Drugs R D (2017) 17:487–488
DOI 10.1007/s40268-017-0185-9

LETTER TO THE EDITOR

Comment on: "Net Budgetary Impact of Ferric Citrate as a First-Line Phosphate Binder for the Treatment of Hyperphosphatemia: A Markov Microsimulation Mode"

Karen Rascati[1]

Published online: 20 May 2017

In 2012, total treatment costs for end-stage renal disease (ESRD) [in-center dialysis and outpatient costs combined] were estimated to be about US$88,000 per person per year [1]. For payers, this represents over US$7000 per member per month (PMPM) in expenses, a substantial burden. Therefore, analyses of ESRD costs are vital. Brunelli et al. conducted a budget impact analysis of a new phosphate binder (PB), ferric citrate (FC), to estimate potential cost savings compared with current PBs [2]. The effectiveness of FC to manage phosphate levels has been shown to be similar to PBs currently on the market. Brunelli et al. indicate that a potential advantage of FC is that it also improves iron absorption, which may lead to decreased doses of erythropoiesis-stimulating agents (ESAs) and intravenous iron. The authors contend that it might also decrease the number of missed dialysis days because of fewer hospitalizations. It should be noted that FC is not approved by the US Food and Drug Administration for reducing iron and ESA, and the effects on iron indices are actually included in the 'Warnings and Precautions' in the approved labeling.

Previous researchers have looked at potential cost savings of FC. Rodby et al. [3] developed a model using data from a randomized controlled trial, and estimated that the reduced ESA and intravenous iron would provide cost savings of about US$175 PMPM. They do address some limitations, including that (1) the population enrolled in the randomized controlled trial was a younger, and probably less severe, population (the patients had to have >1-year life expectancy to be included in the study) than the average patient with ESRD and (2) the costs of PBs was NOT accounted for in the model, and it is expected that new medications will be priced at a higher rate than current comparators. Mutell et al. [4] generated a cost-offset model comparing FC with current PBs. The researchers assumed that the effectiveness and costs for all PBs were equivalent, and estimated cost offsets to be about US$160 PMPM.

For the Brunelli et al. model, shortcomings in the application of phase III data in the model should be noted. The application of the results of the phase III trial assumes perfect adherence to FC prescriptions. As previously reported by Chui et al., approximately 62% of patients are non-adherent to their PB prescriptions [5]. Next, estimates of reductions in ESA utilization may be overstated. The Brunelli et al. article includes a reduction in ESA dose of 36% based on "primary study data from a phase III trial" and references an article by Lewis et al. However, Table 3 in the Lewis article shows only a 23.7% ESA reduction in the 52-week median doses [6].

Additionally, confounding may have occurred because the FC phase III study was conducted between December 2010 and November 2012—about the same period when significant anemia management changes were implemented in response to the Center for Medicare and Medicaid Services new bundled reimbursement to dialysis facilities [7]. It has been estimated that bundling decreased the mean ESA dose by 35% during a similar time period. In addition, current ESA and intravenous iron utilization is lower than

✉ Karen Rascati
krascati@mail.utexas.edu

[1] Health Outcomes and Pharmacy Practice Division, College of Pharmacy, The University of Texas, 1 University Station A1930, Austin, TX 78712-0127, USA

it was during the phase III study. According to the Dialysis Outcomes and Practice Patterns Study practice monitor, at large dialysis organizations, the median weekly erythropoietin dose decreased from 12,718 units in December 2010 to 7203 in October 2016 [8].

While the reduction in hospitalizations played only a small part in cost savings, the "24% lower hospitalization rate" used to determine the expected number of missed treatments comes from a non-significant result from the Rodby et al. article [3]. "There were a total of 181 unique hospitalizations in the FC group of 289 subjects (0.63 hospitalizations per subject) and 123 hospitalizations in the AC group of 149 study subjects (0.83 hospitalizations per subject), $p = 0.08$." Thus, the unique hospitalizations did not differ significantly between the two groups in the original paper.

Brunelli et al. conclude that use of FC would provide 'substantive' savings, and savings are summarized as yearly costs for 100 patients. This estimated savings of US$213,233/year/100 patients can also be presented as US$178 PMPM to the dialysis center, a similar finding to the Rodby and Mutell studies. Over 90% of this savings was owing to the reduction in ESA use, which is a debatable estimate based on the above reasoning. The reductions in intravenous iron use and hospitalization both play a small role in the estimates. For the baseline analysis, the average wholesale price was used to estimate the cost of ESA. Dialysis centers pay much less than the average wholesale price. The sensitivity analysis using 50% of the average wholesale price may be more realistic, and, as expected, it reduces costs savings by half. Considering the average PMPM for a patient with ESRD is more than US$7000, a savings of US$178 results in a 2.5% decrease, which may or may not be seen after realistic reductions in ESA and realistic cost estimates are used.

Instead of using the payer perspective (which would include the costs of PBs), Brunelli et al. used a more narrow perspective of 'the dialysis center.' While this may be important to decision makers at dialysis centers, it provides an incomplete examination of the costs associated with ESRD treatment, known as 'silo' mentality. The International Society For Pharmacoeconomics and Outcomes Research Task Force on Budget Impact Analyses recommends a flexible analysis that includes the larger economic implications of the intervention, including the impact on other budget holders [9].

In conclusion, while there may be a potential for cost savings for some patients with ESRD with iron deficiency, these estimated savings may not be considered 'substantial' when compared with overall ESRD costs or when framed as PMPM estimates. A critical factor that will determine the cost effectiveness of FC has been ignored—the actual cost of this new PB. Although costs of PBs may not currently be bundled into dialysis center costs, ignoring these costs provides only a partial analysis of their overall effect. With a new administration in Washington, DC, scrutiny of the overall costs to insurers, especially Medicare, will be intensified.

Compliance with Ethical Standards

Funding No funding was received for the preperation of this manuscript.

Conflict of interest Karen Rascati has served as a consultant to Fresenius Medical Care.

References

1. Schmid H, Lederer SR. Novel iron-containing phosphate binders for treatment of hyperphosphatemia. Expert Opin Pharmacother. 2015;16(14):2179–91.
2. Brunelli SM, Sibbel SP, Van Wyck D, et al. Net budgetary impact of ferric citrate as a first-line phosphate binder for the treatment of hyperphosphatemia: A Markov microsimulation model. Drugs R D. 2017;17:159–66. doi:10.1007/s40268-016-0163-7.
3. Rodby R, Umanath K, Dwyer J, et al. Ferric citrate, an iron-based phosphate binder, reduces health care costs in patients on dialysis based on randomized clinical trial data. Drugs R D. 2015;15(3):271–9.
4. Mutell R, Rubin J, Bond T, Mayne T. Reduced use of erythropoiesis-stimulating agents and intravenous iron with ferric citrate: a managed care cost-offset model. Int J Nephrol Renovasc Dis. 2013;6:79–87.
5. Chiu Y, Teitelbaum I, Misra M, et al. Pill burden, adherence, hyperphosphatemia, and quality of life in maintenance dialysis patients. Clin J Am Soc Nephrol. 2009;4(6):1089–96.
6. Lewis J, Sika M, Dwyer J, et al. Ferric citrate controls phosphorus and delivers iron in patients on dialysis. J Am Soc Nephrol. 2015;26(2):493–503.
7. Fuller D, Pisoni R, Bieber B, et al. The DOPPS practice monitor for US dialysis care: update on trends in anemia management 2 years into the bundle. Am J Kidney Dis. 2013;62(6):1213–6.
8. US-DOPPS practice monitor, December 2016. http://www.dopps.org/DPM. Accessed 3 May 2017.
9. Sullivan S, Mauskopf J, Shau W, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. Value Health. 2014;17(1):5–14.