All Wales Therapeutics and Toxicology Centre
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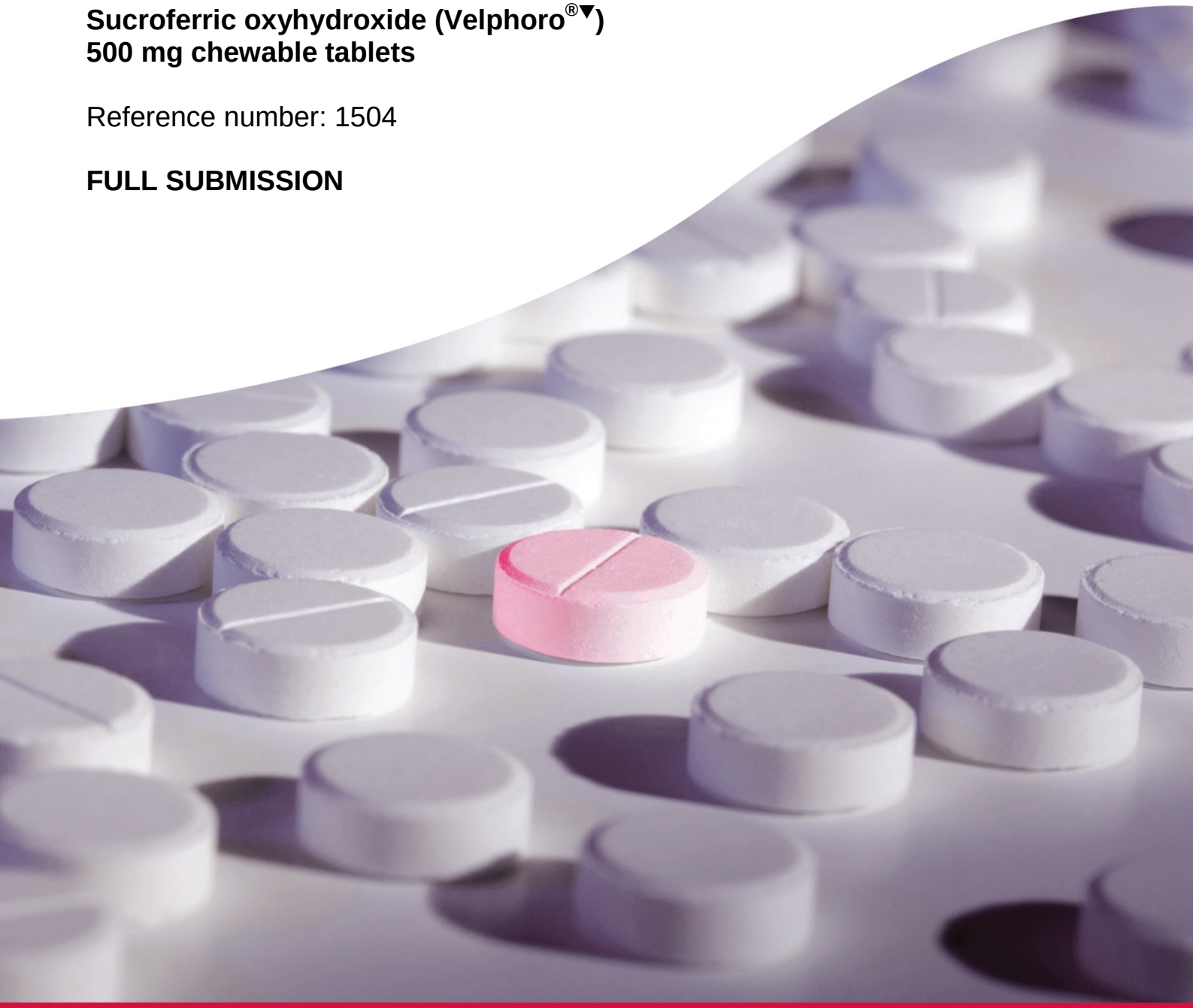
AWMSG SECRETARIAT ASSESSMENT REPORT

Sucroferric oxyhydroxide (Velphoro®▼) 500 mg chewable tablets

Reference number: 1504

FULL SUBMISSION



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AWMSG Secretariat Assessment Report
Sucroferric oxyhydroxide (Velphoro®▼) 500 mg chewable tablets

This assessment report is based on evidence submitted by Fresenius Medical Care UK Ltd[1].

1.0 PRODUCT DETAILS

Licensed indication under consideration	Sucroferric oxyhydroxide (Velphoro®▼) for the control of serum phosphorus levels in adult chronic kidney disease (CKD) patients on haemodialysis (HD) or peritoneal dialysis (PD). Sucroferric oxyhydroxide (Velphoro®▼) should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy vitamin D3 or one of its analogues, or calcimimetics to control the development of renal bone disease[2].
Dosing	The recommended starting dose of sucroferric oxyhydroxide is 1,500 mg iron (three tablets) per day, divided across the meals of the day. Serum phosphorus levels must be monitored and the dose of sucroferric oxyhydroxide up or down titrated in increments of 500 mg iron (one tablet) per day every 2-4 weeks until an acceptable serum phosphorus level is reached, with regular monitoring afterwards. The maximum recommended dose is 3,000 mg iron (six tablets) per day. Refer to the Summary of Product Characteristics (SPC) for further information[2].
Marketing authorisation date	26 August 2014[3]

2.0 DECISION CONTEXT

2.1 Background

Hyperphosphataemia is a common and serious condition occurring in 70% of patients with stage 5 chronic kidney disease (CKD-5) and affects approximately 90% of patients receiving renal replacement therapy[4,5]. It is a predictor of all-cause mortality and fatal and non-fatal cardiovascular events[6] and is significantly associated with all-cause, cardiovascular and fracture-related hospitalisation[7].

For adults with CKD-5 receiving dialysis, the National Institute for Health and Care Excellence (NICE) and the UK Renal Association recommend that serum phosphorus levels are kept between 1.1 and 1.7 mmol/l[8,9]. Hyperphosphataemia is managed through limiting intake of phosphate rich foods, using phosphate binders and partial phosphate removal by dialysis[8]. NICE clinical guideline (CG) 157 recommends that, in addition to dietary management to control serum phosphorus levels, calcium acetate is the first-line phosphate binder for adults with CKD-4 or -5. Calcium carbonate should be considered in patients for whom calcium acetate is not tolerated or is unpalatable[8,10].

Sucroferric oxyhydroxide is an iron-based phosphate binder[2]. Phosphate binding takes place by ligand exchange between hydroxyl groups and/or water and the phosphate ions throughout the physiological pH range of the gastrointestinal (GI) tract. Serum phosphorus levels are reduced as a consequence of the reduced dietary phosphate absorption[2].

The company has proposed that sucroferric oxyhydroxide should be considered for second-line use in adults with CKD-5 whose serum phosphorus levels are not controlled with a calcium-based binder or who are controlled but have high serum calcium levels or low serum parathyroid levels, in line with the recommendations for the use of non-calcium phosphate binders in NICE CG 157[1].

2.2 Comparators

The comparator included in the company submission was the non-calcium-based phosphate binder, sevelamer[1]. Two salts are available in the UK: sevelamer hydrochloride (Renagel®) and sevelamer carbonate (Renvela®, Genthon® and Zentiva®).

2.3 Guidance and related advice

- The UK Renal Association. Clinical practice guideline. Chronic kidney disease mineral and bone disorders (CKD-MBD) (2015)[9].
- NICE. Hyperphosphataemia in chronic kidney disease overview (2014)[10].
- NICE. CG 157. Hyperphosphataemia in chronic kidney disease: Management of hyperphosphataemia in patients with stage 4 or 5 chronic kidney disease (2013)[8].
- Kidney Disease: Improving Global Outcomes (KDIGO) Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of CKD-MBD (2009)[11].
- National Kidney Foundation. American Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines for bone metabolism and disease in chronic kidney disease (2003)[12].

3.0 SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

3.1 Pivotal study

The company submission included a randomised, phase III, multicentre, open-label, two-stage, prospective, parallel-group active controlled pivotal study[1,6,13]. Stage 1 investigated the noninferiority of sucroferric oxyhydroxide versus sevelamer carbonate and stage 2 investigated the superiority of sucroferric oxyhydroxide maintenance-dose (MD) versus sucroferric oxyhydroxide low-dose (LD)[1,6,13].

Patients aged ≥ 18 years with a history of hyperphosphataemia, receiving maintenance haemodialysis (HD) three times a week or peritoneal dialysis (PD) for at least three months, receiving stable doses of phosphate binders for at least one month prior to screening were eligible for study inclusion[1,6,13]. Only patients with serum phosphorus concentrations ≥ 1.94 mmol/l during the washout phase of 2-4 weeks were eligible for randomisation. Antacids containing aluminium, calcium or magnesium, and oral iron therapies/supplements were not permitted during the study. Patients (n = 1,059) were randomised 2:1 to receive either sucroferric oxyhydroxide (1.0–3.0 g/day [2–6 tablets/day]; n = 710) or sevelamer carbonate (2.4–14.4 g/day [3–18 tablets/day]; n = 349) for 24 weeks (stage 1). The dose was titrated for 8 weeks, then adjusted only for tolerability during weeks 9−12, and subsequently for efficacy and tolerability during weeks 13−24. At the end of week 24, those patients on HD who were receiving sucroferric oxyhydroxide were re-randomised to either continue their MD (n = 50), or

begin the LD (250 mg: n = 49), for a further three weeks (to week 27; stage 2), with no dose adjustments permitted[1,6,13].

At week 24, the mean serum phosphorus concentrations were similar in the two treatment groups[1,6,13]. The primary endpoint was met, with sucroferric oxyhydroxide MD demonstrated to be superior to the LD in maintaining control of serum phosphorus levels from week 24 to week 27 (stage 2; $p < 0.001$; see Table 1). The secondary efficacy endpoint was also met, demonstrating noninferiority of sucroferric oxyhydroxide versus sevelamer carbonate in stage 1. The upper bound of the 97.5% one-sided confidence interval (CI) of the least-squares mean difference in the change from baseline to week 12 in serum phosphorus was 0.15 mmol/l; however the predefined noninferiority margin of 0.19 mmol/l[1,6,13] was not justified as clinically relevant. Subsequent superiority analyses showed that the reduction from baseline was statistically significantly greater with sevelamer carbonate than with sucroferric oxyhydroxide, although the difference was small and may not be clinically relevant. The proportion of responders according to the KDOQI target range (1.13–1.78 mmol/l) reflects the treatment goal in clinical practice and is considered an important clinically relevant endpoint. A significantly lower proportion of patients on sucroferric oxyhydroxide achieved KDOQI target serum phosphorus levels compared with sevelamer carbonate (44.8% versus 54.7%, p=0.01) at week 12. An absolute difference of about 7% in responder rates in favour of sevelamer carbonate persisted at 24 weeks in the intention-to-treat (ITT) population[6].

Table 1. Serum phosphorus levels during stage 2 (week 24–27)[1,6,13].

	Sucroferric oxyhydroxide	
	MD (n = 44)	**LD (n = 49)**
Stage 2 baseline (week 24)*		
Mean serum phosphorus level, mmol/l (SD)	1.5 (0.33)	1.6 (0.37)
Week 27, LOCF		
Mean serum phosphorus level, mmol/l (SD)	1.6 (0.35)	2.2 (6.8)
Change from stage 2 baseline (LOCF)		
Mean serum phosphorus level, mmol/l (SD)	0.1 (0.40); p = NR	0.6 (0.47); p = NR
LS means†	0.08	0.62
Difference MD versus LD (95% CI)	0.54 (0.37 to 0.71)	
p-value	< 0.001	

CI: confidence interval; LD: low-dose; LOCF: last observation carried forward; LS: least squares; MD: maintenance-dose; NR: not reported; SD: standard deviation

* Stage 2 baseline was week 24 or latest value available before week 24 when week 24 result was missing. LOCF endpoint was week 27 or includes the latest evaluable measurement after week 24.
† ANCOVA-LOCF: ANCOVA analysis on endpoint results using a mixed model with the maximum likelihood estimation. The model includes treatment, baseline serum phosphorus levels, and region (USA/EU/rest of world) as fixed effects.

3.2 Extension study

All patients who completed the 24-week pivotal study (see Section 3.1), with the exception of those who had received LD sucroferric oxyhydroxide in weeks 25-27 (stage 2), were eligible for inclusion in the open-label 28-week extension study[1,6,14]. Patients continued with their MD of randomised treatment (sucroferric oxyhydroxide: n = 391; sevelamer carbonate: n = 267), with efficacy and safety assessments

performed every four weeks. Serum phosphorus control was maintained with sucroferric oxyhydroxide and sevelamer carbonate throughout the extension study, with no significant difference between treatment groups (see Table 2); control was maintained over the whole year of treatment (pivotal study baseline to end of extension study)[1,6,14]. At each time point throughout the extension study, mean serum phosphorus levels remained within the KDOQI target range for both treatment groups[1,6,14]. However, the absolute difference of about 7% in responder rates in favour of sevelamer carbonate observed in the pivotal study persisted over the 6–12 months when assessed on an ITT basis.

Table 2. Serum phosphorus levels during the 28-week extension study[1,6,14].

	Sucroferric oxyhydroxide (n = 384)	Sevelamer carbonate (n = 260)
Extension study baseline*		
Mean serum phosphorus level, mmol/l (SD)	1.75 (0.48)	1.68 (0.46)
End of 28-week extension study (LOCF)†		
Mean serum phosphorus level, mmol/l (SD)	1.77 (0.54)	1.77 (0.52)
Change from extension study baseline†		
Mean serum phosphorus level, mmol/l (SD)	0.02 (0.52); p = 0.42	0.09 (0.58); p = 0.02
Difference between treatment groups (95% CI)	0.07 (NR)	
p value	p = 0.14	

CI: confidence interval; LOCF: last observation carried forward; NR: not reported; SD: standard deviation.

* Extension study baseline is the last non-missing value prior to or on the date of the first extension study treatment intake.
† LOCF, week 52 endpoint is week 52 result or the latest available measurement after extension study baseline when week 52 is missing.

3.3 Comparative safety

In the pivotal study, the percentage of patients that reported at least one treatment-emergent adverse event (TEAE) was higher in the sucroferric oxyhydroxide group compared to the sevelamer carbonate group (83.2% versus 76.1%, respectively)[1,6,13], but was lower in the extension study (73.9% versus 76.8%, respectively)[1,6,14]. In both studies, the incidence of severe and serious TEAEs and deaths were similar in both treatment groups. Over the course of one year, a higher incidence of TEAEs leading to study withdrawal was observed in patients receiving sucroferric oxyhydroxide versus sevelamer carbonate (20.9% versus 10.3%, respectively), reflecting the higher withdrawal rate due to TEAEs early on in treatment (pivotal study: 15.7% versus 6.6%, respectively; extension study: 8.2% versus 4.9%, respectively)[1,6,13,14]. In both treatment groups in the pivotal study, GI events accounted for large proportions of the TEAEs leading to study withdrawal (54.0% versus 43.5%, respectively). Diarrhoea was the most frequent AE resulting in withdrawal: 2.8% and 0.6% of patients in the sucroferric oxyhydroxide and sevelamer carbonate treatment groups in the pivotal study withdrew on this basis, respectively)[1,6,13].

3.4 AWTTC critique

- The Committee for Medicinal Products for Human Use (CHMP) concluded that sucroferric oxyhydroxide demonstrated a clear benefit in terms of reducing serum phosphorus levels in patients on maintenance dialyses with an acceptable safety profile based on data up to one year[6]. CHMP highlighted that

although the serum phosphorus lowering effect and the tolerability of sucroferric oxyhydroxide is somewhat less than sevelamer carbonate, the long-term efficacy appears comparable[6].

- The tolerability of sucroferric oxyhydroxide is less than for sevelamer carbonate and resulted in more study withdrawals. Despite this, over half of the patients treated with sucroferric oxyhydroxide were included in the long-term extension study and almost half continued treatment for one year[6].
- CHMP noted that around a third of patients were already taking and likely tolerating sevelamer when enrolled in the main trial, which could potentially bias assessment of tolerability in favour of sevelamer; however, sucroferric oxyhydroxide was also commenced in the trial at a dose lower than the SPC-recommended starting dose (1.5 g or three tablets), which could plausibly bias assessment of tolerability in favour of sucroferric oxyhydroxide[1,2,13]. It is not clear whether an increase in dose would improve the proportions achieving, or time to achieve, target serum phosphorus levels.
- Lanthanum, which is also recommended as an option in NICE CG 157, is not included as a comparator in the company submission although it is included in the health economic model as an option for patients who do not respond to sucroferric oxyhydroxide or sevelamer. The company anticipate that sucroferric oxyhydroxide will only displace sevelamer in the second line setting[1,8].
- Most phosphate binders are associated with a high pill burden that can potentially result in poor compliance[13]. The pill burden over one year of treatment was 62% lower with sucroferric oxyhydroxide than with sevelamer carbonate (8.7 versus 3.3 tablets/day, respectively), which may have implications for long-term adherence[14]. There was a trend towards higher adherence with sucroferric oxyhydroxide; however findings should be interpreted with caution as this was based on tablet numbers dispensed and returned, a method with limited reliability[1,13,14].

4.0 SUMMARY OF THE EVIDENCE ON COST-EFFECTIVENESS

4.1 Cost-effectiveness evidence

4.1.1 Context

The company submission describes a base case cost-minimisation analysis (CMA) of sucroferric oxyhydroxide compared against sevelamer hydrochloride[1]. Results of an additional analysis incorporating disutilities associated with AEs are also provided, using a net monetary benefit approach[1].

The company anticipates use of sucroferric oxyhydroxide in adult dialysis patients with CKD-5 whose serum phosphorus levels are not controlled with a calcium-based binder or who are controlled but have high serum calcium or low serum parathyroid levels, in line with the recommendations for the use of non-calcium phosphate binders in NICE CG 157[8]. The economic evidence for sucroferric oxyhydroxide is therefore restricted to its use in a subgroup of its full licensed population[2], in whom sevelamer hydrochloride would be the alternative phosphate binder.

The base case analysis assumes sucroferric oxyhydroxide and sevelamer hydrochloride have equivalent efficacy for lowering of serum phosphorus levels based on an analysis of noninferiority of sucroferric oxyhydroxide compared with sevelamer carbonate as a secondary endpoint at 12 weeks in the pivotal phase III trial (see Section 3.1)[13]. Based on a review of published studies that concluded sevelamer hydrochloride has comparable efficacy to sevelamer carbonate for the lowering of serum phosphorus levels[15], the company assumes that the pivotal study results can be extended to the comparison of sucroferric oxyhydroxide and sevelamer hydrochloride.

Patients discontinuing treatment due to AEs with sucroferric oxyhydroxide and sevelamer hydrochloride (15.7% and 6.9%, respectively, at rates observed in the pivotal study) are assumed to switch to lanthanum at a dose of 1.5 g/day. Such switching is assumed to occur on average after two weeks of sucroferric oxyhydroxide and sevelamer hydrochloride treatment. AEs occurring more frequently with sucroferric oxyhydroxide in the trial included diarrhoea, constipation and nausea/vomiting, which are assumed to impact on quality of life for five days based on the disutilities assumed in the economic model informing NICE CG 157[8]. The impact of these AEs in terms of a net monetary loss is estimated, assuming a willingness to pay threshold of £30,000 per quality-adjusted life year (QALY).

Resource use in the base case analysis relates to medicine acquisition costs only, assuming the mean average daily number of tablets taken per patient on sucroferric oxyhydroxide and sevelamer carbonate (3.1 versus 8.1, respectively) observed across the entire first 24 weeks of treatment in the pivotal study. Scenario analyses include exploration of the impact of incorporation of GP visits for AEs. The base case analysis is based on a 12 month time horizon.

4.1.2 Results

Results of the base case CMA are presented in Table 3. Sucroferric oxyhydroxide is estimated to be cost saving compared with sevelamer hydrochloride by £526 per patient per year, driven primarily by lower daily medicine acquisition costs based on the assumed dosing at 12 weeks in the pivotal study.

Table 3. Base case CMA results over a one-year time horizon[1].

	Proportion of patients	Cost of treatment per day	Days	Total cost
Patients who stay on sucroferric oxyhydroxide throughout	0.843	£6.17	365.25	£1,899.47
Patients who start on sucroferric oxyhydroxide but switch to lanthanum after 14 days	0.157	£6.17	14	£13.56
Costs of lanthanum after switch	0.157	£4.13	351.25	£227.38
Sucroferric oxyhydroxide total cost	–	–	–	**£2,140.41**
Patients who stay on sevelamer hydrochloride throughout	0.93	£7.52	365.25	£2,564.31
Patients who start on sevelamer hydrochloride but switch to lanthanum after 14 days	0.07	£7.52	14	£6.95
Costs of lanthanum after switch	0.07	£4.13	351.25	£95.84
Sevelamer hydrochloride total cost	–	–	–	**£2,667.09**
Difference (sucroferric oxyhydroxide – sevelamer hydrochloride)				**–£526.08**

Incorporation of AEs of sucroferric oxyhydroxide is estimated to result in a loss of 0.0004 QALYs, which at a willingness to pay threshold of £30,000 per QALY results in

a net monetary loss of £11.75 compared with sevelamer hydrochloride. Therefore, taking into account these AEs, the company estimates sucroferric oxyhydroxide is still cost saving by £514.33 compared with sevelamer hydrochloride.

Scenario analyses suggest sucroferric oxyhydroxide is cost saving irrespective of the assumptions on time horizon of analysis, and whether or not switching to lanthanum occurs in those experiencing AEs. Incorporation of GP visits and clinic visits for patients experiencing AEs and requiring treatment switching has little impact on the total cost savings, and use of observed dosing at week 24 in the pivotal study (4.4 versus 11.25 tablets per day [data on file]) increases cost savings to £773.74 per patient per year. Sucroferric oxyhydroxide is no longer cost saving if the assumed mean number of tablets taken per day exceeds 3.93 in the base case (while sevelamer hydrochloride dosing remains at 8.1 tablets/day).

4.1.3 AWTTC critique

The company has presented a base case CMA of sucroferric oxyhydroxide compared against sevelamer hydrochloride, which implicitly assumes therapeutic equivalence of these treatments; however the supporting clinical data suggests there may be differences (see Section 3.0 and bullet points below). An alternative analysis provided by the company, using a net monetary benefit approach considers differences in AEs, but does not consider potential differences in efficacy. The magnitude of cost savings estimated in each analysis are highly sensitive to the assumed daily treatment doses, which are subject to uncertainty.

Sucroferric oxyhydroxide has lower acquisition costs than sevelamer hydrochloride at the doses observed in the clinical trial and the usual doses noted in their SPCs; however, there are several uncertainties in the assumption of therapeutic equivalence based on the available clinical data, and in the magnitude of any cost differences.

Key limitations and uncertainties in the economic evidence include:

- The company has limited its economic evidence to a subset of the sucroferric oxyhydroxide licensed indication, assuming use when sevelamer hydrochloride would be an alternative as per NICE CG 157. Lanthanum, which is also recommended as an option in NICE CG 157[8], is not considered as a potential comparator by the company (see Section 3.4).
- The base case analysis is a CMA, which may be appropriate if therapeutic equivalence of sucroferric oxyhydroxide and sevelamer hydrochloride in all domains of health outcomes can reasonably be assumed. However, there are several uncertainties in this assumption:
  - Sucroferric oxyhydroxide has not been directly compared with sevelamer hydrochloride in the pivotal study on which the assumption of therapeutic equivalence is based; sucroferric oxyhydroxide, at a lower starting dose than is recommended in its SPC[2], was compared against sevelamer carbonate at a starting dose of 4.8 g daily irrespective of baseline serum phosphorus levels, which is then assumed to be equivalent to sevelamer hydrochloride.
  - Noninferiority for reductions from baseline in serum phosphorus levels was assessed as a secondary endpoint at 12 weeks, using a margin for noninferiority that was not justified as clinically relevant (see Section 3.1); CHMP attaches greater clinical relevance to the proportion of patients achieving KDOQI target serum phosphorus levels[6].
  - A significantly lower proportion of patients on sucroferric oxyhydroxide achieved KDOQI target serum phosphorus levels compared with sevelamer carbonate. There was also a difference in responder rates in favour of sevelamer carbonate which persisted (see section 3.1). A lower starting dose of sucroferric oxyhydroxide than is recommended in the SPC was used in the pivotal study, and CHMP notes it remains unknown whether

use of the SPC-recommended starting dose will improve the proportion achieving, or time to achieve, KDOQI target with sucroferric oxyhydroxide[6].
  - More patients discontinued treatment with sucroferric oxyhydroxide due to AEs compared with the sevelamer carbonate in the trial.
- There was potential bias regarding the assessment of tolerability in both sucroferric oxyhydroxide and selevamer carbonate (see Section 3.4).
- The estimated cost savings are very sensitive to the assumed daily treatment doses, which are subject to uncertainties:
  - As the trial used sucroferric oxyhdroxide starting dose lower than recommended in its SPC, the base case analysis may underestimate dosing and overestimate cost savings with sucroferric oxyhydroxide.
  - A scenario analysis using daily doses observed in the trial at 24 weeks (4.4 versus 11.25 tablets per day for sucroferric oxyhydroxide versus sevelamer carbonate, respectively) increased the estimated cost savings. However, the assumed doses in that analysis are somewhat greater than the usual SPC-reported doses[2,16]. At an average dose of 7 g (8.75 tablets) reported for chronic use in the sevelamer hydrochloride SPC[16], and the usual dose for response with sucroferric oxyhydroxide (3–4 tablets) reported in its SPC[2], sucroferric oxyhydroxide remains cost saving, but by an amount that is dependent on the greater switching of patients to the assumed lower cost of lanthanum, which is also subject to uncertainty.
- The analysis incorporating disutilities to account for the differing incidences of AEs is of limited informative value as it does not consider the potential for differences in efficacy highlighted above.

4.2 Review of published evidence on cost-effectiveness

Standard literature searches conducted by AWTTC have identified a published abstract that provides only brief details of a cost utility analysis of sucroferric oxyhydroxide compared against sevelamer carbonate, conducted from the NHS perspective in Scotland[17]. This is based on a Markov model and incorporated risk of mortality related to serum phosphorus levels from the literature, which was adjusted for sucroferric oxyhydroxide and sevelamer carbonate treatment using the observed serum phosphorus levels in the pivotal study and extension study. Over a 10-year time horizon, there were no differences between treatments in accrued QALYs; however, total treatment costs were reported to be marginally less with sucroferric oxyhydroxide, which the authors conclude demonstrates its cost-effectiveness[17]. The reported results are consistent with the CMA approach and results reported by the company for its comparison against sevelamer hydrochloride; however, too few details are provided to fully critique this analysis.

5.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

5.1 Budget impact evidence

5.1.1 Context and methods

Based on UK Renal Registry data[18], the company estimates the net number of patients on dialysis will be 1,278 in 2015[1]. Company-conducted market research data is reported to show 74% (946 patients) of dialysis patients receive phosphate binders, of which 50% (473 patients) receive non-calcium phosphate binder therapy. The company anticipates use of sucroferric oxyhydroxide as second-line therapy after failure on non-calcium phosphate binder therapy, and assumes uptake to be 8% in year one, rising to 20% in year five[1].

The budget impact analysis assumes sucroferric oxyhydroxide would be dosed at 3 tablets/day, and sevelamer hydrochloride at 8 tablets/day[1]. Only medicine acquisition costs are included.

5.1.2 Results

Based on the daily dosing assumed above, the company anticipates cost savings of £532 per patient per year, based on medicine acquisition costs alone[1]. The net budget impact in each of the next 5 years is estimated in Table 4.

Table 4. Company estimates of net cost implications associated with use of sucroferric oxyhydroxide[1].

	Year 1	Year 2	Year 3	Year 4	Year 5
Total number of eligible patients	473	–	–	–	–
Sucroferric oxyhydroxide uptake (%)	8%	12%	15%	18%	20%
Number treated with sucroferric oxyhydroxide	38	57	72	86	96
Total cost without sucroferric oxyhydroxide uptake	£1,281,716	£1,281,716	£1,281,716	£1,281,716	£1,281,716
Total cost with sucroferric oxyhydroxide uptake	£1,261,503	£1,251,397	£1,243,418	£1,235,971	£1,230,652
Overall net cost	**−£20,213**	**−£30,320**	**−£38,299**	**−£45,746**	**−£51,065**

No sensitivity or scenario analyses have been provided.

5.1.3 AWTTC critique

- The company has adopted a pragmatic approach to estimate the number of patients eligible for treatment with sucroferric oxyhydroxide.
- The daily doses of treatments assumed in the budget impact analysis appear to be rounded figures for the doses assumed in the base case CMA in Section 4. These figures may not accurately reflect the daily doses of these agents, and the estimates of cost savings with sucroferric oxyhydroxide are very sensitive to the assumed treatment doses, as noted in Section 4. The impact of assumed treatment doses has not been sufficiently explored in the budget impact analysis.
- Collectively, the budget impact analysis is subject to uncertainty.

5.2 Comparative unit costs

Sucroferric oxyhydroxide is a non-calcium phosphate binder, which is licensed for use in adult dialysis patients[2]. NICE CG 157 recommends use of non-calcium phosphate binders in adult dialysis patients with CKD-5 whose phosphorus levels are not controlled with a calcium-based binder. In those who are controlled but have high serum calcium or low serum parathyroid levels, consideration should be given to use of sevelamer hydrochloride or lanthanum carbonate[8]. The company anticipates use of sucroferric oxyhydroxide where sevelamer hydrochloride would otherwise be used.

Phosphate binder doses need to be individually tailored to patients based on serum phosphorus levels. Example acquisition costs of sucroferric oxyhydroxide and likely comparators, based on the range of SPC-recommended daily maintenance doses, are provided in Table 5.

Table 5. Example annual costs of sucroferric oxyhydroxide and potential comparators.

Treatment	Example maintenance regimen	Annual cost*
Sucroferric oxyhydroxide (Velphoro®▼)	1.5 g to 3 g daily	£2,178 to £4,356
Sevelamer carbonate (Renvela®)	2.4 g to 12 g daily†	£1,016 to £5,081
Sevelamer hydrochloride (Renagel®)	2.4 g to 12 g daily	£1,016 to £5,081
Lanthanum carbonate hydrate (Fosrenol®)	750 mg to 3.75 g daily	£741 to £3,096

This table does not imply therapeutic equivalence of treatments or doses.
See relevant Summaries of Product Characteristics for full dosing details[2,16,19,20].
* Costs based on BNF list prices as of 15 July 2015[21], and company information for sucorferric oxyhydroxide.
† Dose assumed to be the same as for sevelamer hydrochloride (Renagel®)

6.0 ADDITIONAL INFORMATION

6.1 Prescribing and supply

AWTTC is of the opinion that, if recommended, sucroferric oxyhydroxide (Velphoro®▼) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

The company do not anticipate that sucroferric oxyhydroxide (Velphoro®▼) 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: 5 June 2015
Date range of evidence search: No date limits were applied to database searches.

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