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The Cost-Effectiveness and Budget Impact of Introducing Indacaterol into the Colombian Health System

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ABSTRACT

Objectives: The main objectives were to estimate the cost-effectiveness and budget impact of indacaterol (a once-daily, long-acting-beta$_2$-agonist) compared with 1) salmeterol/fluticasone, 2) formoterol/budesonide, and 3) tiotropium for the treatment of chronic obstructive pulmonary disease in Colombia. **Methods:** A Markov model was utilized to simulate the progressive course of chronic obstructive pulmonary disease, distinguished by forced expiratory volume in 1 second predicted according to the four Global Initiative for Chronic Obstructive Lung Disease severity stages by using prebronchodilation values. Efficacy was based on the initial improvement in forced expiratory volume in 1 second, taken from either a network meta-analysis (salmeterol/fluticasone and formoterol/budesonide) or a randomized controlled trial (tiotropium). Colombian direct costs and life tables were incorporated in the adaptation, and analysis was performed from a health care payer perspective, discounting future costs (presented as US dollars) and benefits at 5%. A budget impact model was built to estimate the cost impact of indacaterol in Colombia over 3 and 5 years. **Results:** Indacaterol was found to be dominant (i.e., less costly and more effective) against both salmeterol/fluticasone and formoterol/budesonide per life year and quality-adjusted life-year gained after a 5-year time horizon. The average cost saving against salmeterol/fluticasone and formoterol/budesonide was US $411 and US $909 per patient, respectively. All probabilistic sensitivity analysis simulations indicated indacaterol to be less costly than salmeterol/fluticasone and formoterol/budesonide. Indacaterol was more effective and more costly than tiotropium, corresponding to an incremental cost-utility ratio of US $2584 per quality-adjusted life-year. **Conclusions:** The results indicate that by replacing salmeterol/fluticasone or formoterol/budesonide with indacaterol, there are possible cost savings for the Colombian health care system. This was demonstrated by both cost-effectiveness and budget impact models.

Keywords: Colombia, COPD, cost-effectiveness, indacaterol.

Background

Chronic obstructive pulmonary disease (COPD) is a chronic disease affecting 8.9% [1] of the 14,958,285 [2] Colombians aged 40 years or older. Of these, 31% [1] belong to Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometric classification 2 to 4, as defined by GOLD [3]. In 2005, COPD was ranked as Colombia's seventh most disabling disease, with 9.8 disability-adjusted life-years per patient, and second or third when considering people older than 80 years and between 60 and 79 years old, respectively [4]. This proves that COPD is a major burden to the Colombian health care system. It has been estimated that the weighted average cost of COPD could be US $848.10 per patient per year in Colombia [5]. By using this average per-patient cost, the burden of COPD was found to be US $916 million in 2004, based on a COPD prevalence figure of 1,080,000 patients, and US $1129 million, based on 2012 projections of COPD prevalence, which estimate 1,331,000 patients [2]. This is approximately 0.7% to 0.9% of the Colombian gross domestic product (GDP). About 35% of these costs are related to hospitalizations to treat acute exacerbations [6]. It is unclear whether this estimate includes the cost of long-acting inhaled therapies used as maintenance therapy in COPD. An alternative source indicates that the annual spending on inhaled therapies—long-acting beta$_2$-agonist (LABA), long-acting muscarinic antagonist, and LABA with inhaled corticosteroids (ICSs)—for COPD in Colombia is estimated to be US $5.5 million (0.6% of the total cost of COPD), using data validated by Dr. Luis F. Giraldo [7], with LABA/ICS products being the market leaders (60% market share in COPD).

There are currently four long-acting inhaled products used in the treatment of COPD in Colombia: indacaterol 150 μg; a once-daily LABA, tiotropium 18 μg; a long-acting muscarinic antagonist; and two fixed-dose combinations (FDCs) of LABA and ICS: salmeterol/fluticasone 50/500 μg and formoterol/budesonide 9/320 μg. For the purposes of the current analysis, FDCs were

Conflicts of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article. Machnicki and Kraemer are employees of Novartis, Ariza is a former employee of Novartis, and Thuresson, Mungapen, and Asukai are paid consultants.

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selected as the main comparators because these are most frequently used in GOLD stages 2 to 4. It should be noted, however, that ICSs are not recommended for patients at low risk of COPD exacerbations, such as those with % predicted forced expiratory volume in 1 second (FEV_1) of more than 50% and with zero or one exacerbation in the previous year by the current GOLD strategy [3]. Currently, no long-acting therapies have been included in the Colombian health benefit plan, despite the recommendation in the GOLD strategy. Currently, patients with COPD in Colombia must have their prescriptions approved by the health service on a case-by-case basis.

The decision of whether to include long-acting inhaled products in the national health plan, and if so which products might offer the best value for money, would pose a challenging question to Colombian decision makers. Different tools exist to facilitate the decision-making process on resource allocation, and one such tool is the cost-effectiveness (CE) analysis; it is highly suitable as it considers both the difference in effects gained (i.e., life years [LYs] or quality-adjusted life-years [QALYs]) and costs incurred between two interventions. Another commonly used tool is the budget impact model, which considers the changes in the health care budget when introducing a new therapy. Both tools have therefore been utilized numerous times to evaluate the CE and budget impact of therapies in COPD such as long-acting muscarinic antagonist or LABA alone, or the latter in combination with ICS. To the authors' knowledge, however, this is the first COPD CE study in a Latin American setting and the first CE evaluation of indacaterol compared with a combination of LABA and ICS. A CE analysis will help decision makers who are considering individual patient applications for long-acting inhaled products to treat COPD; it may also help to reconsider the case decision to include certain long-acting inhaled products in the Colombian Health Benefit Plan, thereby eliminating the need to assess patients on a case-by-case basis.

Methods

The CE analysis was performed by using a Markov model constructed in Microsoft Excel 2007, with 3-month cycles. The structure was identical to the model previously published by Price et al. [5] (Fig. 1). Health states were categorized by the ratio of prebronchodilator FEV_1 compared with that of the general population. The states were separated according to the GOLD spirometric classification [8]: mild (GOLD 1: 80%–100%), moderate (GOLD 2: 50%–80%), severe (GOLD 3: 30%–50%), and very severe COPD (GOLD 4: <30%) airflow limitation. The initial distribution of disease severity in the model corresponded to the baseline characteristics observed in the Novartis Indacaterol phase III trial (INHANCE) (1.4%, 42.2%, 45.4%, and 11.0% from stage 1 to 4, respectively) [9]. To ensure that the model results were representative of the Colombian population, a disease severity distribution based on Colombian data was investigated as a scenario analysis based on the Colombian COPD cohort PREPOCOL [1]. Prediction of FEV_1 for the general population was done by utilizing a regression model published by Falaschetti et al. [10]; this was used as no Colombian-specific regression model was available. Each GOLD state in the model could be further subdivided into no exacerbation, nonsevere exacerbation (not requiring hospitalization), severe exacerbation (requiring hospitalization), and those having discontinued therapy. A 7% annual discontinuation rate of therapy was assumed, equal for all treatments.

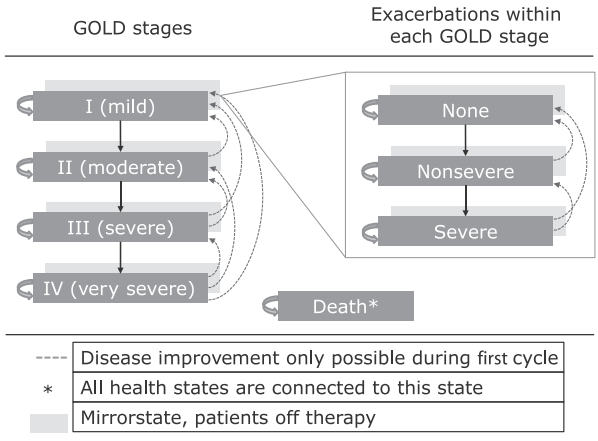

Fig. 1 – Model structure. GOLD, Global Initiative for Chronic Obstructive Lung Disease.

The annual decline in lung function was 54 ml obtained from the OLIN study [11], which gives the rate of decline in prebronchodilator FEV_1. Normal lung function was compared against the lung function predicted by the annual rate of decline for patients with COPD to yield a percentage of predicted lung function for each year. The number of years it took for the percentage predicted value to cross the threshold of a GOLD class was taken as the median time for patients to progress one GOLD class. The median time was then converted into a probability of progressing by using the following equation: $1 - 0.5^{\wedge}(1/(\text{median time}))$.

Two different CE analyses were performed, the first against formoterol/budesonide 9/320 μg and the second against salmeterol/fluticasone 50/500 μg. Because there were no head-to-head trials between indacaterol and LABA/ICS, efficacy was instead based on a published network meta-analysis (NMA) [12]. This NMA used Bayesian statistics to compare all therapies linked in the network at once, considering both direct (i.e., head-to-head trials) and indirect evidence (i.e., via a common comparator) [13]. The NMA included 15 placebo-controlled randomized clinical trials of which 13 contained active treatments of interest: indacaterol 150 μg (n = 5 studies), formoterol/budesonide 9/320 μg (n = 3), salmeterol/fluticasone 50/500 μg (n = 5), excluding those with only an Asian study population. The present analysis uses FEV_1 results reported in the NMA publication: indacaterol 150 μg increased FEV_1 with 180 ml (95% credible interval [CrI] 110–250 ml) after 12 weeks; the corresponding number for formoterol/budesonide 9/320 μg was 90 ml (95% CrI 10–160 ml) and 150 ml (95% CrI 100–230 ml) for salmeterol/fluticasone 50/500 μg (Table 1). The outcome presented above was adjusted for two covariates: the proportion of current smokers and the proportion with severe or very severe COPD. This set of results from the NMA was selected to ensure that the model could properly account for the patient characteristics that would have an impact on the results.

A second analysis was based on the clinical study INHANCE [9], a head-to-head trial of indacaterol versus open-label tiotropium 18 μg, applying the transition matrix published by Price et al. [5].

No exacerbation data were available from the NMA; thus, only FEV_1 was considered in this analysis; however, exacerbation rates were included in the analysis versus tiotropium. These were taken from the INHANCE study. The baseline rate of exacerbations from the placebo arm of the trial was 0.72 per patient-year [9]. Rate ratios were applied to the baseline rate of exacerbation: 0.67 (95% CI 0.46–0.99) and 0.70 (95% CI 0.48–1.03) for indacaterol and tiotropium, respectively. As the exacerbation rates by disease severity (i.e., GOLD stage) were not available, the same rate of exacerbations per year was applied to all four disease severity groups. The impact of such an assumption was tested in a scenario by applying values from a systematic review [14]. Exacerbations were further classified as severe or nonsevere. Exacerbations requiring hospitalizations were considered severe. The distribution of severe to nonsevere exacerbations was derived for each disease severity group on the basis of INHANCE [9].