

The budgetary impact of alemtuzumab in multiple sclerosis in Quito, Ecuador. Payer's perspective

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ABSTRACT

Introduction: Multiple sclerosis is a neurological condition that causes disabilities and is most common in young adults. It imposes high financial costs affecting the quality of life of patients, families, and society. It is critical to measure the budgetary impact of new technologies to treat this disease.

Objective: The aim of the article is to estimate the budgetary impact of introducing alemtuzumab as an escalation therapy in patients diagnosed with Recurrent Remitting Multiple Sclerosis and treated in Quito, Ecuador.

Materials and methods: A cohort of 85 patients receiving treatment with disease-modifying therapies was used, within a 5-year timeframe, between 2021 and 2025. The baseline scenario, including the percentages of administration of the different drugs, is compared with the alternative scenario, including alemtuzumab. The cost assessment included only direct medical resources. To obtain local resources for management of the disease, a neurologist and clinical expert who treats most of the patients in Quito was consulted.

Results: Considering a cohort of 85 patients with active Recurrent Remitting Multiple Sclerosis, the average global budget impact in 5 years would be USD 10,603,230.00 in the base case and USD 9,995,817.00 in the alemtuzumab scenario.

Conclusion: The inclusion of alemtuzumab as escalation therapy represents budgetary savings over the next 5 years (2021-2025).

Keywords: Multiple sclerosis, Interferons, Budgetary impact analysis, Fingolimod, Alemtuzumab, Ocrelizumab, Teriflunomide

Introduction

Multiple sclerosis (MS) is the most common chronic neurological disease in young adults (1) and imposes high financial costs, affecting patients' quality of life, families, and society (2). It is a chronic disorder that can place a significant burden on patients over the years (3). MS affects mostly adult women (4). It most frequently presents as Recurrent Remitting Multiple Sclerosis (RRMS). Approximately 85% of patients are affected by this form of MS, which is characterized by the occurrence of one or two episodes of neurological

deficit per year, which resolve, at least partially, with or without treatment, in days or months (5).

According to information from the Association of Patients with Multiple Sclerosis and Demyelinating Diseases of Ecuador (APEMEDE), as of June 2020, 124 patients with Active RRMS in Ecuador receive care from the Carlos Andrade Marín Specialty Hospital (HECAM) and the Eugenio Espejo Hospital, which are third-level health centers in the city of Quito, capital of Ecuador.

Definitions used in the model

Relapse or flare: The appearance of new neurological symptoms or the worsening of existing ones for a period of time longer than 24 hours (6).

Costs: Direct medical costs, which are expressed in US dollars. The costs were obtained from the Consolidated Ceiling Prices Updated 2020-10-02 (7) and the Benefit Tariff for the National Health System Version Year 2014 (8). The costs associated with the monitoring of each therapy and costs related to the management of the adverse events are included in this analysis, as well as those related to outbreaks, according to their severity.

Escalation: Switch to a high-efficacy drug (9).

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Sensitivity analysis

A series of deterministic univariate sensitivity analyses were performed to verify the robustness of the model results, which evaluated the parameter's impact with the most uncertainty in the analysis, namely, the price of the drug. For this, the economic impact was estimated if 100% of the patients included in the model were administered only one drug. This analysis was carried out for each of the therapeutic alternatives included in the model.

There is no definitive cure for MS to date; hence, treatment aims at modifying the natural course of the disease. In the last decade, there has been a rapid development in the investigation of new disease-modifying therapies (DMTs) for patients with MS (10).

In recent years, new treatments have emerged to slow the progression of RRMS, both immunomodulatory and immunosuppressive. However, the drugs approved to date only allow the modification of the disease's course, delaying its progression and avoiding relapses. Alemtuzumab emerges as a promising and cost-effective therapy, the reason why it has been considered essential to evaluate its budgetary impact at a local level.

Materials and methods

A Budget Impact Analysis predicts how a change in the combination of drugs and other therapies used to treat a particular health condition will impact the trajectory of spending on that condition. It can be used for budget planning, forecasting, and calculating the impact of changes in health technology on health insurance premiums. In the present work, the budget impact model was carried out using the Microsoft Excel 2011 program for Mac, following international recommendations (11).

From a population of 124 patients with RRMS, according to the APEMEDE registry, treated in Quito, a target sample of 85 patients was estimated, undergoing treatment with interferon beta 1a (IFN β -1a) intramuscular (IM), IFN β -1a subcutaneous (SC), ocrelizumab, teriflunomide 14 mg, and fingolimod. The inclusion criteria were RRMS diagnosis in treatment with DMTs, without distinguishing gender, disease status, or age. The exclusion criteria were: patients diagnosed with RRMS under treatment with rituximab (because it was off-label use), natalizumab (there were no patients with this therapy), and those who did not have any DMT. Data was taken from an online query made to APEMEDE.

The study is an adaptation of a budget impact model made for Social Security in Costa Rica (12). The model assumes that there are no transitions between EDSS states throughout the time horizon. The only effect for DMTs included in the model is the number of outbreaks requiring hospitalization or not. In the case of alemtuzumab, the CARE MS II clinical study is used as a reference, a randomized controlled phase III study of alemtuzumab in patients with RRMS previously exposed to another DMT (13). The information is summarized in Table I.

In the base case, a cohort with 85 patients using the following therapies was considered: (18; 85) patients with IFN β -1a IM, (41; 85) patients with IFN β -1a SC, (3; 85) patients

TABLE I - Budget impact model characteristics

Summary	Description
Type of economic analysis	Budget impact model
Intervention	<ul style="list-style-type: none"> • Alemtuzumab
Comparators	<ul style="list-style-type: none"> • Interferon beta-1a intramuscular • Interferon beta-1a subcutaneous • Teriflunomide 14 mg • Fingolimod • Ocrelizumab
Population	Adults on Recurrent Remitting Multiple Sclerosis (RRMS) using a disease-modifying therapy
Perspective	Payer
Time horizon	5 years
Health states	Transitions between states were not considered.
Primary outcome	Both annual and 5-year cost for the population with RRMS
Assumptions	<ul style="list-style-type: none"> • Patients do not switch treatment throughout the time horizon. • The effect of the considered treatment is the reduction of the relapse rate only. • Transfers to Progressive Secondary Multiple Sclerosis (SPMS) are not possible throughout the time horizon.

Source: Authors' research database.

with teriflunomide 14 mg orally, (21; 85) patients with fingolimod tablets, and (2; 85) patients with ocrelizumab, in correspondence with the real data as of July 2020.

In the alternative scenario with alemtuzumab, the same cohort of 85 patients was considered, but with (10; 85) patients using alemtuzumab; (5; 85) patients move from the pool of patients using IFN β -1a SC and (5; 85) patients from those using fingolimod (Tab. II).

Therapeutic alternatives

The therapeutic alternatives evaluated in the analysis included the following drugs, which are used in Quito for the treatment of active RRMS:

First line

IFN β -1a IM
 IFN β -1a SC
 Teriflunomide 14 mg coated tablets

Second line

Fingolimod 0.5 mg hard capsule
 Ocrelizumab concentrate for solution for infusion

For modeling purposes, a reference or base case scenario was used, in which the percentages of use of each of the

TABLE II - Distribution of the cohort of patients with relapsing remitting multiple sclerosis, diagnosed and treated in Quito, Ecuador

PRODUCT	2020		2021		2022		2023		2024		2025		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
BASE CASE (without alemtuzumab)	IFNB-1a IM	18	21.18	18	21.18	18	21.18	18	21.18	18	21.18	18	21.18
	IFNB-1a SC	41	48.24	41	48.24	41	48.24	41	48.24	41	48.24	41	48.24
	Teriflunomide 14 mg tab.	3	3.53	3	3.53	3	3.53	3	3.53	3	3.53	3	3.53
	Fingolimod	21	24.71	21	24.71	21	24.71	21	24.71	21	24.71	21	24.71
	Natalizumab	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	Ocrelizumab	2	2.35	2	2.35	2	2.35	2	2.35	2	2.35	2	2.35
	Total	85	100.00	85	100.00	85	100.00	85	100.00	85	100.00	85	100.00
ALTERNATIVE CASE (with alemtuzumab)	IFNB-1a IM	18	21.18	18	21.18	18	21.18	18	21.18	18	21.18	18	21.18
	IFNB-1a SC	41	48.24	36	42.35	36	42.35	36	42.35	36	42.35	36	42.35
	Teriflunomide 14 mg tab.	3	3.53	3	3.53	3	3.53	3	3.53	3	3.53	3	3.53
	Fingolimod	21	24.71	16	18.82	16	18.82	16	18.82	16	18.82	16	18.82
	Natalizumab	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
	Ocrelizumab	2	2.35	2	2.35	2	2.35	2	2.35	2	2.35	2	2.35
	Alemtuzumab course 1	0	0.00	10	11.76	0	0.00	0	0.00	0	0.00	0	0.00
	Alemtuzumab course 2					10	11.76	0	0.00	0	0.00	0	0.00
	Alemtuzumab course 3							2	2.35	0	0.00	0	0.00
	Alemtuzumab course 4									2	2.35	0	0.00
	Alemtuzumab course 5											1	1.18
	Free of therapy							8	9.41	8	9.41	9	10.59
Total	85	100.00	85	100.00	85	100.00	85	100.00	85	100.00	85	100.00	

IFNB-1a IM = interferon beta 1a intramuscular; IFNB-1a SC = interferon beta 1a subcutaneous.

Source: Association of Patients with Multiple Sclerosis and Demyelinating Diseases of Ecuador (APEMEDE) (with permission).

drugs indicated in the first line and second line for the treatment of patients with active RRMS were included. This base case was compared with a scenario that recreates alemtuzumab's use in 11.76% of the cohort (10; 85) patients, varying the participation percentages of the different treatments currently used. In this way, the incremental cost of the inclusion of alemtuzumab can be calculated.

Time horizon, perspective, and discount rate

The analysis was carried out with a time horizon of 5 years, according to the payer's perspective. A discount rate was not applied due to the limitation, for this work, of obtaining the most appropriate indicator in the health area.

Resources

The analysis has been carried out following the payer's perspective. Only resources related to direct healthcare costs were considered, which are those financed by the health authorities.

Drugs and acquisition costs, for each DMT

Treatment administration

The model assumed that the administration of intravenous therapies is performed by qualified personnel; therefore, intravenous administration is associated with an outpatient visit or hospitalization, depending on the type of therapy. Subcutaneous therapy (Interferons) and oral therapies can be self-administered by the patient.

Management of the disease

The information about the disease's management was obtained from a local expert and the available clinical evidence.

Adverse events

The most frequent and severe adverse events of each of the products were selected according to the pivotal studies



published for each therapy (14-18). Regarding its clinical management, only the clinician's medications for its management and the consultation with the respective service (either the emergency department or the neurology specialist) were considered.

Outbreaks and annualized relapse rate

Annualized relapse rates are based on clinical evidence for each of the products (pivotal studies). For management of outbreaks, the information was collected through a local expert.

Quantification of resources

The estimation and quantification of the resources used are summarized in the tables included in the supplementary materials (Tabs. IV-VII).

Results

Table III shows the total economic impact, broken down into pharmacological, administration, and monitoring costs. The budgetary impact for the cohort of patients with active RRMS in treatment at the Carlos Andrade Marín Hospital,

TABLE III - Model results

Total cost per year for each scenario	2021	2022	2023	2024	2025
Without alemtuzumab	\$2,120,646	\$2,120,646	\$2,120,646	\$2,120,646	\$2,120,646
With alemtuzumab	\$2,418,917	\$2,159,217	\$1,812,638	\$1,807,819	\$1,797,226
Difference	\$298,271	\$38,571	-\$308,007	-\$312,827	-\$323,420
Annual costs breakdown: drugs, administration, monitoring, adverse events, relapse cost					
Drug cost	2021	2022	2023	2024	2025
Without alemtuzumab	\$2,040,156	\$2,040,156	\$2,040,156	\$2,040,156	\$2,040,156
With alemtuzumab	\$2,321,632	\$2,070,874	\$1,738,514	\$1,734,104	\$1,724,821
Difference	\$281,477	\$30,719	-\$301,642	-\$306,052	-\$315,335
Drug administration	2021	2022	2023	2024	2025
Without alemtuzumab	\$1,015	\$1,015	\$1,015	\$1,015	\$1,015
With alemtuzumab	\$12,321	\$7,580	\$1,296	\$1,212	\$1,037
Difference	\$11,306	\$6,565	\$281	\$197	\$22
RRMS and other monitoring cost	2021	2022	2023	2024	2025
Without alemtuzumab	\$34,271	\$34,271	\$34,271	\$34,271	\$34,271
With alemtuzumab	\$39,618	\$35,417	\$31,268	\$31,097	\$30,504
Difference	\$5,347	\$1,146	-\$3,003	-\$3,174	-\$3,767
Adverse event cost	2021	2022	2023	2024	2025
Without alemtuzumab	\$1,139	\$1,139	\$1,139	\$1,139	\$1,139
With alemtuzumab	\$1,379	\$1,379	\$1,121	\$1,110	\$1,073
Difference	\$240	\$240	-\$18	-\$28	-\$65
Relapse cost	2021	2022	2023	2024	2025
Without alemtuzumab	\$44,065	\$44,065	\$44,065	\$44,065	\$44,065
With alemtuzumab	\$43,967	\$43,967	\$40,440	\$40,295	\$39,791
Difference	-\$98	-\$98	-\$3,625	-\$3,770	-\$4,274
Breakdown of total costs per year by medical/pharmacy costs for each scenario					
Medical costs	2021	2022	2023	2024	2025
Without alemtuzumab	\$44,354	\$44,354	\$44,354	\$44,354	\$44,354
With alemtuzumab	\$61,229	\$52,287	\$40,961	\$40,670	\$39,774
Difference	\$16,875	\$7,933	-\$3,393	-\$3,683	-\$4,580
Pharmacy costs	2021	2022	2023	2024	2025
Without alemtuzumab	\$2,076,292	\$2,076,292	\$2,076,292	\$2,076,292	\$2,076,292
With alemtuzumab	\$2,357,688	\$2,106,930	\$1,771,677	\$1,767,148	\$1,757,452
Difference	\$281,396	\$30,638	-\$304,615	-\$309,144	-\$318,840

Source: Authors' research database.





Fig. 1 - Budget impact in base case and alternative case.

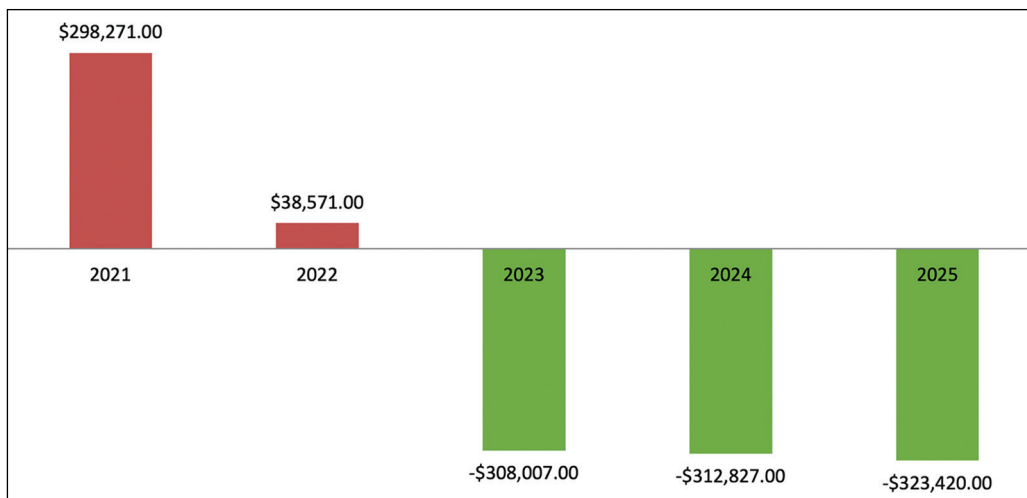


Fig. 2 - Budgetary impact of the inclusion of alemtuzumab.

in the base case, represents a 5-year investment of USD 10,603,230.00 and USD 9,995,817.00 in the alternative scenario with alemtuzumab. The alternative scenario, which includes 11.76% of new patients with alemtuzumab (10; 85), reduces the investment by 5.73% of the total at 5 years, representing an average saving of USD 7,146.00 per patient in 5 years.

Figure 1 shows the budgetary impact by year and an annual decreasing trend is observed in the budgetary impact in the scenario with alemtuzumab, starting the third year.

Figure 2 shows the delta between both scenarios, with a clear impact in favor of the alemtuzumab scenario from year 2. Figure 3 shows the average monthly average cost per year and patient, observing a lower cost in the scenario with alemtuzumab, from the second year of the time horizon.

Sensitivity analysis

Figure 3 shows the budgetary impact in 5 years, with regard to univariate parameter modifications. The pharmacological cost is the parameter with the most significant weight in the analysis. A sensitivity analysis was made based on the hypothetical scenario using each drug in 100% of the patients in the cohort, that is, (85; 85) patients. It is observed that, according to the drug under analysis, the budgetary impact is within a range that increases or decreases investment. This analysis reflects that alemtuzumab constitutes an escalation therapy, positively impacting the payer’s budget.

Discussion and limitations

The analysis of the budgetary impact of introducing new drugs in the treatment of MS could optimize existing



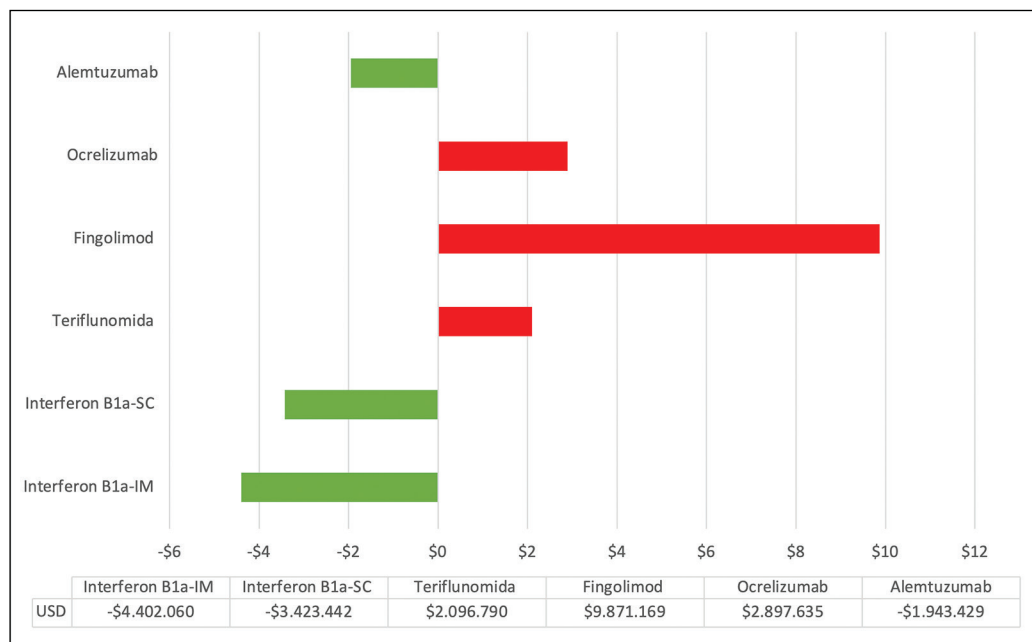


Fig. 3 - Budgetary impact (millions of USD) in a hypothetical case of 100% of patients (85; 85) with each therapy through 5 years.

economic resources. In Ecuador, there are no studies of this nature to date.

Although there is consensus that DMTs can reduce the frequency of relapses, their relative benefit (effectiveness compared to each other) in reducing new relapses or the progression of disability remains unclear due to the limited number of studies with direct comparisons. However, to assess the relative efficacy of the alternatives among themselves, in terms of annualized relapse rate, indirect comparisons can be used, obtained by a Cochrane network meta-analysis carried out in 2015 (19). The network meta-analysis showed that, in terms of the protective effect against relapse recurrence in RRMS, during the first 24 months of treatment, alemtuzumab, natalizumab, and fingolimod outperformed other drugs.

Given the nature of MS, these therapies are chronic in use, representing a significant investment for payers. On the other hand, the economic burden of managing MS is very high. The objective of this study was to estimate the budgetary impact of the inclusion of alemtuzumab, as escalation therapy, in the population with active RRMS.

For first-line treatment of the disease in Quito, beta interferons are available: IFNβ-1a IM and IFNβ-1a SC. Some patients use teriflunomide and fingolimod.

The information collected by APEMEDE (see Supplementary Materials) indicates that, as of June 2020, there were 3 patients with alemtuzumab, 21 patients with fingolimod, 18 patients with IFNβ-1a IM, 41 patients with IFNβ-1a SC, 3 patients with teriflunomide, 2 patients with ocrelizumab, 34 patients with rituximab (off-label use) and 2 patients without DMT.

Important note

At the date of the study, there were no patients treated with other DMTs, for example, natalizumab. Under the above, natalizumab was excluded from the study as it is not

locally used. Rituximab was also excluded as it is used off-label, and this does not allow a fair and referenced comparison with the other DMTs with approved indications to treat the disease under review.

According to the payer’s perspective, this partial economic model provides data on the budgetary impact for local public payers of the management of active RRMS. The inclusion of alemtuzumab to treat 10 of the 85 patients represents a saving of 8.9% of the 5-year budget, compared to the base case budget (current situation), as long as alemtuzumab meets the efficacy and decreasing retreatment rates, evidenced in the pivotal CARE MS II study. The parameter with the most significant influence on the results is the pharmacological cost, which should encourage further discussions on this specific topic.

Within the limitations, it is found that this model considers only the direct costs for the system and does not consider the social impact of MS and the economic impact of disease progression in the long term, which may justify additional studies. On the other hand, the absence of a national registry of the disease makes it necessary to assume that the results of clinical trials can be extrapolated in Ecuador, especially regarding the incidence rates of adverse events.

Another limitation is that the model does not include the impact of health states (expanded disability status scale, EDSS). According to the number of patients, there is no consolidated information published regarding the distribution percentage in each state.

On the other hand, although the collection of unit costs was accurate (considering that it is obtained from direct sources from the Ecuadorian Institute of Social Security and the Ministry of Health), some few costs could not be determined, resulting in the use of values corresponding to the private market.

There is no Local Clinical Practice Guide, so access to information on management of the disease was carried out in consultation of an expert.



Conclusion

Under the assumptions presented in this work, it can be concluded that, from the payer's perspective, the introduction of alemtuzumab, as escalation therapy, represents budgetary savings over a 5-year time horizon. Greater benefits in reducing the retreatment rate and a very manageable short-term dosing regimen in most patients make it possible to recommend, both clinical and economically, the rational and progressive use of the product in this context.

Recommendations

Additional studies are recommended, including the progression of the disease in the cohort, to obtain a dynamic model. It is recommended to expand this work with additional studies, as new DMTs are included in providing services.

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