Economic Impact of Ferric Citrate Versus Standard of Care For Hemodialysis Patients

DaVita Clinical Research

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Introduction

- Hyperphosphatemia is a nearly ubiquitous consequence of end-stage renal disease (ESRD) and is associated with increased risks of mortality and hospitalization.[1-3]
- Phosphate homeostasis in patients receiving dialysis generally requires dietary phosphate restriction and, frequently, the use of phosphate binders to prevent systemic absorption.[4]
- The iron-based phosphate binder ferric citrate coordination complex (FCCC; Keryx Biopharmaceuticals, Inc.) has recently completed phase 3 clinical trials in the United States and Japan.
  - In addition to being safe and efficacious as a phosphate binder, clinical trials have shown that FCCC results in a stable and sustained increase in serum ferritin concentrations and transferrin saturation, without evidence of iron overload.
  - FCCC use also resulted in reduced utilization of ESA and intravenous (IV) iron, with higher hemoglobin (Hb) concentrations and lower hospitalization rates.[5-7]
- Changes to Centers for Medicare and Medicaid Services reimbursement for hemodialysis in recent years have affected dialysis facilities' financial status, with the costs of providing care exceeding payments received for patients with Medicare as primary payer.

Objective

The objective of the current study was to evaluate the budgetary impact of FCCC versus standard of care as first-line phosphate binder from the perspective of a dialysis provider within the context of the current reimbursement paradigm and accounting for the effects of FCCC on ESA and IV iron utilization, Hb concentrations, and the potential for missed hemodialysis sessions resulting from hospitalizations.

Methods

- We constructed a Markov microsimulation model using TreeAge Pro 2013 (TreeAge Software Inc., Williamston, MA). The model considered 21 health states: 20 based on permuted categories of serum phosphate and phosphate binder dose strength; the 21st state was death, which was an absorbing state. We modeled serum phosphate and phosphate binder dose strength as continuous tracer variables and modeled the mutually referential, longitudinal effects between the two (Figure 1).
- For each interval, probability of death, hemodialysis treatment attendance, ESA utilization, and IV iron utilization were probabilistically assigned conditional upon health state.

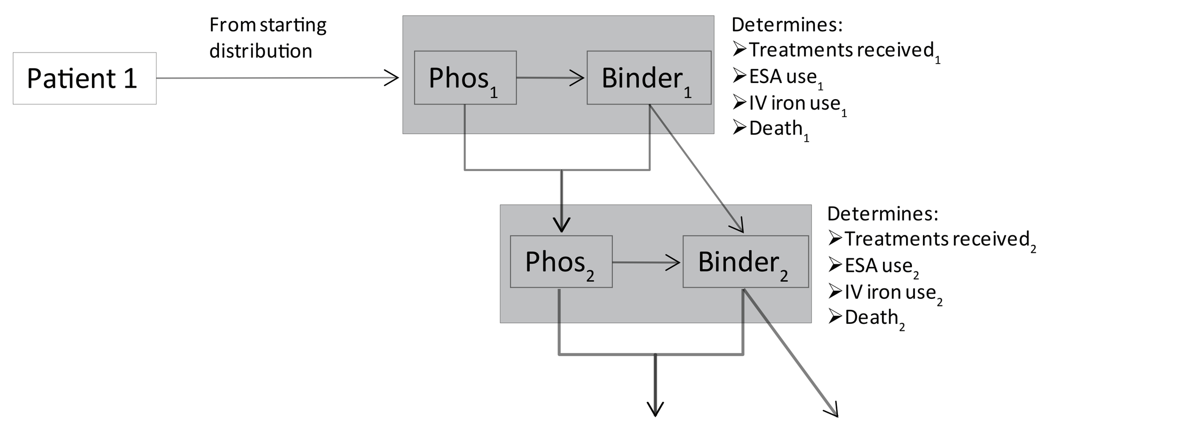

Figure 1. Schematic Depiction of the Microsimulation Model

Patient is probabilistically assigned a starting serum phosphate level ($Phos_1$) based on the empiric distribution of phosphate levels that immediately preceded phosphate binder initation. Phosphate binder dose strength for cycle 1 ($Binder_1$) is assigned probabilitistically conditional on $Phos_1$. $Phos_1$ and $Binder_1$ determine the patient's health state for cycle 1, which probabilistically determines the number of dialysis treatments, total dose of ESA and IV iron, and probability of death during cycle 1. For patients who survive cycle 1, change in phosphate between cycle 1 and cycle 2 is probabilitistically sampled based on $Phos_1$ and $Binder_1$. Change in phosphate binder strength at the start of cycle 2 is probabilistically sampled conditional on $Phos_2$ and $Binder_1$. $Phos_2$ and $Binder_2$ then define the health state for cycle 2. This process iterates forward.

Methods

- We ran the model over a 1-year time horizon and considered a 1-month cycle length. We used combined first and second order Monte Carlo simulation to fit models. Each model considered 1000 second-order trials.
- Model input data were derived from a retrospective analysis of phosphate binder users from a large dialysis organization (LDO). Patients received in-center hemodialysis at the LDO between January 2011 and June 2013, were enrolled in the LDO's pharmacy management program, and were incident users of phosphate binders. Patients were considered for a maximum of 24 months or until censoring (death, transfer, modality change, transplant, end of study period).
- Effects of FCCC were taken from results of the 52-week open-label safety portion of a recently completed phase III clinical trial (Keryx Biopharmaceuticals Inc., data on file).
- Costs and revenues were based on actual rates paid/received by the LDO (proprietary) and were considered in fixed 2013 USD. Costs and revenues considered were revenue for attended treatments, fixed costs of providing dialysis, cost of ESA, remuneration for ESA, cost of IV iron (drug and associated peripherals), and payment for IV iron. Phosphate binder costs were not included in the model as these are not borne by dialysis facilities under current reimbursement policies.

Results

Table 1. Base Case Model Inputs

		Value
Model inputs derived from retrospective analysis of incident phosphate binder users at LDO		
Mean (SD) starting serum phosphate, mg/dL		5.4 (1.6)
Distribution of primary insurance		
Medicare		85%
Private		15%
PB mix (standard of care)		
Calcium acetate		45%
Sevelamer		47%
Lanthanum carbonate		7%
Starting PB strength based on starting serum phosphate[a]		
Serum phosphate < 3.5 mg/dL, starting PB strength	1	19.9%
	1.5	27.7%
	2	52.4%
Serum phosphate = 3.5-5.5 mg/dL, starting PB strength	1	19.6%
	1.5	23.1%
	2	57.4%
Serum phosphate = 5.6-6.5 mg/dL, starting PB strength	1	17.8%
	1.5	21.2%
	2	61.0%
Serum phosphate > 6.5 mg/dL, starting PB strength	1	13.4%
	1.5	17.2%
	2	69.4%
Model inputs derived from FCCC clinical trial		
Effects of FCCC		
ESA dose		36% reduction
Effect of higher Hb on ESA dose		10% additional reduction
IV iron dose		55% reduction
IV iron administrations		59% reduction

a. Phosphate binder dose strength categories:
Dose Strength +1 = calcium acetate 1-2001 mg; sevelamer 1-2400 mg; lanthanum carbonate 1-3000 mg
Dose Strength +1.5 = calcium acetate 2002-4002 mg; sevelamer 2401-4800 mg; lanthanum carbonate 3001-6000 mg
Dose Strength +2 = calcium acetate > 4002 mg; sevelamer > 4800 mg; lanthanum carbonate > 6000 mg

Abbreviations: ESA, erythropoiesis-stimulating agent; FCCC, ferric citrate coordination complex; Hb, hemoglobin; IV, intravenous; PB, phosphate binder; SD, standard deviation

Results

Base-Case Model

- Under base-case assumptions and considered over 1 year, treatment with FCCC versus standard of care was found to have a net budgetary impact of +1,188,337 USD/year for 1,000 patients receiving phosphate binder (**Table 2**).

Table 2. Net Budgetary Impact: Base-Case Model

	Net Budgetary Impact of FCCC vs SOC (USD/year)		
	Mean (SEM)	Median (p25, p75)	P-value
Number of patients treated with phosphate binder			
Per 80 patients	+95,071 (7,385)	+94,948 (+89,842; +100,254)	< 0.001
Per 1,000 patients	+1,188,337 (26,490)	+1,188,885 (+1,170,228; +1,206,570)	< 0.001
Per 10,000 patients	+11,868,830 (83,895)	+11,866,750 (+11,815,720; +11,924,160)	< 0.001
Per 100,000 patients	+118,695,600 (262,404)	+118,698,400 (+118,516,400; +118,873,200)	< 0.001

Abbreviations:FCCC, ferric citrate coordination complex; SEM, standard error of mean; SOC, standard of care; USD, United States dollars

Sensitivity Analyses

- In a phase 3 clinical trial, mean Hb was +0.3 g/dL higher in FCCC-treated compared to control-treated patients. If the magnitude of the Hb differential is sufficient to prompt ESA down-titration in FCCC-treated patients, then further reductions in ESA utilization could result.
  - We assessed scenarios in which the increase in Hb translated into 0%, 10% (base case), 20%, or 30% additional reduction in ESA. Net budgetary impact ranged from +1,042,204 to +1,474,917 USD/year/1,000 patients receiving phosphate binder (**Table 3**).
- Clinical trial data indicate that FCCC use results in a 24% lower hospitalization rate. In base-case models, we assumed that the number of missed treatments corresponded 1:1 with hospitalizations.
  - Varying the ratio of missed sessions to hospitalizations to 1.25:1 or 1.5:1 resulted in a net budgetary impact of FCCC of +1,268,391 and +1,290,981 USD/year per 1,000 patients treated with phosphate binder, respectively (**Table 3**).

Table 3. Net Budgetary Impact: One-Way Sensitivity Analyses

	Net Budgetary Impact of FCCC vs SOC (USD/year/1000 patients treated) Mean (SEM)	P-value
Implication of Hb differential on ESA utilization, +0.3 g/dL higher Hb results in:		
0% further reduction in ESA	+1,042,204 (23,315)	< 0.001
10% further reduction in ESA (*base case*)	+1,188,337 (26,490)	< 0.001
20% further reduction in ESA	+1,331,169 (29,806)	< 0.001
30% further reduction in ESA	+1,474,917 (34,033)	< 0.001
Ratio of missed treatments to hospitalizations:		
1:1 (24% reduction in missed treatments; *base case*)	+1,188,337 (26,490)	< 0.001
1:1.25 (30% reduction in missed treatments)	+1,268,391 (27,204)	< 0.001
1:1.5 (36% reduction in missed treatments)	+1,290,981 (28,400)	< 0.001

Abbreviations: ESA, erythropoiesis-stimulating agent; FCCC, ferric citrate coordination complex; Hb, hemoglobin; SEM, standard error of mean; SOC, standard of care; USD, United States dollars

Conclusions

- This net budgetary impact model demonstrates that if FCCC were adopted in wide clinical practice as a first-line phosphate binder rather than the current standard of care, cost savings to the dialysis provider would be approximately $1.2M per year per 1,000 patients receiving phosphate binder.
  - Estimated cost savings arise principally from reductions in injected drug utilization and missed dialysis sessions.
  - The model assessed net budgetary impact of FCCC under current reimbursement, where oral medications are reimbursed separately from dialysis.
- The potential range of cost savings will depend in part on how physicians adjust ESA dose in response to the +0.3 g/dL differential in Hb concentration seen in FCCC-treated patients compared to control patients; sensitivity analyses suggest a range of $1.0M to $1.5M per year per 1,000 patients receiving phosphate binder.

Limitations of the Model

- Data do not pertain to net budgetary impact in the context of a more comprehensive bundle, under which dialysis providers assume financial responsibility for the costs of oral drugs.
- Cost savings pertain to patients treated with FCCC and not those who do not receive phosphate binders. Payer mix among phosphate binder initators is skewed toward higher prevalence of commercial payers because such patients are, on average, younger than the overall dialysis population. Extrapolation of findings to a facility- or provider-level should therefore be undertaken cautiously.
- Data used to estimate costs were derived based on contracted rates for a single provider; actual costs will vary across provider organizations.

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Acknowledgments

We extend our sincere appreciation to the teammates in more than 1,800 DaVita clinics who work every day to take care of patients and also to ensure the extensive data collection on which our work is based. We thank DaVita Clinical Research® (DCR®), and specifically acknowledge Abigail Hunt, PhD, of DCR for editorial contributions in preparing this poster. DCR is committed to advancing the knowledge and practice of kidney care.

This study was funded by Keryx Biopharmaceuticals, Inc.

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National Kidney Foundation Spring Clinical Meetings, 22-26 April 2014, Las Vegas, Nevada