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A decision-analytic model to assess the cost-effectiveness of etelcalcetide vs cinacalcet

Björn Stollenwerk, PhD,[1,2] Sergio Iannazzo, MBA, EngD,[3] Ron Akehurst, BSc (Econ) (London), Hon MFPHM,[4] Michael Adena, PhD,[5] Andrew Briggs, DPhil,[6] Bastian Dehmel, MD[1,7] Patrick Parfrey, MD, FRCPC, OC, FRSC,[8] Vasily Belozeroff, PhD[7]

1 – Amgen Europe (GmbH), Dammstrasse 23, 6301 Zug, Switzerland

2 – Helmholtz Zentrum München, Ingolstädter Landstr. 1, 85764 Neuherberg, Germany

3 – SIHS Health Economics Consulting, Via Sebastiano Caboto, 45, 10129 Torino, Italy

4 – BresMed, North Church House, 84 Queen Street, Sheffield, S1 2DW, UK; University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA, UK

5 – Datalytics Pty Ltd, 19/12 Trevillian Quay Kingston ACT 2603, Australia

6 – Health Economics & Health Technology Assessment, University of Glasgow, UK

7 – Amgen Inc., One Amgen Center Drive, Thousand Oaks, CA 91320, USA

8 – Memorial University, St. John's, NL A1C 5S7, P.O. Box 4200, Newfoundland, Canada

Correspondence regarding this paper should be addressed to:

Björn Stollenwerk,

Amgen (Europe) GmbH, Dammstrasse 23

P.O. Box 1557, CH-6301 Zug, Switzerland

T: +41(0) 413690383

M: +41(0)795437898

bjoerns@amgen.com

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ABSTRACT

Introduction and objective: Etelcalcetide is a novel intravenous calcimimetic for the treatment of secondary hyperparathyroidism (SHPT) in haemodialysis patients. The clinical efficacy and safety of etelcalcetide (in addition to phosphate binders and vitamin D and/or analogs; PB/VD) was evaluated in three phase 3 studies, including two placebo-controlled trials and a head-to-head study versus the oral calcimimetic cinacalcet. The objective of this study was to develop a decision-analytic model for economic evaluation of etelcalcetide compared to cinacalcet.

Methods: We developed a life time Markov model including potential treatment effects on mortality, cardiovascular events, fractures, and subjects' persistence. Long term efficacy of etelcalcetide was extrapolated from the reduction in parathyroid hormone (PTH) in the phase 3 trials and the available data for outcomes study in cinacalcet (EVOLVE trial). Etelcalcetide was compared to cinacalcet, both in addition to PB/VD. We applied unit costs averaged from five European countries and a range of potential pricing options assuming parity price to weekly use of cinacalcet and varying it 15% or 30% higher.

Results: Compared with cinacalcet, the incremental cost-effectiveness ratio of etelcalcetide was €1.355 per QALY, €24,521 per QALY and €47,687 per QALY for the three prices explored. The results were robust across the probabilistic and deterministic sensitivity analyses.

Conclusions: Our modelling approach enables cost utility assessment of the novel therapy for SHPT based on the observed and extrapolated data. This model can be used for local adaptations in the context of reimbursement assessment.

KEY POINTS FOR DECISION MAKERS

- While no hard outcomes data are available for etelcalcetide, its superior efficacy in reducing parathyroid hormone, compared to the oral calcimimetic cinacalcet, enables extrapolation to improved rate of survival, cardiovascular events, fractures and parathyroidectomy.

- We provide a model which can be used to assess the cost-effectiveness of etelcalcetide compared to cinacalcet, both in addition to phosphate binders and vitamin D analogs.

1 Introduction and objective

Secondary hyperparathyroidism (SHPT) is a disease characterized by the excessive secretion of parathyroid hormone (PTH) and associated with hyperplasia of the parathyroid glands. This disorder is a common complication in patients with chronic kidney disease (CKD) on haemodialysis. SHPT is linked to the risk of extra skeletal calcification, reduced bone density and strength [1], bone fractures [2] morbidity and mortality [3,4,5]. The prevalence of SHPT within dialysis population ranges between 30%-49% in Europe and Australia and is estimated at about 54% in North America. [6]

The traditional treatment of SHPT includes treatment with active forms of vitamin D or its analogs and phosphate binders. In the past years, cinacalcet, the first calcimimetic agent, has been established as an additional effective therapy for this indication. For patients with severe SHPT who fail to respond adequately to medical therapy, surgical removal of parathyroid glands (parathyroidectomy) is also a viable option. The National Kidney Foundation through its Kidney Disease Outcomes Quality Initiative (K/DOQI) has established clinical practice guidelines for bone metabolism and disease in CKD. These clinical practice guidelines also specify target levels of PTH, serum calcium, and serum phosphorus [7].

Etelcalcetide is a novel D-amino peptide calcimimetic approved in the EU and US for the treatment of SHPT in adult haemodialysis patients. Etelcalcetide is administered intravenously three times per week at the end of each dialysis session. This route of administration, from the patient perspective, has been shown to be more convenient (preferred) over an oral drug[8]. Etelcalcetide is an allosteric activator that binds to, and activates, the calcium-sensing receptors in the parathyroid gland, resulting in reduced PTH secretion. The efficacy of etelcalcetide in reducing PTH levels has been established by three Phase 3 studies, two parallel placebo-controlled trials [9], and a head-to-head study comparing etelcalcetide to cinacalcet [10]. In the head-to-head study, etelcalcetide met the

primary endpoint of non-inferiority measured as the proportion of patients achieving a greater than 30% PTH reduction from baseline during the efficacy assessment phase, and the secondary endpoints of superiority (>50% and >30% reduction in PTH).

The objective of this study was to develop a decision-analytic model for economic evaluation of etelcalcetide compared to cinacalcet. We expect that this model can be adapted to local settings and will be applied to inform reimbursement decisions.

2 Methods

We developed a Markov cohort state transition model using a 3-month cycle length, and a life-time horizon. . We followed the current best practice modelling and reporting guidelines [11,12] and considered previously published cinacalcet cost-effectiveness models as a context [13, 14]. We conducted model validation based on the AdViSHE validation tool (see electronic supplementary material) [15]. Furthermore, we applied a life-table half-cycle correction [16, 17]. Both costs and outcomes were discounted at an annual rate of 3%. Treatment with etelcalcetide was compared to cinacalcet. Both calcimimetics were assumed to be administered in addition to phosphate binders and vitamin D,or its analogs (PB/VD). As an option, we explored the comparison of etelcalcetide to 'no calcimimetics' (i.e. PB/VD alone) which would represent a clinical decision to use etelcalcetide after cinacalcet discontinuation (see electronic supplementary material). The characteristics of the model population were aligned with etelcalcetide trials [9,10] and the 'EValuation Of Cinacalcet Hydrochloride (HCl) Therapy to Lower CardioVascular Events' (EVOLVE) trial [18]. EVOLVE was a global, multi-center, placebo-controlled, double-blind, event-driven trial, that assessed the impact of cinacalcet on outcomes in an SHPT dialysis population [18]. The primary endpoint was a composite of all-cause mortality and major cardiovascular (CV) events. Other clinical events such as fractures and parathyroidectomy (PTx) were

registered as secondary endpoints [18, 19]. EVOLVE is the only long-term randomized clinical trial that directly measured the impact of calcimimetics on SHPT clinical outcomes.

The design of the model is depicted in Figure 1. Simulated subjects enter the model in the "Event free" state. During the simulation, the subjects can experience CV events and fractures as a consequence of the disease, or die. Subjects who do not persist with calcimimetic treatment switch to PB/VD alone. Lastly, the occurrence of PTx was simulated as this event can generate costs and short-term health consequences.

The decision model compares long-term outcomes (survival and quality-adjusted life-years, QALYs) and overall costs. Calcimimetic treatment results in more controlled levels of SHPT biomarkers (PTH, serum calcium, and phosphorus), which are related to mortality as well as the incidence of CV events, fractures and PTx. The efficacy compared with 'no calcimimetic treatment' was parameterized as a hazard ratio (HR) by type of event (i.e. all-cause mortality, non-fatal CV events, fractures and PTx). Rates of clinical events, while on calcimimetic treatment, were obtained by applying HRs to the baseline rates (no calcimimetic treatment) (Table 1) [18,20].

The HRs for cinacalcet compared to 'no calcimimetics' were derived from EVOLVE [18] based on the event- specific HRs published by Belozeroff et al. [13]. Among the reported HRs, the lag-censored estimates (6-months lag) were most consistent with our model structure. This is, because both the model structure and the censoring approach distinguish between subjects on vs. off treatment. The EVOLVE pre-specified 6-month lag in the referenced source accounts for the delay between the drug intake and the treatment effect. As a sensitivity analysis to using lag-censored hazard ratios, we presented an intention-to-treat (ITT)-based approach (see electronic supplementary material).

No study is available that measured the incidence of clinical events in SHPT patients treated with etelcalcetide. Therefore, the cinacalcet efficacy has been extrapolated based on

the ability to lower PTH (see electronic supplementary material). The extrapolation was used separately for each type of event (i.e. mortality, CV events, fractures and PTx), and was based on the primary outcome of the etelcalcetide trial (i.e. the ability of the treatment to achieve a PTH reduction of at least 30% compared to baseline). More specifically, the proportion of subjects achieving the 30% PTH reduction was calculated separately for each treatment arm (etelcalcetide, cinacalcet, and placebo) across three etelcalcetide trials. Because the HR for cinacalcet is known for each event type, we used placebo as a reference and applied the share of subjects that met the primary endpoint to approximate the efficacy of etelcalcetide.

The treatment effect in the model is applied as long as subjects persist on the calcimimetic treatments. As soon as subjects discontinue, the baseline incidence rates are applied. As a consequence, on a population basis, the treatment effect of the calcimimetic treatment fades out continuously.

We modelled discontinuation with a parametric Weibull function (see electronic supplementary material). For the base case, we used the United States (US) real world data [21]. To test the sensitivity of the model to persistence assumptions, we applied EVOLVE trial persistence as an upper bound, and the lowest observed real-world persistence in Europe as a lower bound (one-year persistence: EVOLVE 73%, US 27%, France 27%, Germany 22%, Italy 16%). Given that no significant persistent difference (p=0.60) was observed within the head-to-head trial, the same discontinuation probabilities were applied for both calcimimetics.

The utility values (EQ-5D, Dolan algorithm) for each of the health states in the model were derived from a published EVOLVE analysis [22] using separate estimates for 'myocardial infarction', 'hospitalization for unstable angina', 'heart failure' and 'peripheral vascular event'. To derive a combined utility estimate for CV events, the number of events in

EVOLVE were used for weighting. The corresponding standard error was derived via error propagation [23].

The cost perspective of the third-party payer was applied; the total cost was estimated as the sum of drug consumption, management of clinical events, and routine monitoring. Dosing for calcimimetics was quantified based on the efficacy assessment phase of the head-to-head trial [10]. Consistent with the modelling approach from Garside et al. [14], the same background PB/VD drug usage was assumed for all treatment strategies (Table 2).

To parameterize this generic cost-effectiveness model, we applied crude averages of published drug prices and event costs across five European countries (Italy, Spain, Portugal, Switzerland, Czech Republic) [24]. These illustrative costs refer to the year 2010. Three potential etelcalcetide pricing scenarios were illustrated: 1) same weekly calcimimetic drug cost (WCDC), 2) 15% higher WCDC ('+15% WCDC') and 3) 30% higher WCDC ('+30% WCDC'). We used the weekly costs because the frequency of administration differs between calcimimetics. The ratio of average drug usage was taken for price calculation.

To assess the robustness of the model, a distribution-based probabilistic sensitivity analysis was conducted with key parameters varied simultaneously in 1,000 replications. The parameters of the uncertainty distributions were based on the point estimate and the standard error or confidence interval. The uncertainty of the primary endpoint of the etelcalcetide trials was sampled via the bootstrap approach. Hazard ratios of the cinacalcet treatment effect based on the EVOLVE trial were sampled via the Log-normal distribution. Baseline event rates were sampled via the Gamma distribution. Persistence-adjustment and extrapolation of efficacy based on the primary endpoint in the etelcalcetide study was re-calculated for the sampled values.

The Gamma distribution was also applied to sample resource usage and costs. Utility decrements were sampled based on the Normal distribution, whereas absolute utility values were sampled based on the Beta distribution. The results of probabilistic sensitivity analysis were displayed as a scatter plot on the cost-effectiveness plane and as cost-effectiveness acceptability curves.

We conducted a deterministic sensitivity analysis (DSA), where parameters were varied to the upper and lower bound of their 95% confidence intervals. For grouped parameters, or parameters without available standard errors (i.e. age-specific mortality, utility decrements, event costs, monitoring costs), plus/minus 20% of the point estimate were applied. The results of the DSA were displayed via a tornado diagram.

We performed structural sensitivity analyses including a different approach to estimate the treatment effect (i.e. ITT hazard ratios), and different sources to quantify discontinuation. Lastly, to assess the uncertainty due to PTx, we included a scenario where the PTx incidence rate has been set to zero.

3   Results

Lifetime total costs and outcomes by treatment are reported in Table 3. Etelcalcetide was more effective, providing 0.032 additional discounted QALYs compared with cinacalcet. This limited QALY gain reflects the high calcimimetic discontinuation rate. If the weekly calcimimetics treatment costs were kept constant, the increased life-expectancy resulted in a cost increase of €49. If a price mark-up was allowed, a 30% cost increase, combined with the effect of increased life-expectancy, resulted in additional costs of €1,518 compared with cinacalcet. These incremental costs are based on the assumption that no additional administration costs are associated with etelcalcetide treatment. (Table 3)

Compared with cinacalcet, the incremental cost-effectiveness ratio (ICER) of etelcalcetide was €1,355 per QALY, €24,521 per QALY and €47,687 per QALY for the three pricing options explored.

In the probabilistic sensitivity analysis, etelcalcetide consistently yielded more QALYs than cinacalcet (Figure 2).

The tornado plot of the DSA is displayed in Figure 3 (for illustration purposes based on an increase of 15% of weekly calcimimetic treatment costs). The parameters with the highest impact on the ICER were the calcimimetic doses and the HR (etelcalcetide vs. cinacalcet) to reduce mortality. The order of these variables varied by pricing assumption. Other inputs with a high impact on the outcomes were the HRs on CV events, fractures, and PTx.

The results of the structural sensitivity analyses are displayed in Table 4. A higher persistence led to increased ICERs. This is because at the later stages of the Markov model the treatment costs were equal, but the expected QALYs gained per event avoided decreased. When setting the PTx rate to zero, the ICER slightly increased. Incorporating ITT efficacy into the model resulted in a higher ability of etelcalcetide to reduce events. This is because of the implicit assignment of the spill-over treatment effect post discontinuation to the treatment period. For the +15% and the +30% treatment scenarios this resulted in slightly improved ICERs. For the pricing scenario where the weekly calcimimetic treatment costs do not differ between calcimimetics, the reduced mortality shifts people into later life-time cycles, where at similar costs to avoid one event, the QALYs per event avoided decreases, resulting in a slight increase of the ICER.

4   Discussion and conclusions

We developed a model to assess the cost-effectiveness of etelcalcetide vs. cinacalcet. The rationale for selecting cinacalcet as the comparator was that in most settings it

corresponds to the current standard of care. The purpose of this article was not to calculate the cost-effectiveness of etelcalcetide itself. Neither did we intend to calculate for a given price and a given willingness-to-pay (WTP) threshold, how effective etelcalcetide would have to be.

The efficacy of cinacalcet was directly based on the hard outcome trial EVOLVE. In contrast, though based on a randomized trial, the efficacy of etelcalcetide was extrapolated via a surrogate parameter. No hard outcomes study directly comparing etelcalcetide to cinacalcet exists, nor is there any observational studies as the therapy is just entering the markets. Thus, for the life-time analysis, the decision-analytic model needs to rely on surrogate parameters and efficacy extrapolation. However, this is a usual practice for economic analyses, and is also very common in the context of dialysis care where hard outcomes trials are very rare: Among eight previous studies reporting on the economics of SHPT treatment [13, 14, 20, 24, 25, 26, 27, 28] only two did not use surrogate parameters [13, 28]. However, as the treatment effect is an explicit input to our model, the model can easily be updated once alternative estimates become available.

The efficacy estimates in this publication were based on the lag-censored approach. Though not in the context of cost-effectiveness analysis, the usage of lag-censored estimates has been questioned [29], and the ITT approach may be preferable, particularly to assess whether a drug has a treatment effect. In the context of economic analyses, however, the purpose is to provide a point estimate of cost-effectiveness. The ITT-based HRs are inconsistent with the model structure. Still, we found that compared to the ITT sensitivity analysis, the lag-censored estimates were more conservative. This is because the ITT-based HRs do not capture the complete spill-over effect post discontinuation.

A limitation of the analysis is that the treatment effect does not vary by patient characteristics such as age. Assuming constant HRs over a wide range of potential subpopulation is a common approach in decision-analytic modelling, and is also often

assumed in meta-analyses. In the current case, we applied the published efficacy estimates based on the EVOLVE trial. No robust evidence exists that could be used to quantify a treatment effect by population subgroup. Furthermore, subgroup analyses also reduce the sample size, which makes it harder to detect significant differences.

The current model was inspired by three previous cinacalcet cost-effectiveness models [13, 14, 26]. Our definition of health states and the clinical events is generally consistent with these models. However, in the NICE PenTAG model [14] PTx affects PTH levels and thus indirectly the incidence of fractures and CV events. In our model, aligned with the other two analyses [13, 26] PTx only affects the estimation of costs and quality of life. As outlined below, this choice was based on the large uncertainty of PTx outcome data.

Furthermore, in contrast to previous models, the etelcalcetide model explicitly simulates the discontinuation. This is important, as real-world studies on cinacalcet discontinuation have demonstrated that persistence is a key success factor of calcimimetic treatment. Based on the phase 3 trial data, we assumed the same persistence for both calcimimetics. In real world, however, due to the intravenous administration and potential improvements of gastrointestinal events, persistence may be better for etelcalcetide.

In our illustration of this cost-effectiveness model, the third-party payer perspective was applied. For some settings, the considered corresponding costs may have limitations. In particular, for some settings, it may be relevant to also consider patients' out-of-pocket costs or costs for administration.

The presented model assigns equal probability of PTx to all possible transition states. A more complex model could have explicitly distinguished whether subjects can tolerate calcimimetic therapy, or it could have accounted for potential associations between the risk of fracture, CV events and PTx. Furthermore, a short-term utility decrement is accrued after PTx, but PTx has not been modelled to reduce risk of future complications and mortality.

Such decision rules, however, would not only have increased model complexity, but would also have required robust input data for quantification. Increasing model complexity beyond the level of available inputs does not increase the accuracy of the results, and a higher complexity often leads to criticism. The available data on consequences of PTx is very limited: No clinical trial exists that would compare the effectiveness of PTx vs. calcimimetics. Furthermore, PTx does not automatically lead to calcimimetics discontinuation [30].

In this model we followed the established approach of not including dialysis costs [13, 31, 32, 33]. Dialysis *per se* is not a cost-effective procedure and the inclusion of its high costs tends to drive the outcome of cost-effectiveness analyses so that even low-priced therapies might end up with high ICERs just because they are life-extending.

The results of the presented cost-effectiveness analysis strongly depend on the price of the innovative drug. This is not uncommon, in particular if there are already alternative treatments on the market. However, it may be found difficult to conclude from the results which price for etelcalcetide would be appropriate. The purpose of this article, however, was not to make suggestions on which price would be reasonable, but was to present an economic model which can be adapted to various settings. In this context, we would also like to point out how substantial input parameters may differ from country to country. For example, in the US drug and event costs have been observed to be higher than in European settings [13, 26].

In conclusion, within the limits of the modelling approach, we created a model that could be used to assess the cost-effectiveness of etelcalcetide. The cost-effectiveness of etelcalcetide itself may depend on country settings, such as country specific prices, further model inputs, and willingness-to-pay.

5   Data Availability Statement

The authors declare that all input data to parameterize the decision-analytic model is available within the article and its electronic supplementary material. The model can entirely be re-built based on the information provided.

6   Compliance with Ethical Standards

7   Author Contributions

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published. The authors thanks Amgen biostatistical department for the support provided.

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TABLES

Table 1 – Clinical input parameters

Parameter	Point estimate	SE or [95%CI]	Notes	Sources
Baseline event rates (events per person year)				
All-cause death			Age-specific annual	[20]
- 18-34 years old	0.045		mortality rates for	
- 35-44 years old	0.074		dialysis patients	
- 45-54 years old	0.094		with elevated levels	
- 55-64 years old	0.126		of PTH, Ca, and P	
- 65-74 years old	0.165			
- 75-84 years old	0.219			
- 85+ years old	0.261			
Non-fatal CV			EVOLVE trial,	EVOLVE
- first event	0.098	0.005	analysis of patient-	
- subsequent event	0.620	0.047	level data	
Non-fatal fracture				
- first event	0.045	0.003		
- subsequent event	0.114	0.024		
PTx	0.049	0.003		
HR clinical events, cinacalcet vs. placebo				
All-cause mortality	0.80	[0.69-0.91]		[13]
CV events	0.78	[0.67-0.91]		
Fractures	0.73	[0.59-0.92]		
PTx	0.25	[0.19-0.33]		
HR clinical events, etelcalcetide vs. placebo				
All-cause mortality	0.75	[0.62-0.89]		[9, 10, 13]
CV events	0.72	[0.59-0.88]		
Fractures	0.67	[0.50-0.89]		
PTx	0.17	[0.11-0.25]		
HR clinical events, etelcalcetide vs. cinacalcet				
All-cause mortality	0.94	[0.88,0.98]		[9, 10, 13]
CV events	0.93	[0.87,0.98]		
Fractures	0.91	[0.83,0.98]		
PTx	0.66	[0.51,0.81]		
Parametric functions to model the persistence of calcimimetics				

Gamma parameter	0.459		Weibull function (time in months)	[21]
Lambda parameter	0.409			
HRQoL utilities				
Utility while on dialysis	0.71	0.013		[22]
Absolute utility decrements				
- CV event months 1-3	0.19	0.014	Aggregated among CV events	[22]
- CV event after month 3	0.14	0.014		
- fracture months 1-3	0.31	0.035		
- fracture after month 3	0.12	0.020		
- PTx months 1-3	0.06	0.020		
- PTx after month 3	0	0	Assumption, based on non-significance (p=0.653)	
- Calcimimetic treatment	0	0	Conservative assumption, as published point estimate implied a slight utility increase	

HR: hazard ratio; CV: cardiovascular; PTx: parathyroidectomy; SE: standard error; CI: confidence interval; na: not applicable

Table 2 – Input parameters on drug usage and costs

Parameter	Point estimate	SE	Sources
Calcimimetic drug consumption (mg per day)			
Etelcalcetide	3.11	0.08	Efficacy assessment phase of etelcalcetide trials [9,10]
Cinacalcet	64.18	2.78	
Vitamin D and/or analogs consumption (μg per day)			
Alfacalcidol (oral)	0.07	0.005	Etelcalcetide trials [9,10]§
Alfacalcidol (IV)	0.009	0.002	
Calcitriol (oral)	0.05	0.003	
Calcitriol (IV)	0.006	0.0014	
Doxercalciferol (oral)	0.0005	0.00035	
Doxercalciferol (IV)	0.27	0.018	
Paricalcitol (oral)	0.02	0.005	
Paricalcitol (IV)	0.35	0.024	
Phosphate binders consumption (g per day)			
Aluminum containing	0.04	0.007	Etelcalcetide trials [9,10] §
Calcium (Ca) containing	0.57	0.031	
Lanthanum carbonate	0.21	0.016	
Mg containing	0.03	0.005	
Mg and Ca containing	0.005	0.0023	
Sevelamer	1.73	0.058	
Unit costs (*)			
Cinacalcet (€/mg)	€ 0.218	n.a.	Average of published cost data [24]
CV event costs	€ 3,184	€ 1,163	
Fracture event costs	€ 2,627	€ 1,053	
PTx event costs	€ 4,249	€ 2,097	
Monitoring costs (per quarter)	€ 72.9	€ 4.8	[14]
Vitamin D & phosphate binders	Costs were set to zero for this illustrative analysis.		
Etelcalcetide	Varies by scenario; results from the cinacalcet price via the dose ratio (multiplier) and a potential multiplier (1, 1.15, 1.3) to account for an increase in treatment costs		

CV: cardiovascular; PTx: parathyroidectomy; SE: standard error; CI: confidence interval; IV: intravenous; n.a., not applicable.

(*) Three price scenarios are explored for etelcalcetide: 1) same weekly calcimimetic drug cost – WCDC; 2) +15% WCDC and; 3) +30% WCDC.

§ Safety analysis set, sum of cumulative doses divided by total exposure days; SE based on bootstrapping.

Table 3 - Base case results of the cost-effectiveness analysis

	LYs		QALYs		Costs (discounted)		
	undiscounted	discounted	undiscounted	discounted	Same WCDC	+15% WCDC	+30% WCDC
Etelcalcetide	7.575	6.348	4.749	4.032	€14,195	€14,932	€15,670
Cinacalcet	7.520	6.304	4.771	4.000	€14,152	€14,152	€14,152
Increments							
Etelcalcetide vs. cinacalcet	0.055	0.043	0.039	0.032	€43	€780	€1,518
ICER							
Etelcalcetide vs. cinacalcet					€1,355/QALY	€24,521/QALY	€47,687/QALY

QALY: quality-adjusted life-years; ICER: incremental cost-effectiveness ratio; LY: life-years; PB/VD: phosphate binders and vitamin D and/or analogs alone;

WCDC: weekly calcimimetic drug cost.

Table 4 – Structural sensitivity analysis on the incremental cost-effectiveness ration

| ICER (€ per QALY)	Same WCDC	+15% WCDC	+30% WCDC
Base case	1,355	24,521	47,687
No parathyroidectomy	1,727	24,915	48,103
EVOLVE persistence	1,700	26,576	51,451
16% one-year persistence	502	21,866	43,229
Efficacy based on ITT disaggregation approach	1,848	23,614	45,380

QALY: quality-adjusted life-years; ICER: incremental cost-effectiveness ratio; WCDC: weekly calcimimetic drug cost; ITT, intention to treat.

FIGURES

Markov Component A: Health States
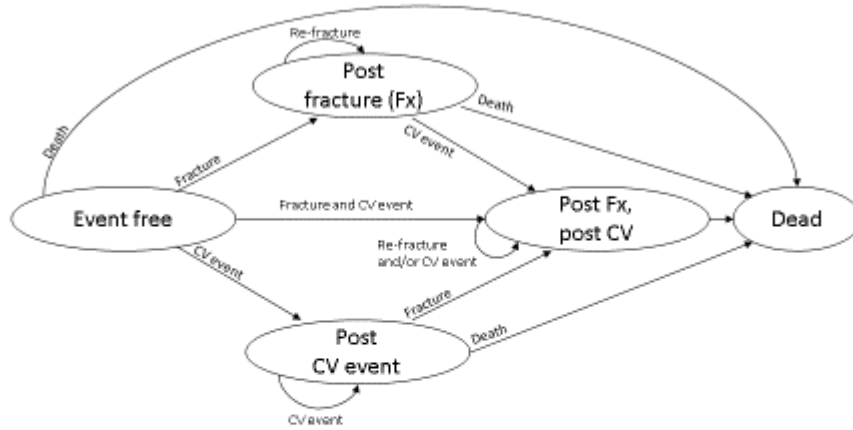
Markov Component B: Current Treatment
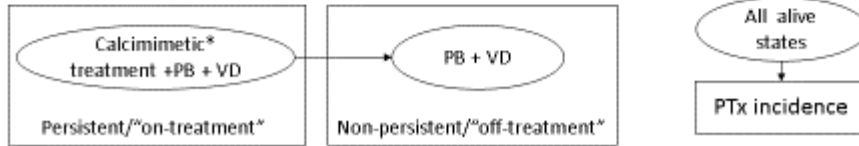
*Etelcalcetide or cinacalcet
PB, Phosphate binders ; VD, vitamin D; PTx, parathyroidectomy; CV, cardiovascular

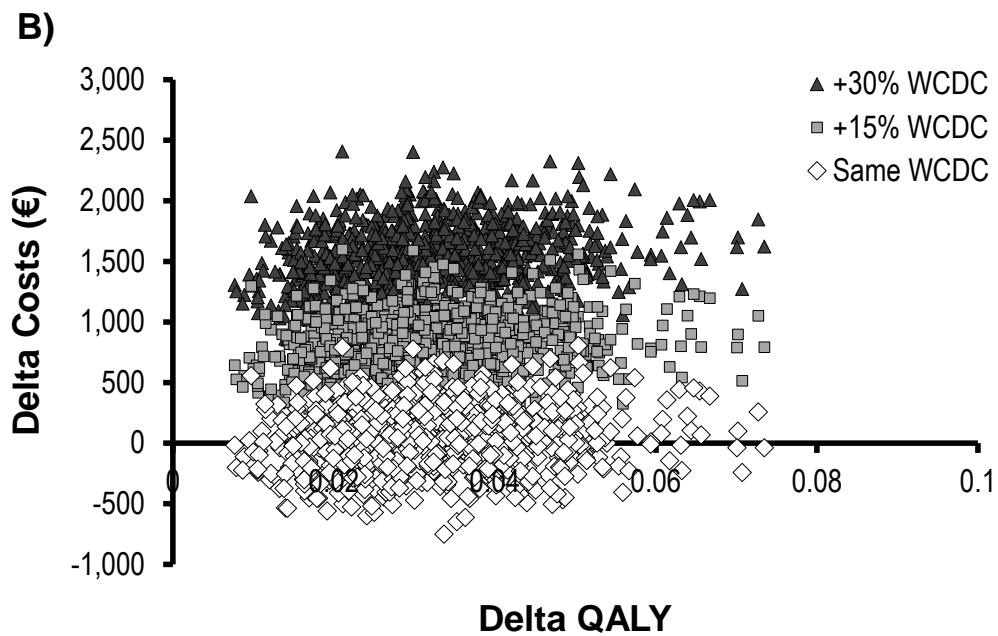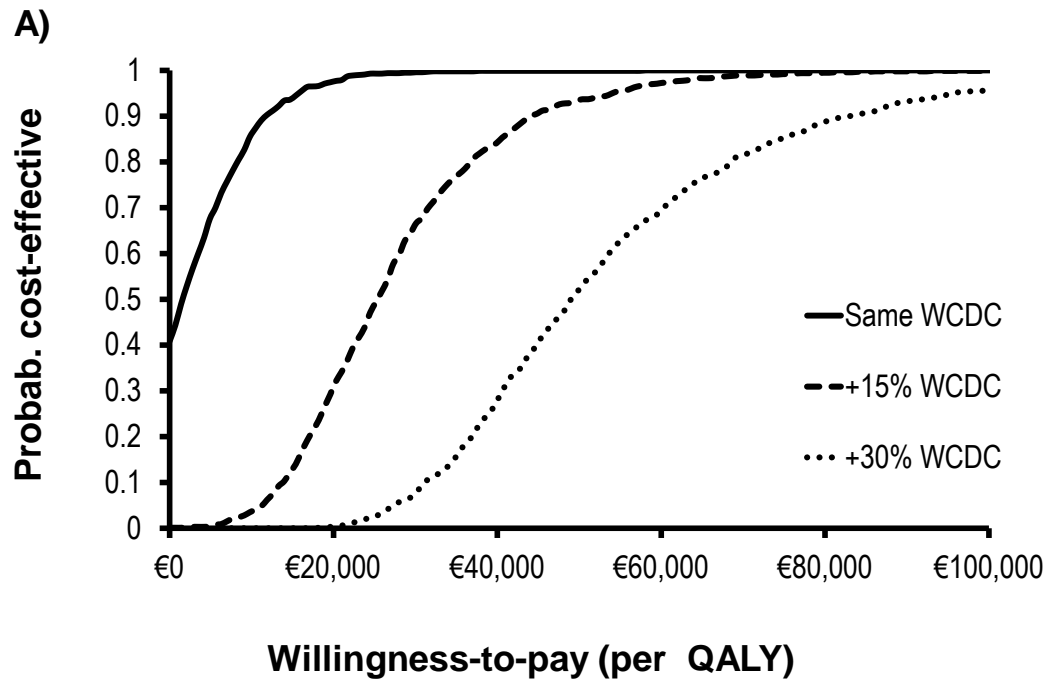Figure 1 - Illustration of the decision-analytic model

Figure 2 – Results of the probabilistic sensitivity analysis of etelcalcetide vs. cinacalcet. A) cost-effectiveness acceptability curves; B) scatter plot of 1000 PSA iterations in the cost-effectiveness plane. WCDC: weekly calcimimetic drug cost; WTP: willingness to pay; QALY: quality-adjusted life-years.
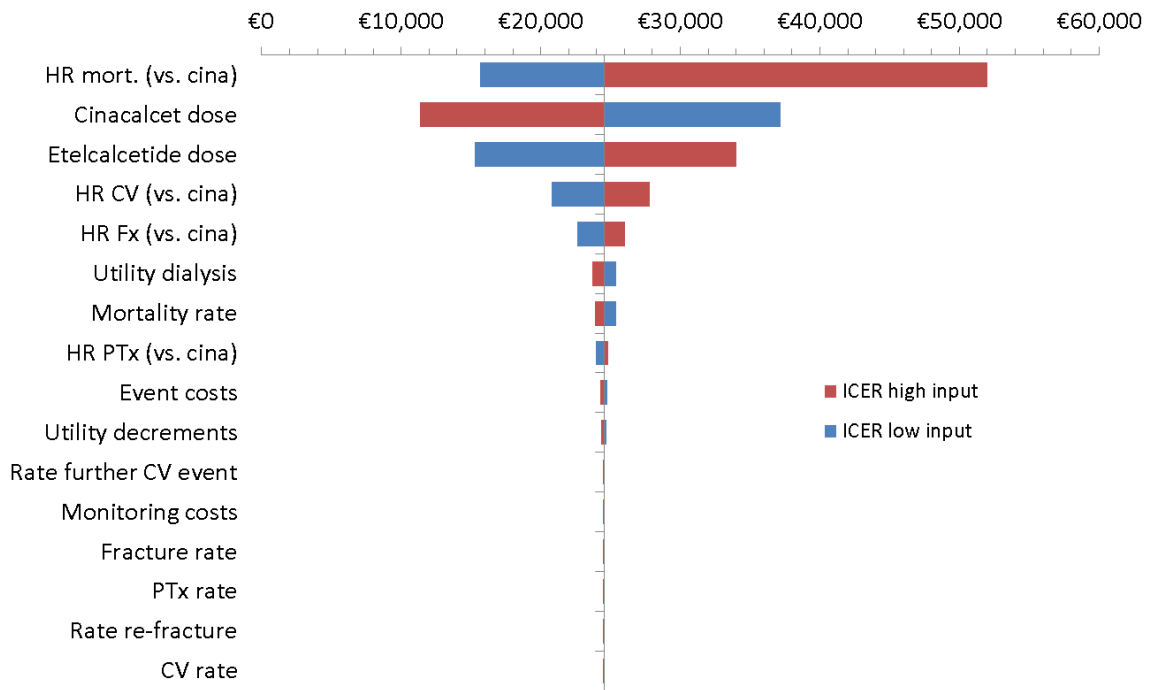
Figure 3 – Tornado diagram on the impact on the incremental cost-effectiveness ratio (ICER), illustrated based on a cost increase of 15% of the weekly calcimimetic treatment costs.

CV, cardiovascular; HR, hazard ratio; PTx, parathyroidectomy; Fx, fractures