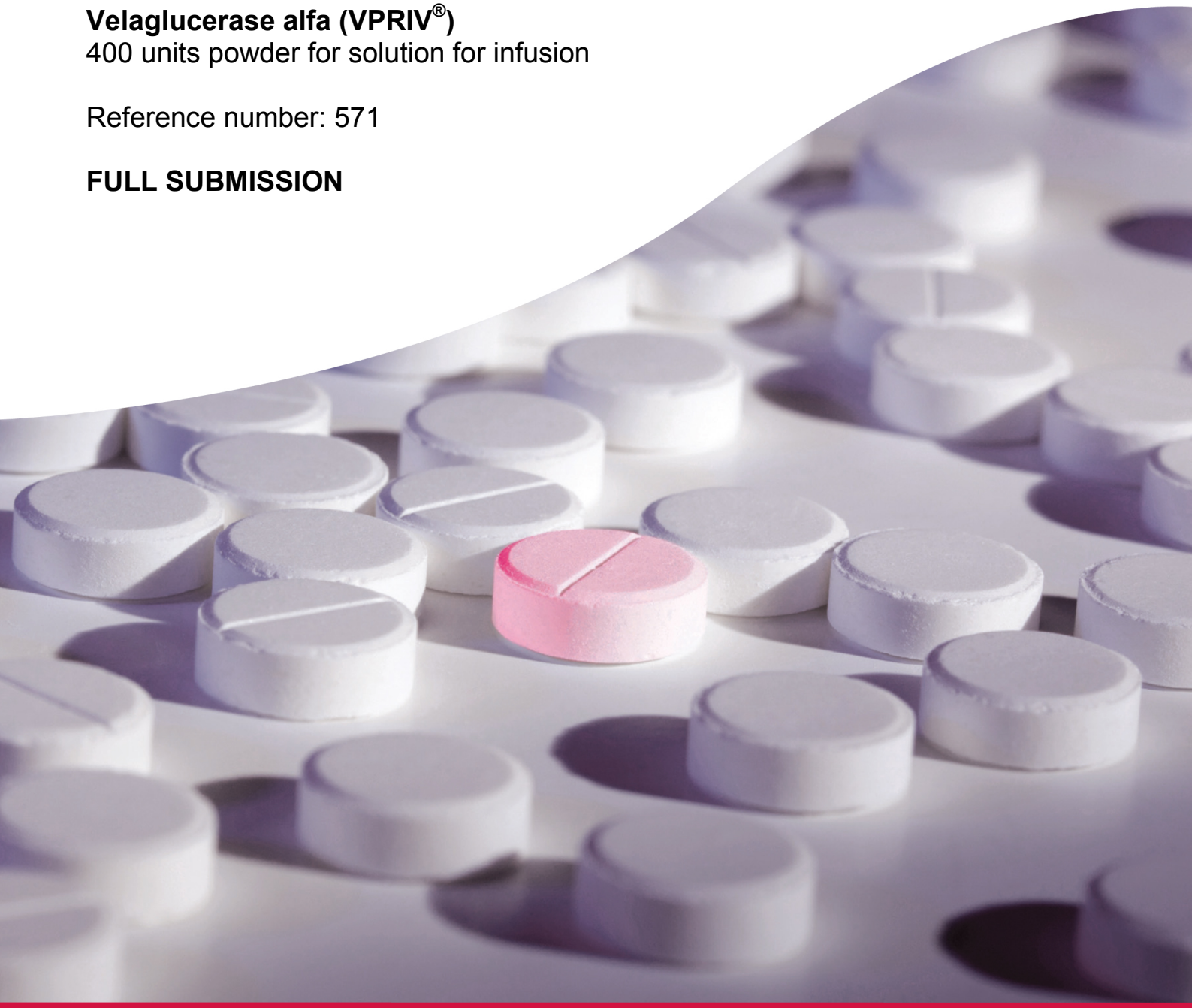
All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG SECRETARIAT ASSESSMENT REPORT

Velaglucerase alfa (VPRIV®)
400 units powder for solution for infusion

Reference number: 571

FULL SUBMISSION



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AWMSG Secretariat Assessment Report
Velaglucerase alfa (VPRIV®) 400 units powder for solution for infusion

This assessment report is based on evidence submitted by Shire Pharmaceuticals Ltd on 31 January 2014[1].

1.0 PRODUCT DETAILS

Licensed indication under consideration	Velaglucerase alfa (VPRIV®) is indicated for long-term enzyme replacement therapy in patients with type 1 Gaucher disease[2].
Dosing	The recommended dose of velaglucerase alfa is 60 units/kg administered every other week as a 60-minute intravenous infusion. Dose adjustments can be made on an individual basis based on achievement and maintenance of therapeutic goals. Patients currently treated with imiglucerase enzyme replacement therapy for type 1 Gaucher disease may be switched to velaglucerase alfa, using the same dose and frequency. Home administration under the supervision of a healthcare professional may be considered only for patients who have received at least three infusions and were tolerating their infusions well. Refer to the Summary of Product Characteristics (SPC) for further information[2].
Marketing authorisation date	26 August 2010[2].

2.0 DECISION CONTEXT

2.1 Background

Gaucher disease is a rare, autosomal recessive, lysosomal glycosphingolipid storage disorder. Glucosylcerebroside (GlcCer) is a type of fat molecule that is broken down by the enzyme beta-glucocerebrosidase (GCase)[3,4]. Individuals with Gaucher disease lack GCase and this leads to an accumulation of GlcCer in cells, which are known as Gaucher cells[2–4]. Gaucher disease can be classified into three clinical types: type 1 (non-neuronopathic) disease, where partial deficiency of GCase is associated with parenchymal disease of the liver, spleen, bone marrow and, in severe cases, the lung; and types 2 and 3 (acute neuronopathic and sub-acute neuronopathic, respectively), where severe deficiency of GCase is additionally associated with neurological manifestations[5]. Type 1 Gaucher disease varies in severity, partly as a result of varying residual enzyme activity, ranging from mild asymptomatic cases (which may go undiagnosed) to severe, life threatening disease[4]. Gaucher disease has been estimated to affect approximately 0.3 patients in 10,000 people in the European Union[6], of which type 1 is the most common subtype[7].

Beside palliative therapies, such as splenectomy and blood transfusions, the aim of treatment is to reduce GlcCer accumulation in affected tissues of patients with Gaucher disease, improving haemoglobin concentration and platelet count while reducing spleen and liver volumes[3,8]. The preferred first line therapy for patients with type 1

Gaucher disease is enzyme replacement therapy (ERT)[4,9], consisting of complementation of endogenous lysosomal enzyme activity by intravenous infusion of GCase[10]. Velaglucerase alfa is an ERT, consisting of GCase produced by gene activation in a human cell line, and contains the same amino acid sequence as the naturally occurring human enzyme[2–4]. However, the carbohydrate content has been engineered to contain predominantly high mannose-type-linked glycans, which facilitates uptake into the phagocytic target cells via the mannose receptor[3,4]. In adult patients where ERT is not a therapeutic option, the recommended treatment is substrate reduction therapy (SRT)[4], using medicines such as miglustat (Zavesca®), where the aim is to suppress production of glycosphingolipids, such as GlcCer, reducing intracellular concentration to a level where residual enzyme activity is sufficient to prevent accumulation[11].

2.2 Comparators

The comparator included in the company submission was imiglucerase.

2.3 Guidance and related advice

- Paediatric Gaucher disease in England: guidelines for assessment, monitoring and enzyme replacement therapy (2012)[9].
- Adult Gaucher disease standard operating procedures (2012)[4].
- Guidelines for the management of paediatric Gaucher Disease in the United Kingdom (2005)[12].
- UK National Guideline for Adult Gaucher Disease (2005)[10].

3.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

As evidence of clinical effectiveness, the applicant company has provided a pivotal phase III study (HGT-GCB-039), which compared velaglucerase alfa and imiglucerase for the first line treatment of type 1 Gaucher disease (see Section 3.1)[1]. The company submission also includes studies TKT034 and HGT-GCB-058, which investigated the safety and efficacy of switching from treatment with imiglucerase, and studies HGT-GCB-044 and TKT025/TKT025EXT, which provided evidence of long-term safety and effectiveness (see Section 3.2).

Additionally, the applicant company presented the dose-finding study TKT032 as supporting evidence[1]. This study does not add to the evidence of the effectiveness of velaglucerase alfa in comparison with imiglucerase and so will not be discussed further.

3.1 Study HGT-GCB-039

This was a nine-month, multicentre, randomised, double-blind, parallel-group, noninferiority trial that evaluated the safety and efficacy of velaglucerase alfa compared with imiglucerase for the treatment of type 1 Gaucher disease[13]. Patients (n = 35) were randomised (1:1) to receive either velaglucerase alfa or imiglucerase, both of which were administered as a continuous 60-minute intravenous infusion at a dose of 60 units/kg every other week for 39 weeks (20 infusions). Eligible patients were ≥ 2 years of age, diagnosed with Gaucher disease characterised clinically as type 1, had not received treatment for this disease ([Commercial in confidence data removed]) within the past 12 months, and had disease-related anaemia along with at least one of the following symptoms: disease-related thrombocytopenia, moderate splenomegaly (if not splenectomised), or enlarged liver by palpation[13,14]. All four patients aged 2–4 years were recruited into the imiglucerase treatment group; no patients aged < 4 years received treatment with velaglucerase alfa[3].

The primary endpoint was the mean change in haemoglobin concentration from baseline to week 41, which was 1.624 g/dl in the velaglucerase alfa group and 1.488 g/dl in the imiglucerase treatment arm (treatment difference: 0.135 g/dl; lower bound of the 97.5% one-sided confidence interval [CI]: −0.596 g/dl). This met the criteria for demonstrating the noninferiority of velaglucerase alfa (lower bound of 97.5% one-sided CI within the predefined margin of −1.0 g/dl). This was supported by analysis of secondary endpoints (see Table 1)[13]; although changes in platelet count were numerically higher in the imiglucerase group, this was not statistically significant and a post-hoc analysis suggest that there is no relevant difference[3]. Comparable changes were also observed in responses from 13 adult patients to the Short Form 36 (SF36) questionnaire (six patients from the velaglucerase alfa group and seven from the imiglucerase group), a self-reported measure of quality of life; only one paediatric patient (aged 5–17 years) from each group provided quality-of-life data. Consequently, due to the small numbers involved no conclusions could be drawn[3].

Table 1. Analysis of endpoints from study HGT-GCB-039[13].

	Velaglucerase alfa (n = 17)	Imiglucerase (n = 17)	Treatment difference
Primary endpoint			
Mean change from baseline haemoglobin concentration (g/dl)	1.624	1.488	0.135 (lower bound of 97.5% one-sided CI: −0.596)
Secondary and ancillary endpoints			
Mean change from baseline platelet count (x 10^9/l)	108.0	146.7	−38.7 (95% two-sided CI: −88.4 to 11.0)
Mean change from baseline liver volume (% body weight)	−1.24	−1.17	−0.07 (95% two-sided CI: −0.43 to 0.29)
Mean change from baseline spleen volume* (% body weight)	−1.86	−1.94	0.08 (95% two-sided CI: −0.52 to 0.68)
* population data available for seven patients in each group.			

3.2 Supporting studies

3.2.1 Switching from treatment with imiglucerase to velaglucerase alfa

Study TKT034 was a 12-month, open-label, phase II/III study designed to evaluate the safety of velaglucerase alfa in 40 patients with type 1 Gaucher disease (≥ two years old) who were clinically stable on imiglucerase therapy (dose range 15–60 units/kg for a minimum of 30 consecutive months)[15]. Patients were switched to velaglucerase alfa administered at the same dose and frequency as their imiglucerase dose; 25 of 40 eligible patients received velaglucerase alfa as a home infusion at least once. Investigators had the option of increasing the patient's dose by 15 units/kg if a clinically significant deterioration occurred; however, no dose adjustments were made during the study and no patient was withdrawn because the investigator wished to increase the dose above 60 units/kg. Results indicated that haemoglobin concentrations, platelet counts and spleen and liver volumes were sustained at therapeutic levels through 12 months of treatment, thus demonstrating preservation of treatment effect after switching from imiglucerase to velaglucerase alfa[15].

Study HGT-GCB-058 was an open-label, phase III study designed to evaluate the safety of velaglucerase alfa in 211 patients (≥ two years old) with type 1 Gaucher disease[1]. Of these patients, 205 were previously treated with imiglucerase and received velaglucerase alfa infusions every other week at the same number of units as imiglucerase within the range of 15–60 units/kg; [Commercial in confidence data removed].

3.2.2 Long-term cohort studies

Study HGT-GCB-044 was a multicentre, open-label, phase III, cohort study conducted over 62 months and designed to evaluate the long-term safety and efficacy of velaglucerase alfa in patients with type 1 Gaucher disease[1]. Eligible patients had completed studies TKT032, TKT034, and HGT-GCB-039; patients receiving imiglucerase as part of study HGT-GCB-039 were also included. Patients (n = 93) received velaglucerase alfa (dose range: 15–60 units/kg) as an intravenous infusion every other week. The primary outcome was long-term safety, but secondary outcomes assessed efficacy, and demonstrated that changes in haemoglobin concentrations, platelet counts and spleen and liver volumes were sustained at therapeutic levels at 24 months following first administration of study drug in original study[1].

Study TKT025 was a phase I/II, open-label, single-arm, single-centre study, where 12 patients with type 1 Gaucher disease received velaglucerase alfa over nine months and demonstrated significant improvements in haematological parameters and organomegaly[1,17]. Study TKT025EXT was an open-label, phase I/II, extension study that evaluated the long-term safety and efficacy of velaglucerase alfa in patients with type 1 Gaucher disease who had previously completed study TKT025. Of the 11 patients that completed study TKT025, 10 enrolled in the long-term extension study and continued to receive velaglucerase alfa every other week (dose: 30–60 units/kg). Results demonstrated the long-term therapeutic effect of velaglucerase alfa on haemoglobin concentrations, platelet counts and spleen and liver volumes was maintained over five years[1,17].

3.3 Comparative safety

Evidence of comparative safety comes from study HGT-GCB-039, where 8/17 (47.1%) patients in the velaglucerase alfa group experienced adverse events (AEs) considered treatment-related, compared with 6/17 (35.3%) in the imiglucerase group[13]. These were most commonly infusion-related events (five patients in the velaglucerase alfa group versus four in the imiglucerase group). Four treatment-emergent serious AEs were reported in three patients from the velaglucerase alfa group only, of which one AE was considered potentially related to study treatment (allergic dermatitis)[3,13]. Two patients receiving velaglucerase alfa had a severe or life-threatening AE considered probably related to study medication (severe prolonged activated partial thromboplastin time [aPTT] and severe allergic dermatitis) versus one patients from the imiglucerase group (severe chills)[3,14]. No deaths or discontinuations due to AEs were reported; however, one patient receiving imiglucerase withdrew consent following multiple infusion-related reactions[13]. Four patients in the imiglucerase group developed antibodies to imiglucerase; no patients in the velaglucerase alfa group developed anti-drug antibodies[3].

HGT-GCB-044 (see Section 3.2.2) provided safety data for up to 5.8 years of follow-up[1]. Investigators concluded that there were no new safety signals observed among the 95 patients (73 adults and 22 paediatric patients) over the course of the study.

[Commercial in confidence data removed]

At the time of licensing, the Committee for Medicinal Products for Human Use (CHMP) stated that the overall AE profile observed during study HGT-GCB-039 was comparable between velaglucerase alfa and imiglucerase, with the exception of the incidence of serious AEs and the case of aPTT[3], which is reflected in the velaglucerase alfa SPC[2]. The AE profile of patients transitioned from imiglucerase to velaglucerase alfa was not considered to reveal any unexpected findings. Additionally, CHMP considered the long-term safety of velaglucerase to appear comparable to that observed up to nine months, but stated that the small numbers make it impossible to draw any conclusions[3].

3.4 AWTTC critique

- Analysis of submitted studies is restricted by low patient numbers, limiting the extent to which conclusions can be drawn on the safety and effectiveness of velaglucerase alfa; however, given the low prevalence of type 1 Gaucher disease, CHMP considered patient exposure to be adequate[3]. Additionally, the applicant company has suggested that the clinical trial registration programme for velaglucerase alfa is the largest and most comprehensive for an approved ERT in type 1 Gaucher disease[1].
- Based on evidence from study HGT-GCB-039, UK guidance concludes that from a clinical perspective, velaglucerase alfa and imiglucerase are broadly equivalent as ERT for type 1 Gaucher disease[4]. Similarly, CHMP has concluded that velaglucerase alfa has an equivalent clinical efficacy and safety profile to that of imiglucerase[3].
- Although uncontrolled, cohort studies suggest that the beneficial effects of velaglucerase alfa are sustained or improved over longer-term treatment[3], evidence of comparative effectiveness beyond nine months is unavailable.
- There is a lack of quality-of-life data available to compare velaglucerase alfa and imiglucerase, especially in paediatric patients; however, in adult patients, the limited data available appears to show comparable improvements[3].
- Use of velaglucerase alfa in patients aged 4–17 years is supported by evidence from controlled studies, comprising 20/94 (21.3%) patients treated with velaglucerase alfa, and safety and efficacy profiles were demonstrated to be similar between paediatric and adult patients[2]. However, no data are available for children under the age of four years.
- CHMP noted that velaglucerase alfa, like imiglucerase, appears to induce antibodies including neutralising antibodies and that antibody formation appears to be numerically higher in patients on imiglucerase than on velaglucerase alfa. However, absolute numbers were considered to be low and therefore no definite conclusions could be drawn[3].
- There were several imbalances in baseline characteristics among patient groups in study HGT-GCB-039 that had the potential to affect outcomes, including haemoglobin levels, platelet count, spleen volume and the number of children aged 2−4 years[3,13]. However, an analysis adjusting for the baseline haemoglobin levels confirmed the primary efficacy analysis, while baseline platelet count differences were not considered clinically meaningful and changes in spleen volume indicated a comparable response between the groups. The overall effect of the imbalance of patients aged 2–4 years is uncertain, but post hoc analyses suggest that patients in this age group skewed results from the analysis of platelet count change[3].
- Long-term registry data for the use of imiglucerase is available from the International Collaborative Gaucher Group (ICGG) Gaucher Registry, and this registry data has been included in the imiglucerase SPC[18,19]. Data regarding the long-term safety of velaglucerase alfa in clinical trials is included in the submission[1], but real-world data is not yet available. The Gaucher disease Observational Survey, however, has been undertaken as an ongoing, long-term, observational database that will collect additional data on treatment with velaglucerase alfa (see Section 6.2)[1], as noted in the Risk Management Plan[3].
- Like imiglucerase, initial treatment with velaglucerase alfa is also required to be undertaken in hospital[2,18,19]. However, while administration of imiglucerase at home may be considered for patients who are tolerating infusions well for several months[18,19], home administration of velaglucerase alfa may be considered for patients who have received at least three infusions[2].
- The applicant company has advised that although two vial strengths (200 units and 400 units) are licensed, only the higher strength will be available in the UK[1]. Imiglucerase is available in both 200 unit vials and 400 unit vials[18,19], providing more flexibility and potentially less wastage.

- While both velaglucerase alfa and imiglucerase are licensed for use in patients with type 1 Gaucher disease[2,18,19], imiglucerase is also indicated for use in patients with type 3 Gaucher disease who exhibit clinically significant non-neurological manifestations of the disease[18,19].

4.0 SUMMARY OF THE EVIDENCE ON COST-EFFECTIVENESS

4.1 Cost-effectiveness evidence

4.1.1 Context

The applicant company submitted a cost-minimisation analysis (CMA) comparing velaglucerase alfa to imiglucerase, the only other licensed ERT for patients with type 1 Gaucher disease[1].

The CMA assumes therapeutic equivalence based on the efficacy and safety results for velaglucerase alfa and imiglucerase from study HGT-GCB-039[13]. Medicine costs, assuming no wastage, are estimated in the CMA. Other costs associated with treatment initiation, administration, titration, monitoring and management of AEs and health benefits are assumed to be the same for patients receiving velaglucerase alfa or imiglucerase. The modelled population is patients with a mean weight of 75 kg, receiving a dose of 32 units/kg body weight every two weeks at baseline. Dosage is informed by advice received from Welsh clinicians. Medicine costs are obtained from the British National Formulary (BNF). An NHS and Personal Social Services perspective and a lifetime horizon of analysis are adopted.

A discounted price for velaglucerase alfa is available through a Wales Patient Access Scheme (WPAS).

4.1.2 Results

Table 2 presents the base case results. Lifetime costs comprise medicines (99% of the costs), plus administration and disease management costs. Only medication costs vary between the options.

Table 2. Results of base case analysis per treated patient with type 1 Gaucher disease.

	Imiglucerase	Velaglucerase alfa		Difference	
		No WPAS	With WPAS	No WPAS	With WPAS±
Medicine cost per vial	£1071.29 per 400 unit vial and £535.65 per 200 unit vial	£1410.20 per 400 unit vial	†	£339	†
Medicine cost per annum*	£167,121	£219,991	†	£52,870	†
Discounted (at 3.5%) lifetime costs of medicine, administration and disease management	£3,903,338	£5,120,956	†	£1,217,619	†

* Based on 75 kg body weight and 32 units/kg body weight every two weeks. Assumes no wastage.
† Commercial in confidence figures removed.

In the base case analysis without the WPAS, patients receiving velaglucerase alfa incur a total lifetime discounted cost of £5,120,956 compared to £3,903,338 for patients receiving imiglucerase, giving an incremental cost of £1,217,619 for velaglucerase alfa.

[Commercial in confidence data removed]

The results of sensitivity analyses on baseline weight and different doses are presented in Table 3. The individual patient weight analysis attributes a weight to each patient based on age. The proportional weight of each patient, relative to the total population, is multiplied by the average dose to derive a patient specific dose. The mean of the weights is 77.5 kg, slightly higher than the base case mean weight of 75 kg. Use of 200 unit vial only for imiglucerase (not shown) does not change the cost from base case because of the assumption in the base case of no wastage.

Table 3. Results of sensitivity analyses on discounted lifetime costs per patient with type 1 Gaucher disease.

	Imiglucerase	Velaglucerase alfa		Difference	
		No WPAS	With WPAS	No WPAS	With WPAS
Base case analysis Weight: mean 75 kg Dosing: 32 units/kg	£3,903,338	£5,120,956	*	£1,217,619	*
Patient weight					
Individual patient weight	£4,126,730	£5,482,129	*	£1,355,399	*
As per pivotal trial[13] (52 kg at baseline)	£2,620,379	£3,854,333	*	£1,233,954	*
Dosing of velaglucerase alfa and imiglucerase					
15 units/kg	£1,658,163	£2,165,501	*	£507,338	*
60 units/kg	£7,110,735	£9,765,244	*	£2,654,509	*
* Commercial in confidence figures removed.					

The magnitude of the differences is sensitive to weight and dose, with savings increasing as weight and dose increase. The net savings [Commercial in confidence data removed] from imiglucerase relative to velaglucerase alfa at 52 kg baseline arises because the latter does not provide 200 unit vials. This analysis assumes precise dosing is adopted in clinical practice.

All sensitivity analyses are judged plausible, with the possible exception of a dose of 15 units/kg. Clinical guidelines for adult disease advise that maintenance doses of 15–30 units/kg are adequate for most adult patients[4], but the paediatric guidelines state that the dose should not fall below 30 units/kg[9].

4.1.3 AWTTC critique

The reliability of the CMA presented by the company is dependent upon the extent to which velaglucerase alfa is considered to be therapeutically equivalent to imiglucerase. As noted in Section 3.3, CHMP has concluded that velaglucerase alfa has an equivalent clinical efficacy and safety profile to that of imiglucerase[3]. The other key assumption is no wastage, with doses adjusted to vial size prescribing.

Strengths of the economic evidence include:

- The CMA is supported by a robust clinical trial[13].
- The CMA uses appropriate comparator and unit costs of the medicines.
- Base case mean dose of 2,400 units (32 units/kg and average weight of 75 kg) is similar to the mean dose of 2,395 units adopted in a health technology assessment[20], which was sourced from the National Gaucher's Registry.
- Cost results are conservative, because they exclude cost savings from providing velaglucerase alfa using homecare paid for by the applicant company (see Section 6.1).
- A range of sensitivity analyses are presented.

- A transparent and comprehensive Markov model of disease progression and associated costs and utilities is provided and described in the submission. The CMA is a subset of the potential outcomes for the model. With the CMA, all parameter values, other than the price of the medicines, are identical in the two arms.

Weaknesses of the economic evidence include:

- The clinical trial used doses of 60 units/kg every two weeks for 39 weeks[13]. Therapeutic equivalence has not been demonstrated for maintenance doses of 32 units/kg.
- No wastage is assumed, with doses adjusted to nearest 400 units per infusion. The company does not offer 200 unit vials, unlike the comparator, imiglucerase. The analysis assumes no penalty in terms of clinical effectiveness from adopting vial size prescribing. If this approach is not adopted and exact doses administered each time, with unused medication disposed of, then velaglucerase alfa will not always be the cheaper option. For example, if the mean body weight is 68 kg using a maintenance dose of 32 units/kg, the infusion of velaglucerase alfa required would be 2,176 units[2]. This would require six 400 unit vials of velaglucerase alfa per treatment; however, the same dose could be administered with less expense by using five 400 unit vials and one 200 unit vial of imiglucerase instead[18,19,21]. [Commercial in confidence data removed].

4.2 Review of published evidence on cost-effectiveness

Standard literature searches identified two studies. A Canadian CMA[22], comparing velaglucerase alfa with imiglucerase, concluded velaglucerase alfa could increase costs by $5,720 or be cost-saving by $157,560 per patient per year, depending on doses and wastage. Clinical non-inferiority was based on the pivotal randomised control trial[13].

A cost-utility analysis, set in Spain, compared the same medicines and concluded that velaglucerase alfa was slightly cheaper over a 39-year time horizon (€7.265 million per patient compared to €7.328 million per patient with imiglucerase); both yielded identical quality-adjusted life-year (QALY) gains (25.55)[23]. However, this data is presented in a conference abstract and as such a breakdown of costs is not available.

5.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

5.1 Budget impact evidence

5.1.1 Context and methods

The applicant company estimates 15 patients may have type 1 Gaucher disease in Wales, but not all may require treatment. It is aware of 12 patients currently receiving treatment and the base case uses this figure. Incidence is estimated at less than one patient per year. Annual mortality rates used in the Gaucher Disease Health Economic model (0.98%) are applied. Market share is estimated to rise from 50% in year one to 75% in year three and remain stable thereafter, with imiglucerase being displaced. As part of the WPAS, the applicant company will provide homecare support for patients treated in the community, [Commercial in confidence data removed]. Figures are provided in Table 4.

5.1.2 Results

Table 4. Company-reported costs and savings associated with the use of velaglucerase alfa to treat patients with type 1 Gaucher disease (with WPAS).

	Year 1 (2014)	Year 2 (2015)	Year 3 (2016)	Year 4 (2017)	Year 5 (2018)
Number of eligible patients	12	13	14	15	16
Uptake (%)	50%	70%	75%	75%	75%
Treated patients	6	9	11	11	12
Costs and savings					
Velaglucerase alfa costs*	*	*	*	*	*
Imiglucerase costs displaced £167,121/year/patient*	£1,002,727	£1,504,091	£1,838,334	£1,838,334	£2,005,455
*	*	*	*	*	*
Annual net savings in medicine costs*	*	*	*	*	*
Total annual savings*	*	*	*	*	*
* Commercial in confidence figures removed.					

The applicant company did not provide formal sensitivity analysis but noted that the budget impact of switching to velaglucerase alfa from imiglucerase would always be cost-saving with the WPAS because of the lower medicine cost and homecare provision.

5.1.3 AWTTC critique

The applicant company did not provide the total cost of medicines displaced or annual net savings from medication but these could be calculated from the information provided. No sensitivity analyses were provided for a without WPAS option. The limitations of the economic analysis apply to the budget impact analysis, particular the assumption of no wastage.

5.2 Comparative unit costs

Table 5 provides unit costs for velaglucerase alfa and imiglucerase for treating patients with type 1 Gaucher disease.

Table 5. Cost per infusion of velaglucerase alfa and imiglucerase for patients with type 1 Gaucher disease.

Regimens	Example dose	Cost per dose	Cost per year
Velaglucerase alfa (VPRIV®) 400 units powder for solution for infusion (no WPAS)	By intravenous infusion, 60 units/kg once every two weeks, adjusted according to response Typical dose: 2,400 units (32 units and 75 kg).	£8,461	£219,991
Velaglucerase alfa (VPRIV®) 400 units powder for solution for infusion (with WPAS)		*	*
Imiglucerase (Cerezyme®) 200 units and 400 units powder for concentrate for solution for infusion		£6,428	£167,121
* Commercial in confidence figures removed. Costs based on BNF prices as of 25 February 2014[21]. This table does not imply therapeutic equivalence of the medicines and doses listed. See SPCs for full dosing details[2,18,19].			

6.0 ADDITIONAL INFORMATION

6.1 Prescribing and supply

AWTTC is of the opinion that, if recommended, velaglucerase alfa (VPRIV®) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

The company anticipate that velaglucerase alfa (VPRIV®) may be supplied by a home healthcare provider under certain conditions[2]. The cost of providing the treatment using homecare is covered by Shire Pharmaceuticals Ltd[1].

6.2 Ongoing studies

The company submission highlighted one ongoing study that is likely to be available within 6–12 months*:* the Gaucher disease Outcome Survey (GOS), which is an ongoing, global, long-term, real-world observational database recording the medical outcomes of patients with Gaucher disease. The applicant company reports that, as of September 2013, there were a total of 530 patients participating in this survey, at 22 sites located in a total of four countries[1].

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: 10 February 2014.
Date range of evidence search: No date limits were applied to database searches.

6.5 Consideration of AWMSG policy relating to ultra-orphan medicines

Velaglucerase alfa was designated as an orphan medicinal product on 06 June 2010 for the treatment of Gaucher disease[6]. The applicant company states that there are extremely limited data on Wales-specific incidence rates due to the rarity of the disease and consequent limited research[1], but cited one published paper that used an estimation of approximately 1 in 30,000−40,000 patients with type 1 Gaucher disease in the UK[7]. This is in contrast to another estimate of prevalence in the EU of 1 in 100,000 for type 1 Gaucher disease[25]. AWMSG policy states that ultra-orphan medicines are orphan drugs that are licensed for the treatment of diseases with a prevalence of less than 1 in 50,000 persons in the European Union at the time of submission of the designation application to the European Medicines Agency[24]. At the time of orphan designation, Gaucher disease affected approximately 0.3 in 10,000 people in the European Union[6].

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