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Budget impact of a 10% ready-to-use intravenous immunoglobulin in the treatment of primary immunodeficiency in Belgium

Steven Simoens

Research Centre for Pharmaceutical Care and Pharmaco-economics, Katholieke Universiteit Leuven, Leuven, Belgium;
steven.simoens@pharm.kuleuven.be

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ABSTRACT

The aim of this study is to compute the budget impact of adopting Kiovig, a new ready-to-use 10% liquid immunoglobulin preparation, as a treatment for primary immunodeficiency from the perspective of the Belgian health care payer. The analysis compared the "world with Kiovig" to the "world without Kiovig" and calculated how a change in the mix of immunoglobulins used to treat primary immunodeficiency would impact drug spending during 2010-2014. Data on the number of patients, immunoglobulin market shares and drug unit costs were derived from the IMS Health hospital disease database and from Belgian sources. The number of Belgian patients suffering from primary immunodeficiency is expected to increase from 2,378 patients in 2010 to 2,447 patients in 2014. The budget impact of adopting Kiovig is likely to be modest, raising the immunoglobulin drug budget for this patient population by 0.4%-1.3% per year. The budgetary increase originated from the higher price of Kiovig as compared with other products, although the impact of Kiovig was limited by its anticipated slow market penetration. There is a need for more and better data on the Belgian immunoglobulin market.

Keywords: Immunoglobulins; Intravenous; Primary Immunodeficiency; Budget Impact; Belgium

1. INTRODUCTION

Primary immunodeficiency (PID) disorders are characterised by low or undetectable immunoglobulin levels [1] and are associated with an increased patient susceptibility to recurrent respiratory tract and gastrointestinal infections [2]. Since the 1950s, immunoglobulin products have been administered to treat infections in PID, and patients often require lifelong therapy [3]. Immunoglobulin therapy in PID replaces functionally deficient or absent immunoglobulins, reduces the incidence of infections, and prevents organ damage caused by infections [4]. Immunoglobulin therapy is administered via the intramuscular, intravenous or subcutaneous route.

Kiovig (Baxter International Inc.), a ready-to-use 10% liquid immunoglobulin preparation, is medically indicated for the treatment of, amongst other indications, PID disorders [5]. This plasma-derived product consists of a highly purified preparation of human immunoglobulin. It is supplied as a ready-to-use liquid formulation with a pH of 4.6 to 5.1. Three dedicated virus clearance steps are integrated in the manufacturing process and the resulting product exhibits an intact immunoglobulin molecule with complete functional activity. Kiovig is supplied in single-dose vials that nominally contain 1 g, 2.5 g, 5 g, 10 g and 20 g protein per vial. The European Commission granted a marketing authorisation valid throughout the European Union for Kiovig in January 2006 [6].

With a view to assessing a drug reimbursement application, regulatory agencies in an increasing number of countries require data about, amongst other things, the budgetary impact of the drug on national, regional or local budgets [7]. A budget impact analysis examines the financial impact of the adoption and diffusion of a drug within a particular setting and, thus, considers the affordability of a drug. Specifically, a budget impact analysis explores how a change in the current mix of treatment strategies by the introduction of a new drug will impact spending on a disease. However, to date, budget impact analyses have rarely been published in the international literature [8].

In a context of spiralling health care costs and limited resources, policy makers and health care payers are concerned about the budget impact of Kiovig and other intravenous immunoglobulins. Therefore, the aim of this study is to compute the budget impact of adopting Kiovig as a treatment for PID from the perspective of the Belgian health care payer.

2. METHODS

2.1. Analytic Technique

The methodology of budget impact analysis is still developing, although principles of good practice for budget impact analysis have recently been proposed [9]. The budget impact analysis assessed the financial consequences of adopting Kiovig as a treatment for PID from the perspective of the health care payer in Belgium. More specifically, the budget impact analysis compared the "world with Kiovig" to the "world without Kiovig" and calculated how a change in the mix of immunoglobulins used to treat PID would impact the trajectory of drug spending on this condition. The general model for conducting the budget impact analysis of Kiovig is outlined in **Figure 1**.

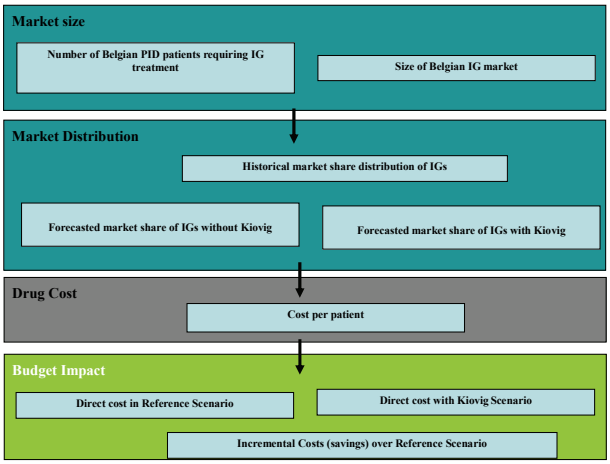
The budget impact analysis consisted of four modules. First, the Market Size was estimated by identifying the number of PID patients requiring immunoglobulin treatment. Second, the Market Distribution module estimated the market share of Kiovig as well as the impact of the adoption of Kiovig on the market shares of other immunoglobulins. Third, the Drug Costs scenario calculated annual immunoglobulin costs per patient. Fourth, the Budget Impact module calculated total drug costs in the reference scenario ("world without Kiovig") and the new drug scenario ("world with Kiovig"). The cost difference between these two scenarios revealed the budget impact of adopting treatment with Kiovig. The time horizon of the budget impact analysis was five years from 2010 until 2014.

2.2. Market Size

The number of Belgian people suffering from PID was derived from the IMS Health hospital disease database and was expressed as a proportion of the Belgian population. The analysis assumed that the percentage of the Belgian population who suffers from PID would remain constant over time. This implies that, in line with the growing size of the Belgian population over time [10], the number of PID patients is expected to increase.

2.3. Market Distribution

Based on the reimbursement value of intravenous immunoglobulins in 2007 as derived from the IMS Health hospital disease database, the market share of intravenous immunoglobulin products was estimated at 50% for Multigam, 45% for Sandoglobuline, 5% for Gammagard S/D, and 0% for Octagam. No data were available on the market shares of other intravenous immunoglobulins (i.e. Nanogam) and subcutaneous immunoglobulins (i.e. Subcuvia and Vivaglobin) available on the Belgian market. The analysis assumed that immunoglobulin market shares observed in 2007 would persist in the future in the reference scenario.



Notes: IG = immunoglobulin; PID = primary immunodeficiency.

Figure 1. Model structure of budget impact analysis.

Table 1. Intravenous immunoglobulin market shares in new drug scenario.

	2010	2011	2012	2013	2014
Gammagard S/D	4.84%	4.75%	4.67%	4.59%	4.49%
Kiovig	3.20%	5.00%	6.60%	8.10%	10.20%
Multigam	48.40%	47.50%	46.70%	45.95%	44.90%
Sandoglobuline	43.56%	42.75%	42.03%	41.36%	40.41%
Total	100%	100%	100%	100%	100%

In the new drug scenario, Baxter expects Kiovig to gain a market share of 3.2% in 2010, 5% in 2011, 6.6% in 2012, 8.1% in 2013, and 10.2% in 2014. Kiovig was assumed to take its market share evenly from Gammagard S/D, Multigam and Sandoglobuline (see **Table 1**).

The associated number of patients in the reference scenario and in the new drug scenario was calculated by multiplying the estimated market share of each immunoglobulin product by the size of the target population.

2.4. Drug Costs

Hospital prices (including value-added tax of 6%) per patient were calculated assuming an immunoglobulin consumption of 24 g for a patient weighing 60 kg. This was based on an average monthly dose of 0.4 g per kg of body weight [1,3]. The average hospital price per gram was calculated based on the different doses available for a particular immunoglobulin product. Immunoglobulin unit cost data for 2008 originated from Belgian sources and were assumed to persist in the future. **Table 2** presents the cost per gram, monthly costs and annual costs for immunoglobulin products on the Belgian market.

2.5. Budget Impact

This study estimated the market size by identifying the number of PID patients requiring immunoglobulin treat-

Table 2. Intravenous immunoglobulin costs per patient in 2008.

Drug	Cost per gram	Monthly costs	Annual costs
Gammagard S/D	44.86 €	1,076.64 €	12,919.68 €
Kiovig	49.01 €	1,176.24 €	14,114.88 €
Multigam	41.29 €	990.96 €	11,891.52 €
Sandoglobuline	45.58 €	1,093.92 €	13,127.04 €

Table 3. Estimated target population.

	2010	2011	2012	2013	2014
Number of Belgian people	10,807,396	10,886,032	10,965,473	11,044,878	11,123,330
Percentage of people with primary immunodeficiency	0.022%	0.022%	0.022%	0.022%	0.022%
Number of primary immunodeficiency patients	2,378	2,395	2,412	2,430	2,447

Table 4. Estimated patient numbers.

Reference scenario						New drug scenario					
	2010	2011	2012	2013	2014		2010	2011	2012	2013	2014
Gammagard S/D	119	120	121	121	122	Gammagard S/D	115	114	113	111	110
						Kiovig	76	120	159	197	249
Multigam	1,189	1,197	1,206	1,215	1,224	Multigam	1,151	1,138	1,126	1,117	1,099
Sandoglobuline	1,070	1,078	1,085	1,094	1,101	Sandoglobuline	1,036	1,023	1,014	1,005	989
Total	2,378	2,395	2,412	2,430	2,447	Total	2,378	2,395	2,412	2,430	2,447

Table 5. Budget impact of adopting Kiovig.

Total drug costs in reference scenario (€)						Total drug costs in new drug scenario (€)					
	2010	2011	2012	2013	2014		2010	2011	2012	2013	2014
Gammagard S/D	1,537,442	1,550,362	1,563,281	1,563,281	1,576,201	Gammagard S/D	1,485,763	1,472,844	1,459,924	1,434,084	1,421,165
						Kiovig	1,072,731	1,693,786	2,244,266	2,780,631	3,514,605
Multigam	14,139,017	14,234,149	14,341,173	14,448,197	14,555,220	Multigam	13,687,140	13,532,550	13,389,852	13,282,828	13,068,780
Sandoglobuline	14,045,933	14,150,949	14,242,838	14,360,982	14,452,871	Sandoglobuline	13,599,613	13,428,962	13,310,819	13,192,675	12,982,643
Total	29,722,392	29,935,460	30,147,293	30,372,460	30,584,292	Total	29,845,247	30,128,141	30,404,860	30,690,219	30,987,193

Budget impact of adopting Kiovig					
	2010	2011	2012	2013	2014
Absolute budget impact (€)	122,855	192,681	257,567	317,759	402,900
Relative budget impact (%)	0.41	0.64	0.85	1.05	1.32

ment. Annual costs for a specific immunoglobulin product were calculated by multiplying the number of patients taking that product with the annual cost of that product. Summing annual costs over all immunoglobulin products generated total drug costs.

3. RESULTS

Table 3 presents estimates of the Belgian number of patients suffering from PID over the 2010-2014 time horizon. The number of Belgian PID patients is expected to increase from 2,378 patients in 2010 to 2,447 patients in 2014. Multiplying the estimated market share of each immunoglobulin product by the size of the target population generates estimates of the number of PID patients taking a particular immunoglobulin product in the reference scenario and in the new drug scenario (see **Table 4**). In both scenarios, the highest number of patients would

be expected to take Multigam, followed by patients taking Sandoglobuline and patients taking Gammagard S/D. In the new drug scenario, the number of patients treated with Kiovig is expected to increase from 76 patients in 2010 to 249 patients in 2014.

Table 5 shows total drug costs in the reference scenario ("world without Kiovig") and the new drug scenario ("world with Kiovig"), respectively. In the reference scenario, total drug costs are expected to increase from 29.7 million € in 2010 to 30.6 million € in 2014. In the new drug scenario, total drug costs would rise from 29.8 million € in 2010 to 31 million € in 2014. The estimated budget impact of treatment with Kiovig is the difference in total drug costs between the new drug scenario and the reference scenario. **Table 5** demonstrates that the absolute budget impact of adopting treatment with Kiovig increases from 0.1 million € in 2010 to 0.4 million € in 2014. Overall, treatment with Kiovig raises the 2010-2014 budget by 1.3 million € (or 0.86% of the reference drug budget).

4. DISCUSSIONS

The budget impact analysis compared the "world with Kiovig" to the "world without Kiovig". The analysis took into account the market size, immunoglobulin market shares and unit costs with a view to estimating the budget impact of Kiovig. The findings showed that, from the perspective of the Belgian health care payer, the budget impact of adopting Kiovig in the treatment of PID is likely to be limited.

The adoption of Kiovig would raise the immunoglobulin drug budget by 0.4%-1.3% per year. The budgetary increase originated from the higher price of Kiovig as compared with other intravenous immunoglobulins, although the impact of Kiovig was limited by the slow market penetration of Kiovig as predicted by Baxter. The analysis used conservative estimates of the market share of Kiovig over time given that similar products are expected to enter the market in the future.

The budget impact analysis was based on a number of assumptions in the absence of data. First, the analysis focused on some, but not all intravenous immunoglobulin therapies available on the Belgian market and did not include subcutaneous immunoglobulin therapies. Second, the immunoglobulin market evolves so that, even though the most recent market share data relating to 2007 were used, the data may no longer reflect the current market situation. Third, the assumption was made that a patient would require an immunoglobulin consumption of 24 g per month. This is in line with estimates used by the Belgian Commission for Drug Reimbursement [11]. In light of these assumptions, the findings give an idea of the order of magnitude of the budget impact of Kiovig, but do not represent the exact budget impact. These shortcomings highlight the need for more and better data on the Belgian immunoglobulin market size and the market distribution.

It should be noted that the budget impact is only one of the factors informing the decision whether to reimburse Kiovig. Other factors that are taken into account in Belgium are the therapeutic value, price, importance in medical practice in terms of therapeutic and social needs, and cost-effectiveness.

Kiovig has a favourable pharmacokinetic, safety and effectiveness profile in the treatment of PID patients. Three prospective, open-label, multi-centre studies 160001 [12], 160101 [13] and 160002 [14] have demonstrated that Kiovig attains the required minimum trough levels and pharmacokinetic parameters in PID patients. The European Public Assessment Report of Kiovig reveals no special risk for humans based on the exploration of safety pharmacology and toxicity [15]. The outcome measures of incidence of infections, antimicrobial use and the number of days off school or work were similar to those of other intravenous immunoglobulins.

In Belgium, Kiovig tends to be more expensive than other intravenous immunoglobulins, amounting to an increase in the hospital price per gram (excluding VAT of 6%) of 0%-18% as compared with Gammagard S/D, 5%-27% as compared with Multigam, -4% to 21% as compared with Nanogam, and 8%-28% as compared with Octagam in 2008.

In addition to Kiovig, other intravenous immunoglobulins are available on the Belgian market, including Gammagard S/D, Multigam, Nanogam, Octagam and Sandoglobuline. Furthermore, Subcuvia and Vivaglobin are available for subcutaneous administration. As compared with other immunoglobulins, Kiovig benefits from: a manufacturing process consisting of three dedicated virus reduction steps; a formulation containing no sucrose or sodium and containing more than 98% immunoglobulin G; a ready-to-use liquid presentation obviating the need for reconstitution; the ability to store at room temperature; a faster infusion speed and lower infusion volume; and the potential for home-based administration [4,5].

To date, the cost-effectiveness of Kiovig as compared with other intravenous immunoglobulins is unknown. The previous sections point to a similar effectiveness and higher price of Kiovig as compared with other products. To determine the cost-effectiveness of Kiovig, there is a need for an economic evaluation alongside a head-to-head clinical trial comparing Kiovig with other intravenous immunoglobulins.

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