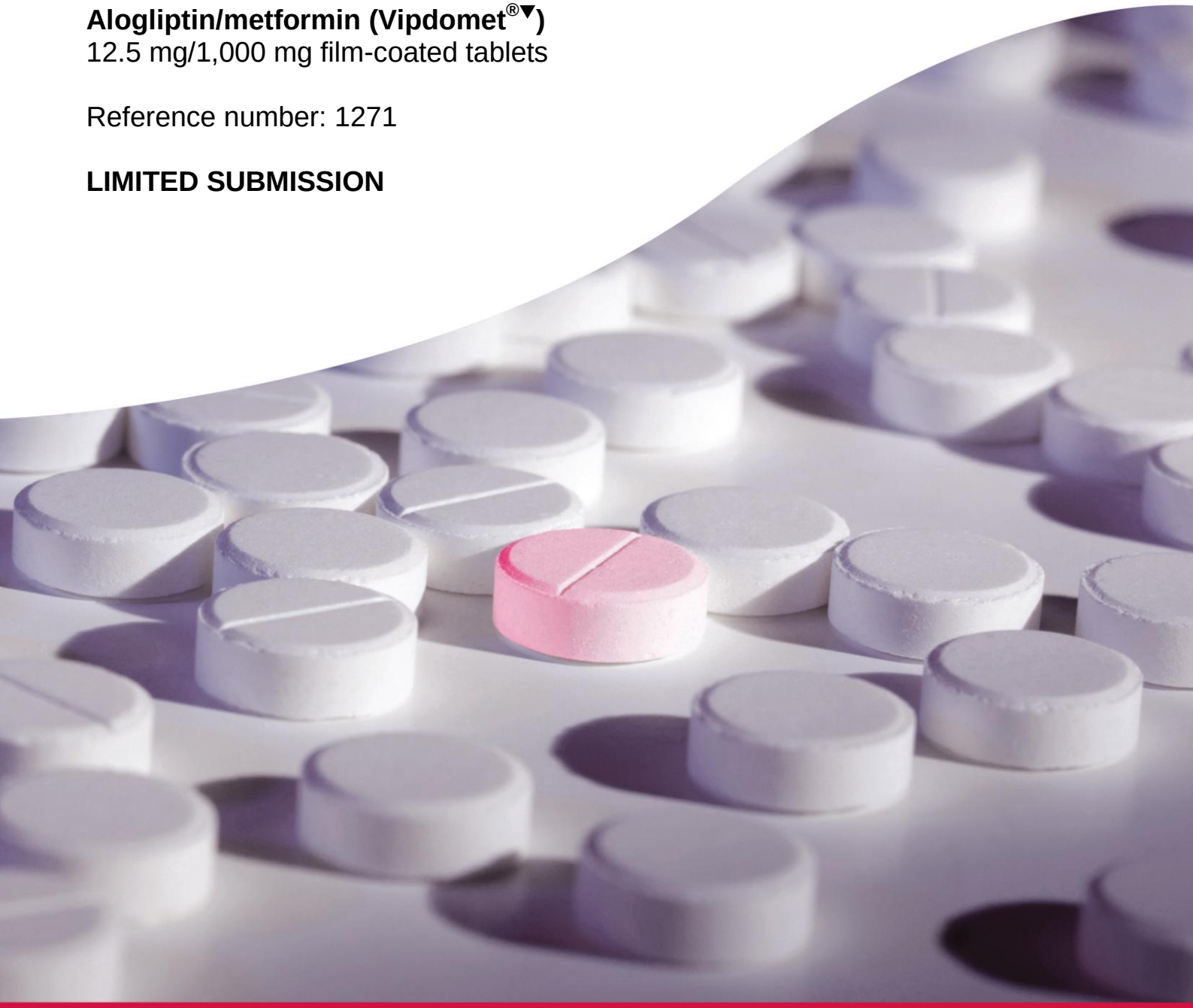
All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG SECRETARIAT ASSESSMENT REPORT

Alogliptin/metformin (Vipdomet®▼)
12.5 mg/1,000 mg film-coated tablets

Reference number: 1271

LIMITED SUBMISSION



This report has been prepared by the All Wales Therapeutics and Toxicology Centre (AWTTC), in collaboration with the Centre for Health Economics & Medicines Evaluation, Bangor University.

Please direct any queries to AWTTC:

All Wales Therapeutics and Toxicology Centre (AWTTC)
University Hospital Llandough
Penlan Road
Llandough
Vale of Glamorgan
CF64 2XX

awttc@wales.nhs.uk
029 2071 6900

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AWMSG Secretariat Assessment Report
Alogliptin/metformin (Vipdomet®▼) 12.5 mg/1,000 mg film-coated tablets

This assessment report is based on evidence from a limited submission by Takeda UK Ltd on 13 February 2014[1].

1.0 PRODUCT AND APPRAISAL DETAILS

Licensed indication under consideration	Alogliptin/metformin (Vipdomet®▼) is indicated in the treatment of adult patients aged 18 years and older with type 2 diabetes mellitus: • As an adjunct to diet and exercise to improve glycaemic control in adult patients, inadequately controlled on their maximal tolerated dose of metformin alone, or those already being treated with the combination of alogliptin and metformin; • In combination with pioglitazone (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled on their maximal tolerated dose of metformin and pioglitazone; • In combination with insulin (i.e. triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control in patients when insulin at a stable dose and metformin alone do not provide adequate glycaemic control[2].
Dosing	The recommended dose is one tablet of 12.5 mg/1,000 mg twice daily with meals, corresponding to 25 mg alogliptin plus 2,000 mg metformin daily. 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]
Comparators	The comparator included in the company submission was the individual components, alogliptin (Vipidia®▼) and metformin.
Limited submission details	Alogliptin/metformin (Vipdomet®▼) for the above indication met the following criteria for eligibility for a limited submission: • Significant new formulation with a pro-rata or lower cost per treatment. • Anticipated usage in NHS Wales is considered to be of minimal budgetary impact.

2.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

The All Wales Medicines Strategy Group (AWMSG) appraises a medicine within the whole of its licensed indication. However, the applicant company has requested that AWMSG considers alogliptin/metformin as an adjunct to diet and exercise to improve glycaemic control in adult patients, inadequately controlled on their maximal tolerated dose of metformin alone, or those already being treated with the combination of

alogliptin and metformin. The applicant company suggest that alogliptin/metformin should be considered for use in patients for whom a combination of alogliptin and metformin is an appropriate choice of therapy and only when the addition of a sulphonylurea to metformin monotherapy is not appropriate[1].

2.1 Evidence of clinical effectiveness

The Committee for Medicinal Products for Human Use (CHMP) concluded that the bioequivalence of the combination alogliptin/metformin tablet to individual alogliptin and metformin tablets was demonstrated[4]. The company highlighted clinical studies of co-administration of alogliptin and metformin as separate tablets to support the efficacy and safety of the combination tablet of alogliptin/metformin[1].

The safety profile was consistent with that of the individual components as demonstrated in clinical trials for alogliptin and from the comprehensive data available for metformin[1,2]. CHMP concluded that when compared with other dipeptidyl-peptidase-4 (DPP-4) inhibitors there were no potential new adverse events for the alogliptin component[4].

2.2 Points to note

- AWMSG is concurrently appraising alogliptin (Vipidia®▼) for the treatment of adults with type 2 diabetes mellitus (T2DM)[5].
- The applicant company suggest that alogliptin/metformin should be considered within its licensed indication, for use in patients for whom a combination of alogliptin and metformin is an appropriate choice of therapy (i.e. dual therapy only)[1]. The company envisage that patients would receive alogliptin/metformin fixed dose combination product if they are inadequately controlled on their maximal tolerated dose of metformin alone or if they are already being treated with the combination of alogliptin and metformin as separate tablets[1].
- The usual recommended individual dose of alogliptin is 25 mg once-daily[6]. As one alogliptin/metformin tablet is taken twice daily, the individual dose of alogliptin is halved (12.5 mg)[1,2]. Clinical results indicated that there was no difference in efficacy when alogliptin is administered once-daily versus twice-daily[4].
- The fixed dose combination of alogliptin/metformin is only available in the UK at a strength of 12.5/1,000 mg; therefore, the combination tablet is only appropriate for patients able to tolerate a total daily dose of metformin of 2,000 mg.

3.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

3.1 Budget impact evidence

The applicant company estimates the total number of adult patients in Wales with T2DM as 155,969[7,8]. Based on incidence rates for diabetes in Wales[8] and mortality rates in the diabetes population[9], the applicant company assume that there would be 156,765 patients with T2DM in year one increasing to 182,407 patients in year five[1].

Based on estimates from the National Institute for Health and Care Excellence (NICE) costing template for dapagliflozin, the applicant company assume that 90% of patients with T2DM receive treatment[10]. The applicant company estimates the proportion of patients on fixed dose combinations of a DPP-4 inhibitor plus metformin in NHS Wales to be 0.2%, which is reflected in the budget impact estimates provided in Table 1. It is assumed that 10% of those receiving dual therapy with a DPP-4 inhibitor will receive alogliptin/metformin in year one, increasing to 50% in year five[1]. The applicant company anticipates that all patients treated with alogliptin and metformin as individual components will be eligible to receive alogliptin/metformin.

Table 1. Incremental budget impact when using alogliptin/metformin fixed-dose combination as dual therapy for the treatment of adult patients with T2DM[1].

	Year 1	Year 2	Year 3	Year 4	Year 5
Proportion of patients on fixed dose combinations of DPP-4 inhibitor plus metformin	282	294	305	317	328
Proportion of patients treated with alogliptin/metformin	10%	20%	30%	40%	50%
Number of patients treated with alogliptin/metformin	28	59	92	127	164
Incremental cost per patient	−£45.36	−£45.36	−£45.36	−£45.36	−£45.36
Budget impact	**−£1,270**	**−£2,676**	**−£4,173**	**−£5,761**	**−£7,439**
Figures are rounded up or down to nearest whole number.					

3.1.1 AWTTC critique

- The sources used for estimating prevalence, incidence and the proportion of patients eligible to receive treatment for the indication under consideration appears reasonable.
- Patients receiving fixed dose combinations of DPP-4 inhibitors plus metformin includes those taking sitagliptin, saxagliptin, linagliptin and vildagliptin fixed dose combinations; the company has not estimated the relative market share of these comparators.
- The company has not estimated the number of patients likely to receive alogliptin and metformin as individual components.
- The incremental cost per patient appears to be based entirely on the displacement costs of alogliptin plus metformin as individual components and does not include the costs of displacement of other DPP-4 inhibitors plus metformin fixed dose combinations.
- The company estimated budget impact analysis is therefore subject to uncertainty; however, cost savings are anticipated due to the lower acquisition cost of fixed dose alogliptin/metformin.

3.2 Comparative unit costs

Table 2 provides an example of the comparative annual acquisition costs for alogliptin/metformin and other DPP-4 inhibitors in combination with metformin as fixed dose combinations, in addition to alogliptin plus metformin as individual components.

Table 2. Examples of annual costs for alogliptin/metformin and fixed-dose combination comparators for the treatment of adult patients with T2DM.

Medicine	Example regimen*	Annual cost †
Alogliptin (Vipidia®▼) 6.25 mg, 12.5 mg and 25 mg film-coated tablets **Metformin (non-proprietary)** 500 mg and 850mg tablets	25 mg once-daily plus 1,000 mg twice-daily	£392.11
Alogliptin/metformin (Vipdomet®▼) 12.5 mg/1,000 mg film-coated tablets	12.5 mg/1,000 mg twice-daily	£346.75
Saxagliptin/metformin (Komboglyze®) 2.5 mg/850 mg and 2.5 mg/1,000 mg film-coated tablets	2.5 mg/1,000 mg twice-daily	£411.93
Vildagliptin/metformin (Eucreas®) 50 mg/850 mg and 50 mg/1,000 mg film-coated tablets	50 mg/1,000 mg twice-daily	£413.42
Linagliptin/metformin (Jentadueto®▼) 2.5 mg/850 mg and 2.5 mg/1,000 mg film-coated tablets	2.5 mg/1,000 mg twice-daily	£433.57
Sitagliptin/metformin (Janumet®) 50 mg/1,000 mg film-coated tablets	50 mg/1,000 mg twice-daily	£433.57

*Regimen based on SPC dosing instructions[2,6,11–15]
† Costs are based on Monthly Index of Medical Specialities (MIMS) list prices as of July 2014[16].

This table does not imply therapeutic equivalence of medicines or the stated doses.
Refer to the SPCs for full dosing details[2,6,11–15].

4.0 ADDITIONAL INFORMATION

4.1 Prescribing and supply

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

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

4.2 AWMSG review

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

4.3 Evidence search

Date of evidence search: 27-30 June 2014
Date range of evidence search: No date limits were applied to database searches.

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