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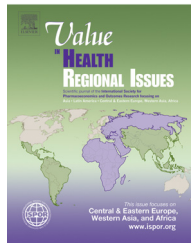

Cost-Minimization Analysis of Direct Cost of Sevelamer Carbonate and Lanthanum Carbonate in the Treatment of Patients with Chronic Kidney Disease Not on Dialysis in Bulgaria

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ABSTRACT

Background: Hyperphosphatemia is associated with significant pathophysiology in chronic kidney disease (CKD). Control of hyperphosphatemia in patients with stage 3 to 5D CKD is now regarded as a high priority. **Objective:** The primary purpose of this study was to perform an economic analysis of the newly available treatments sevelamer carbonate (SC) and lanthanum carbonate (LC) for the treatment of hyperphosphatemia in patients not on dialysis in Bulgaria. **Methods:** Both treatment options demonstrate equal efficacy in controlling hyperphosphatemia, as well as having a similar safety profile in regard to adverse effects. To differentiate between them, a cost-minimization analysis was performed. A time period of 4 years was chosen to perform a budget impact analysis. The robustness of the results was tested through sensitivity analysis using Tornado diagrams. **Results:** The estimated cost per patient per year with SC and LC would be €1441.75 and €1569.50, respectively, at the weighted average daily dose regimen of 4000 mg SC and 2000 mg LC, whereas the cost would be €2306.80 and €2354.25 for 6400 mg SC and 3000 mg LC, respectively. Expected cost savings (discounted) for the 4-year period of the analysis can reach between €1,363,601 and €2,727,201 at 4000 mg SC and 2000 mg LC dose regimen, whereas these can reach between €506,480 and €1,012,961 at 6400 mg SC and 3000 mg LC, respectively. **Conclusions:** The equal efficacy, similar adverse effect profile, and lower cost of SC when used for the treatment of hyperphosphatemia in patients with CKD not on dialysis should make it a preferred alternative.

Keywords: cost-minimization, hyperphosphatemia, lanthanum carbonate, patients not on dialysis, sevelamer.

Introduction

Chronic kidney disease (CKD), the progressive deterioration of kidney function, affects approximately 5% to 10% of the world's population [1]. It is most often caused by diabetes and hypertension, which together account for approximately two-third of CKD cases [2]. Similar numbers were reported for the Bulgarian population [3]. Compared with the general population, patients with CKD are at an increased risk of vascular calcification and mineral and bone disorders, leading to an increased risk of cardiovascular disease and mortality [1,4,5]. The sequel of mineral and bone disorders that accompany CKD has been termed chronic kidney disease-mineral and bone disorder. It is a systemic disorder of mineral and bone metabolism that occurs early in the pathophysiology of CKD, when loss of kidney function leads to progressive deterioration of the balance of minerals such as phosphorus and calcium, hormones, and other metabolites. Hyperphosphatemia or elevated phosphorus level in the blood is common in patients with CKD-mineral and bone disorder and independently and significantly contributes to morbidity and mortality in these patients [1,4–8]. Decrease in the glomerular filtration rate below 59 ml/min is classified as mild to moderate loss of kidney function, whereas that below 29 ml/min is classified as severe according to Levin et al. [4]. Hyperphosphatemia leads to increased risk of calcification [5], 70% increased risk of starting dialysis [7,9], a 30% greater risk of cardiovascular events [10,11], and increased risk of all-cause and cardiovascular-related mortality [11–13]. Early and aggressive management of mineral imbalance, especially phosphorus, is a priority for patients with CKD and can achieve significant savings to health authorities by decreasing hospitalization rates within patients with higher serum phosphate. Managing serum phosphorus in CKD can lead to a decrease of 25% in the rate of cardiovascular events, 4 times lesser mortality,as the risk of starting dialysis and transplantation is reduced by 70% [7,9,14–17]. The goal of phosphorus management is to maintain levels within the normal range of 2.5 to 4.5 mg/dL (0.81–1.45 mmol/L) according to the Kidney Disease: Improving Global Outcomes guideline [1].

Phosphate binders are an essential component of managing hyperphosphatemia. Treatment with phosphate binders is

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independently associated with improved outcomes, including improved overall survival in patients with CKD [18]. Traditional binders such as those containing calcium or heavy metals are effective at reducing serum phosphorus, but they pose health risks associated with the accumulation of calcium or metal in the body [19].

For part of the patients with CKD not on dialysis not eligible for calcium- or other metal-based phosphate binders because of vascular calcifications and toxicity, new alternatives were included in the positive list in Bulgaria, but these are still not marketed effectively in the country—Renvela 800 mg × 180 tablets (sevelamer carbonate [SC]; Genzyme, BV, The Netherlands) and Fosrenol 1000 mg × 90 tablets (lanthanum carbonate [LC]; Shire, Ltd., UK).

Renvela (SC) is a second-generation sevelamer (polymeric amine) compound with the same active moiety and mechanism of action as its predecessor Renagel (sevelamer hydrochloride [SH]). SC differs from SH only in the replacement of chloride with carbonate as the counterion, which serves to increase buffering capacity and reduce the risk of gastrointestinal (GI) adverse events (AEs) and acidosis related to decreased serum bicarbonate concentrations. Such improvements in the chemical structure of SC may reduce the need for monitoring chloride and bicarbonate levels and may reduce the risk of acidosis [20].

In three head-to-head randomized studies, SC and SH were shown to provide equivalent serum phosphorus control [21–23]. Given their structural similarities and equivalence in terms of serum phosphorus control and safety, it is reasonable to expect that SC will demonstrate an impact on other clinical outcomes (e.g., calcification and mortality) that is similar to that of SH.

Both SC and LC are significantly reducing serum phosphorus in patients with CKD. They are well tolerated, where the predominant AEs are of a GI nature with no serious events [21–29].

In light of the increased incidence of CKD, constantly increasing health care spending, and cost-containment policies concerning medicines, there is a rising need for better allocation of scarce resources through informed decisions from the stakeholders.

We sought to investigate the evidence for efficacy and safety and to compare the direct cost of SC and LC in the treatment of hyperphosphatemia in patients with CKD not on dialysis in Bulgaria from the health authority perspective, that is, the National Health Insurance Fund (NHIF). Another study objective was to investigate the budget impact both products would have on entering the market effectively.

Methods

Search Strategy

A comprehensive search to identify all relevant studies was carried out. PubMed, Scopus, The Cochrane Library, NHC Evidence Search, and Google Scholar were searched (1998–August 2014). The following key words and phrases were used: sevelamer, lanthanum carbonate, clinical trial/study or efficacy or safety, hyperphosphatemia, cost-effectiveness, and cost-minimization.

Selection Criteria

Each potentially relevant study was independently assessed by two reviewers for inclusion in the study. For assessing the efficacy and safety, studies meeting the following criteria were eligible for inclusion: controlled clinical trials in which the efficacy and safety are examined in adults, with prevalence of white ethnicity (>50%), with end-stage renal disease or patients with CKD not on dialysis treated with SC, SH, and LC compared with any phosphate binder or placebo.

Type of Analysis and Study Perspective

The two studies that concern patients not on dialysis allow for an indirect comparison [24,28], with SH being the common arm for the indirect comparison of SC and LC. The indirect comparison provides a similar AE profile and efficacy in controlling phosphate levels in patients with CKD not on dialysis, justifying a cost-minimization analysis (CMA).

As per approved label in Bulgaria, both SC and LC can be used for the treatment of hyperphosphatemia in patients with CKD not on dialysis, the cost of which is reimbursed at 75% by the NHIF. For this reason, the present study was carried out from the payer perspective.

Cost-Minimization Analysis

Both medicines are administered orally, with no considerable differences within the AEs' profiles, which can lead to hospitalization and/or increase in treatment cost. CMA was performed using the direct cost, that is, only unit cost per tablet of SC and LC incurred from the NHIF.

The prices were retrieved online from the officially published registries on the National Council for Pricing & Reimbursement's Web site [30]. An exchange rate of 1,95,583 BGN for €1 was used.

The daily/yearly costs of both therapies were calculated using the weighted average dose regimens, under which it was assumed that meaningful clinical outcomes will be achieved, that is, 4000 mg of SC versus 2000 mg of LC and 6400 mg of SC versus 3000 mg of LC, respectively [31,32].

Forecasting the Budget Impact to the NHIF

The budget impact was fulfilled for a 4-year period (2015–2018). We explored three scenarios in which the patient's allocation between the two treatment options SC and LC was 100:0, 50:50, and 0:100.

The budget impact model is prevalence based. The target population was calculated by using the prevalence of CKD in Bulgaria [3] within the population according to the last census 2011 [33].

Data regarding the prevalence considered for this analysis were obtained from the national representative epidemiological study of endocrine and kidney diseases in Bulgaria [3].

Patients eligible for treatment are those in CKD stage 3 to 4 who cannot be treated with calcium- and other metal-based phosphate binders because of vascular calcification and toxicity.

Following the data published on the NHIF Web site, Intercontinental Marketing Services (IMS) data for the market share, and market trends when a new product is launched in Bulgaria, as well as the cost-containment rules limiting the number of eligible patients, we made several assumptions:

- An increase of 0.2% per year, corresponding to the prevalence of CKD among the overall population within stage 3 to 4, as well as a 0.2% yearly increase in the number of patients eligible for treatment with SC and LC.
- Having in mind the very restrictive insurance policy, it is also assumed that treatment will be received from 20% of the eligible patients in 2015 as for 2016, 2017 and 2018, the coverage will be 45%; 65% and 80% respectively.

The discount rate used was 3.5% as per National Institute of Health and Care Excellence recommendations [34].