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ORIGINAL RESEARCH

Budget Impact Analysis of Lebrikizumab for Treating Severe Atopic Dermatitis

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ABSTRACT

***Introduction*:** Lebrikizumab is a novel monoclonal antibody that targets interleukin-13, a pivotal factor in atopic dermatitis (AD). Previous studies revealed a positive benefit–risk profile of lebrikizumab as treatment for patients with moderate-to-severe AD. In Italy, lebrikizumab has been approved and reimbursed as treatment for patients with severe AD (aged 12 years or older and with an Eczema Area and Severity Index (EASI) ≥ 24). However, data on economic impact of lebrikizumab in these subjects are still scarce. This study aimed to assess the budget impact of lebrikizumab in Italian patients with severe AD, according to Italian Medicine Agency (AIFA) reimbursement criteria, from the Italian National Healthcare System (NHS) perspective.

***Methods*:** The budget impact analysis model was used to estimate the economic impact of lebrikizumab as treatment of patients with severe AD by comparing the total budget expenditure under two scenarios: scenario A, which includes the current standard of care with biologic agents (dupilumab and tralokinumab), and scenario B, which includes dupilumab and tralokinumab along with the introduction of lebrikizumab. The analysis was conducted by adopting the Italian NHS perspective and a 3-year time horizon. The clinical data input was based on published evidence, pivotal clinical trial, and expert opinion. Cost data was retrieved from the Italian tariff and literature. One-way sensitivity analysis was conducted to assess the robustness of the model.

***Results*:** The base case analysis, conducted over a 3-year period, estimated that the number of patients treated with lebrikizumab increased from 1198 in the first year to 5849 in the final year of the simulation. The adoption of lebrikizumab for patient treatment resulted in a cumulative cost-saving of €3.3 million in 3 years (€786 thousand in the first year, −€1.7 million in the second year, and −€2.4 in the last year).

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The number of patients potentially eligible to the treatment, the injection site reaction cost, and the injection site reaction rate were the main drivers of the findings.
***Conclusion*:** The availability of lebrikizumab as treatment for patients with severe AD would result in cost savings for Italy. Given the paucity of economic data on lebrikizumab, new economic studies should be conducted to confirm these findings.

Keywords: Lebrikizumab; Budget impact analysis; Severe atopic dermatitis; Italy; Pharmacoeconomics

Key Summary Points

Why carry out this study?

Atopic dermatitis (AD) is a skin disease with significant clinical, humanistic and economic impact. Economic evaluation is essential to ensure the efficient allocation and prioritization of healthcare resources. This study aimed to evaluate the budget impact of introducing lebrikizumab for the treatment of patients with severe AD.

What was learned from the study?

The use of lebrikizumab in Italy is associated with cost saving and improvement in patient management over three-year simulation.

Considering the significant economic, clinical, and humanistic impact of severe AD, the findings provide valuable information for healthcare decision makers to optimize resource allocation.

Given the increased availability of therapeutic alternatives, periodic pharmacoeconomic assessments should be conducted to ensure the affordability of therapies for healthcare systems treating patients with severe AD.

INTRODUCTION

Atopic dermatitis (AD) is a common chronic relapsing inflammatory skin disease, with a prevalence of up to 25% in children and up to 10% in adults [1–4]. The most frequent symptoms associated with AD include eczema, dry scaly and lichenified skin, and pruritus [3, 5–7].

AD results from a complex pathogenesis involving the interplay of several factors, such as genetic predisposition, impaired skin barrier function, alterations in the skin microbiome, and immune dysregulation, characterized by the release of cytokines, especially Th2 cytokines [8, 9]. These cytokines, including interleukin(IL)-4, IL-13, and IL-31, play a key role in the inflammatory cascade [9]. Specifically, among the different pathways, IL-13 is considered one of the main drivers for AD pathogenesis, directly contributing to the occurrence of signs and symptoms [2, 6, 10]. IL-13 acts both directly and indirectly by increasing collagen deposition and fibrotic tissue remodelling. It induces expression of matrix metalloproteinases, which mediate cells migration and tissue remodelling, ultimately resulting in fibrosis with excessive collagen deposition. Additionally, IL-13 is involved in peripheral itch-sensory neurons, leading to increased pruritus symptoms [6]. For these reasons, IL-13 has been considered a pharmacological target for at least three approaches: (1) small molecules interfering with interactions between cytokines and their receptors; (2) small molecules interacting with intracellular signalling pathways; and (3) biologics that block IL-13 binding to its receptor site [6].

Recent guidelines recommend using more advanced therapies when symptoms are not adequately controlled with topical agents such as emollients, corticosteroids, and calcineurin inhibitors. Systemic therapies include immunosuppressants (i.e., cyclosporine, methotrexate, azathioprine, mycophenolate mofetil), biologic agents (i.e., dupilumab and tralokinumab), and Janus kinase (JAK) inhibitors (such as upadacitinib, abrocitinib, and baricitinib) [11–13]. Lebrikizumab is a humanized IgG4 monoclonal antibody targeting IL-13 recently approved by international regulatory agencies for the treatment of patients with moderate-to-severe AD aged ≥ 12 years who are eligible for systemic

therapy [14, 15]. In Italy, lebrikizumab has been approved and reimbursed by the Italian Medicine Agency (AIFA) as treatment for adult patients with severe AD and adolescent aged ≥ 12 years, weighing at least 40 kg, and with severe disease (Eczema Area and Severity Index (EASI) ≥ 24) (AIFA reimbursement criteria). Lebrikizumab specifically binds IL-13, inhibiting only IL-4Ra/IL-13Ra1 heterodimerization, while allowing IL-13 to interact with IL-13Rα2, with consequent alteration of its endogenous regulation [6, 16]. The favorable benefit–risk profile of lebrikizumab has been demonstrated in four pivotal clinical trials: ADvocate1, ADvocate2, ADhere, and Adore [17–20].

The annual costs of AD in the USA were estimated to be $5.3 billion, while in Europe, the annual societal costs were estimated at €30 billion, with approximately half attributed to productivity losses [21–23]. A European study reported that 57% of patients with AD missed at least 1 day of work in the previous year because of the disease [24]. More specifically, the cost per patient has been detected across European countries. For example, the mean costs were €3616 in Germany and €4331 in Hungary [25, 26]. In Italy, the estimated annual total cost per patient for AD management was €7041, with direct healthcare costs (€3291) accounting for 46.7% of total expenditure. The primary driver of these costs was pharmacological treatment (€3156) [27].

In recent decades, healthcare systems have faced with increasing expenditure, leading to resource constraints that necessitate tools for the efficient allocation and prioritization of healthcare resources. In this context, budget impact analysis is a crucial tool for assessing the economic impact of introducing new medical technologies. Therefore, the aim of this study was to evaluate the budget impact of introducing lebrikizumab for the treatment of patients with severe AD over a 3-year time horizon from the perspective of the Italian National Healthcare system (NHS).

METHODS

Overall Model Structure

A budget impact model was developed to estimate the financial consequences of the adoption and diffusion of lebrikizumab as a new treatment within the current healthcare system. Specifically, the model predicts how changes in the therapeutic landscape will impact healthcare expenditure for management of patients with severe AD.

The model was developed using Microsoft Excel to simulate an annual cohort of patients with severe AD who are eligible for systemic treatment, as reported by the reimbursement criteria of AIFA [28]. It adopted the perspective of the Italian NHS. The model incorporated data on the target population, projected market share, treatment acquisition costs, and costs associated with managing disease flares and adverse events (AEs). These data were combined to estimate the annual costs in two different scenarios: scenario A, where lebrikizumab is not marketed in the country and the standard of care includes dupilumab and tralokinumab; and scenario B, where lebrikizumab is available in Italy, thus considering three therapies: dupilumab, tralokinumab, and lebrikizumab. As for other budget impact models, this study was performed using inputs informed by previously conducted studies. For this reason, ethical approval is not necessary.

Time Horizon

The model evaluated the change in healthcare expenditures associated with the introduction of lebrikizumab as a therapeutic option for patients with severe AD, considering it as an alternative option to existing treatments over a 3-year time horizon, following AIFA guidelines.

Model Input Data

Four categories of input data were collected: (1) eligible population, (2) real-world market shares, (3) cost input, and (4) clinical inputs. All data

and relevant assumptions were reviewed and validated by Italian clinical experts.

Population

The process for selecting the target population for inclusion in the budget impact model is reported in Table 1. The model included patients with severe AD (EASI ≥ 24), aged ≥ 12 years, and weighing at least 40 kg and as indicated by the AIFA reimbursement criteria, drawn from a hypothetical cohort of 53 million health plan members. In the general population there were 198,763 individuals with severe AD [29, 30]. Among individuals with severe AD, 2% were treated with advanced systemic treatment (18,520 patients). Within the patients treated with systemic treatments, 64.6% were treated with monoclonal antibodies (mab); therefore, the target population included 11,978 patients with severe AD as reported by market research conducted by IQVIA for the Italian system. On the basis of this population, the model assumed an average growth of the population treated with systemic therapy of 25%, as indicated by clinical expert opinion. Therefore, the target population increased to 14,973 in the first year of the simulation, 18,716 in the second year, and 23,395 in the third year.

Market Share

To estimate the number of patients treated with specific therapies in the market share (MS) scenarios with and without lebrikizumab, the utilization rates of each individual drug were applied to the estimated eligible patient population for each simulated year. The MS data for the scenario without lebrikizumab (scenario A) was obtained from a recent market research study conducted by IQVIA for the Italian system [32].

In the scenario without lebrikizumab (scenario A), patients were treated with either tralokinumab or dupilumab. Specifically, in the first year of simulation, 20% of patients were treated with tralokinumab and 80% with dupilumab, in the second year 22% with tralokinumab and 78% with dupilumab, and

Table 1 Target population

	Number of individuals/ percentage (%)	Reference
Italian population ≥ 12 years old	53,472,097	[31]
Number of individuals with AD	3,312,709	[29]
Number of individuals with severe AD	198,763	[30]
% of individuals with severe AD treated with systemic therapies	2.00%	[32]
Number of individuals with severe AD and treated with systemic therapies	18,520	
% of individuals treated with mab	64.6%	[32]
Number of individuals with severe AD and treated with mab	11,978	
Annual growth rate	25.00%	Assumption
Number of eligible patients in the first year	14,973	
Number of eligible patients in the second year	18,716	
Number of eligible patients in the third year	23,395	

in the third year 25% with tralokinumab and 75% with dupilumab.

In the new scenario with lebrikizumab (scenario B), it was assumed that a proportion of patients would receive lebrikizumab instead of receiving dupilumab and tralokinumab. It was assumed that the number of patients treated with lebrikizumab increased during the simulated period: 8% in the first year, 14% in the second, and 25% in the third year of simulation. The number of individuals treated with dupilumab decreased from 74% during the first year to 59% during the last year of simulation, while patients treated with tralokinumab decreased from 18% in the first year to 16% in the last year of simulation (base case scenario) (Table 2).

Clinical Data

In the model, efficacy data for the included treatments were retrieved from a network meta-analysis (NMA) [33]. Specifically, the estimated response rate, defined as the patients achieving an EASI 75 and Investigator Global Assessment (IGA) 0/1 with a reduction of ≥2 points, were incorporated into the analysis. This outcome was selected by clinical experts as the most appropriate one to reflect the assessment of treatment efficacy in clinical practice. The response rates were 46.8%, 49.17%, and 31.35%, for lebrikizumab, dupilumab, and tralokinumab, respectively.

The model included data on the flare rate, converted into annual rate, of disease flare occurrence during treatment, as well as the 16-week rate, converted into annual rate, of AEs occurrence [34]. The following AEs were considered: injection site reaction, allergic conjunctivitis, infectious conjunctivitis, oral herpes, upper respiratory tract infection, and acne. The annual rates of disease flare and AEs occurrence were based on data reported in the UK National Institute for Health and Care Excellence (NICE) Technology evaluation (TA986–NICE) [34].

Costs and Healthcare Resource Use

In accordance with the chosen analysis perspective, the model incorporated only direct medical healthcare costs covered by the Italian NHS. These costs included drug acquisition and treatment-specific disease costs, and flare and AEs management costs.

The drug acquisition costs for each therapy were computed as an annual expense by multiplying the unit cost by the number of injections per year. Specifically, for each treatment, the first year included an induction phase (weeks 0–16) followed by a maintenance phase (weeks 17–52). In subsequent years, only the annual maintenance frequency was considered. The dose and treatment regimens for each therapy were obtained from the European public assessment report (EPAR) provided by European Medicines Agency (EMA) and from the Summary of Product Characteristics (SmPC) as documented on the AIFA website. The ex-factory price per package, adjusted for the statutory discount (– 5%, followed by – 5%) was considered in compliance with legal requirements for each reimbursed drug. Table 3 shows the prices for each drug

Table 2 Market share in the scenario without lebrikizumab (scenario A) and in the scenario with lebrikizumab (scenario B) (base case analysis)

	Scenario without lebrikizumab (scenario A)			Scenario with lebrikizumab (scenario B)		
	Year 1	Year 2	Year 3	Year 1	Year 2	Year 3
Lebrikizumab	0%	0%	0%	8%	14%	25%
Dupilumab	80%	78%	75%	74%	66%	59%
Tralokinumab	20%	22%	25%	18%	20%	16%

Table 3 Healthcare resource utilization and costs input

	Value	Reference
Lebrikizumab 250 mg costs (ex factory)	2310 €	
Dupilumab 200 mg/1.4 ml costs (ex factory)	1155 €	[35]
Dupilumab 300 mg/2 ml cost (ex factory)	1155 €	[35]
Tralokinumab 150mg/1 ml costs (ex factory)	1155 €	[36]
Number of visits per annum in responders		
Dermatologist outpatients consultation (number per year)	2	Expert opinion
GP consultation	3	Expert opinion
FBC	2	Expert opinion
Number of visits per annum in non-responders		
Dermatologist outpatients consultation	4	Expert opinion
GP consultation	5	Expert opinion
FBC	5	Expert opinion
Visit costs		
Dermatologist outpatients consultation	16 €	[37]
GP consultation	21 €	[38]
FBC	3 €	[37]
Distribution of flare medication for lebrikizumab		
TCS potent	21%	[34]
TCS very potent	20%	[34]
Systemic steroid	14%	[34]
TCI	14%	[34]
Distribution of flare medication for dupilumab		
TCS potent	20%	Expert opinion
TCS very potent	20%	Expert opinion
Systemic steroid	16%	Expert opinion
TCI	20%	Expert opinion
Distribution of flare medication for tralokinumab		
TCS potent	25%	Expert opinion
TCS very potent	68%	Expert opinion
Systemic steroid	29%	Expert opinion
TCI	21%	Expert opinion

Table 3 continued

	Value	Reference
Cost per flare		
TCS potent	39 €	Expert opinion; model estimation
TCS very potent	9 €	Expert opinion; model estimation
Systemic steroid	2 €	Expert opinion; model estimation
TCI	16 €	Expert opinion; model estimation
Cost per flare in responders	530 €	Expert opinion; model estimation
Cost per flare in non-responder	1166 €	Expert opinion; model estimation
Adverse event cost		
Injection site reaction	361 €	[39]
Allergic conjunctivitis	21 €	[37]
Infectious conjunctivitis	36 €	[37]
Oral herpes	21 €	[37]
Upper respiratory tract infection	21 €	[37]
Acne	21 €	[37]

included in the analysis, as referenced from the Italian official gazettes.

The model included the costs associated with disease management according to the response status of patients (responders vs non-responders). The following healthcare resources were considered: dermatologist outpatient consultations, general practitioner (GP) visits, and full blood count (FBC) tests. The annual costs of disease management were computed by multiplying the number of responders and non-responders by the number of each healthcare resource used and its corresponding unit cost.

In the model, the costs associated with managing disease flares were included. These were estimated by multiplying the cost of healthcare resources used for flare management by the annual flare occurrence.

The model included also the costs associated with the management of the following AEs: injection site reactions, allergic conjunctivitis, infectious conjunctivitis, oral herpes, upper respiratory tract infections, and acne. The annual costs associated with managing these events were computed by multiplying the number of events per year for each treatment by the cost of healthcare resources used for their management. Specifically, for injection site reactions, the cost of emergency department visit was considered; for infection conjunctivitis the cost of specialist visit plus antibiotics treatment was included; whereas for all other adverse events, only the cost of specialist visit was considered.

Statistical Analysis

The model output was the budget impact of lebrikizumab in Italian patients with severe AD according to AIFA reimbursement criteria. The total budget impact was estimated on an annual basis as the difference in total costs between the market scenario with and without lebrikizumab. The total costs in both scenarios, in each year and overall, were estimated as the sum of total costs of drug acquisition, disease management, and AEs management incurred in each year of simulation.

To assess the robustness of the study findings, a one-way sensitivity analysis was conducted. Specifically, the impact of each parameter included in the model was assessed. An iterative replacement approach of individual model inputs was performed by using their ± 20% change while holding other inputs constants. Subsequently, the resulting set of sensitivity analyses were ranked by the absolute magnitude of deviation from the base case to assess which input parameter had the most significant impact on the results.

Finally, to account for potential different market penetration of lebrikizumab, three sensitivity analyses with different market share were conducted. Specifically, the first sensitivity analysis included a reduction of 25% of use of lebrikizumab, the second sensitivity analysis a 50% reduction, and the third sensitivity analysis a reduction of 75% (Table 4).

RESULTS

Figure1 reports the estimated number of individuals treated with severe AD, who were potentially eligible for the study treatment, according to AIFA reimbursement criteria, over the 3-year simulation period. Specifically, the projected number of eligible patients over a 3-year timeframe was 14,973, 18,716, and 23,395 in the first, second, and third year, respectively. As depicted in Fig. 1, in scenario B the number of subjects treated with lebrikizumab increased from 1198 in the first year to 5849 in the third year. Furthermore, since an increase in the use of tralokinumab was anticipated in the scenario without lebrikizumab (scenario A), the introduction of lebrikizumab led to a more pronounced reduction in the number of patients treated with tralokinumab by the third year.

The budget impact results are reported in Table 5. As reported in the table, the use of lebrikizumab yielded an overall budget reduction of €3,302,934 over the 3-year period.

The availability of lebrikizumab led to an expenditure of €785,594 in the first year of simulation, followed by cost savings of €1,693,126, and €2,395,402 during the second and third year of simulation, respectively (Table 5).

The main driver of the budget impact was drug acquisition costs. In the scenario without lebrikizumab it accounted from €126,232,192 during the first year of simulation to €190,312,787 during the last year. Similarly, in the scenario with lebrikizumab it accounted from €127,046,433 during the first year of simulation to €188,254,685 during the last year. This

Table 4 Market share in the sensitivity analyses

	Sensitivity analysis 1 (reduction of 25% for lebrikizumab compared with base case scenario)			Sensitivity analysis 2 (reduction of 50% for lebrikizumab compared with base case scenario)			Sensitivity analysis 3 (reduction of 75% for lebrikizumab compared with base case scenario)		
	Year 1	Year 2	Year 3	Year 1	Year 2	Year 3	Year 1	Year 2	Year 3
Lebrikizumab	6%	11%	19%	4%	7%	13%	2%	4%	6%
Dupilumab	76%	68%	64%	77%	71%	69%	79%	74%	74%
Tralokinumab	18%	21%	17%	19%	22%	18%	19%	22%	20%

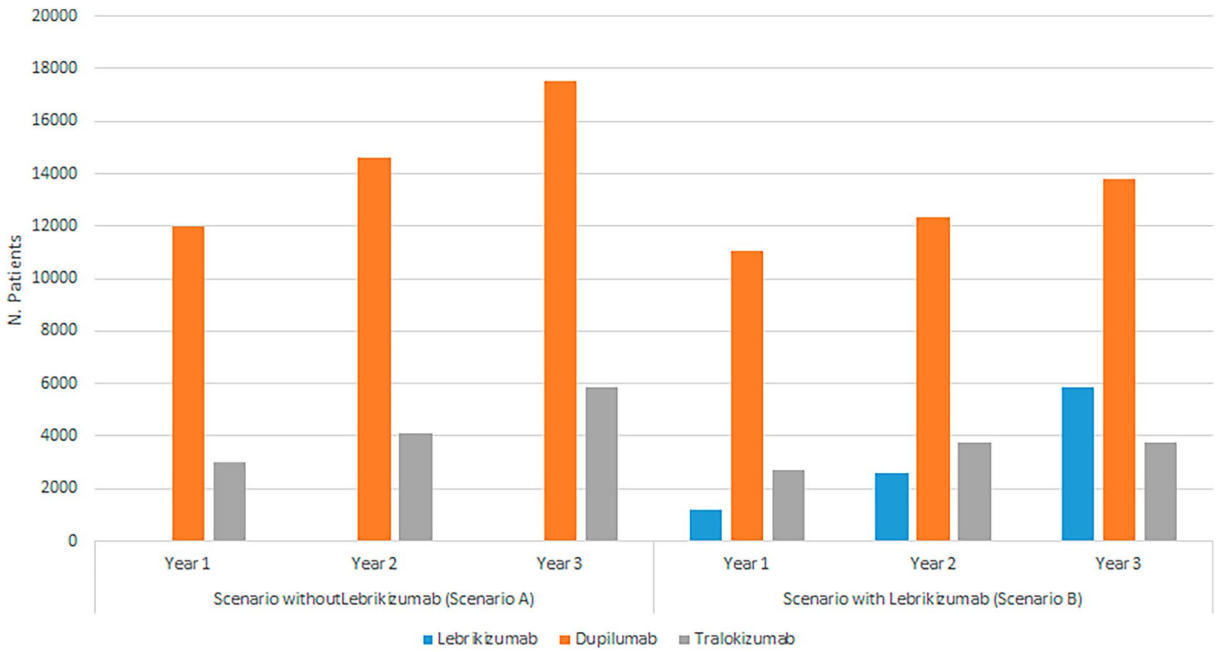

Fig. 1 Number of treated individuals with each therapy within the scenario without lebrikizumab (scenario A) and the scenario with lebrikizumab (scenario B)

Table 5 Budget impact results scenario with lebrikizumab (scenario B) vs scenario without lebrikizumab (scenario A)

	Year 1	Year 2	Year 3	Overall
Scenario without lebrikizumab (€)				
Overall	129,671,131	164,800,471	205,285,589	499,757,191
Treatments and administration costs	126,232,192	152,797,506	190,312,787	469,342,485
Disease management costs	1,716,595	9,867,315	12,335,639	23,919,549
Adverse event management	1,722,344	2,135,650	2,637,163	6,495,157
Scenario with lebrikizumab (€)				
Overall	130,456,725	163,107,345	202,890,187	496,454,257
Treatments and administration costs	127,046,433	151,235,284	188,254,685	466,536,402
Disease management costs	1,715,961	9,867,843	12,329,711	23,913,515
Adverse event management	1,694,332	2,004,218	2,305,791	6,004,341
Delta between the scenario with lebrikizumab and the scenario without lebrikizumab (€)				
Overall	785,594	− 1,693,126	− 2,395,402	− 3,302,934
Treatments and administration costs	814,241	− 1,562,222	− 2,058,101	− 2,806,082
Disease management costs	− 634	528	− 5928	− 6035
Adverse event management	− 28,012	− 131,432	− 331,372	− 490,817

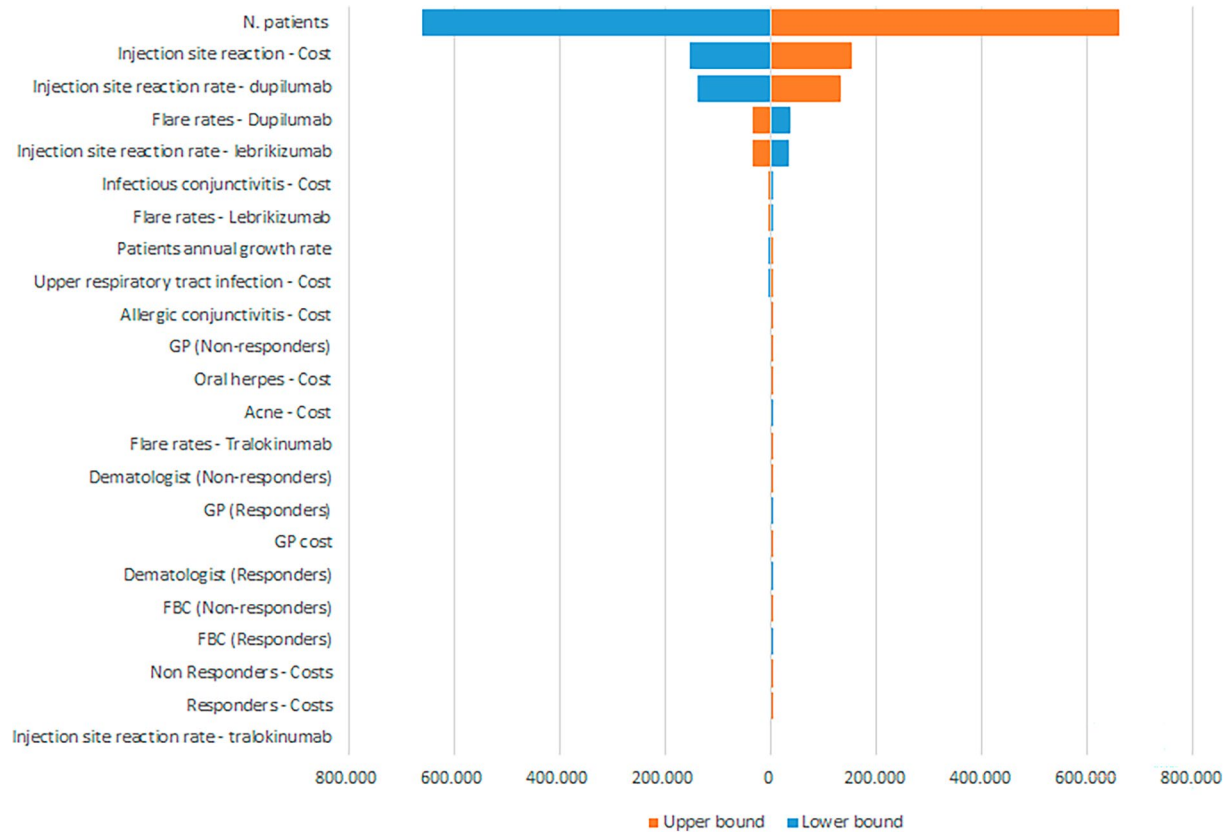

Fig. 2 One-way sensitivity analysis

resulted in a cost expenditure of drug acquisition from €814,241 during the first year to a cost saving of −€2,058,101 in the last year of simulation.

As reported in the one-way sensitivity analysis results in Fig. 2, the number of patients potentially eligible for the treatment and the injection site reaction management costs were the factors with the largest impact on the results.

Scenario sensitivity analyses indicated a decrease in cost saving compared to the base case scenario when assuming a reduced market penetration for lebrikizumab (Table 6). Specifically, a 25% reduction in yearly lebrikizumab use resulted in a cost saving of −€2,298,235 over 3 years of simulation. This cost saving further decreased to −€161,829 when assuming a 75% reduction in lebrikizumab use compared to the base case scenario.

DISCUSSION

This is the first study to evaluate the financial impact of administering lebrikizumab to patients with severe AD according to AIFA reimbursement criteria. The study, by adopting the perspective of the Italian NHS, suggested that the use of lebrikizumab resulted in an overall budget saving of €3.3 million over 3 years. In addition, the study revealed that lower use of lebrikizumab resulted in lower overall budget saving.

Data on the risk–benefit profile of new medications should be complemented by economic evaluations to ensure their affordability for the Italian NHS. For this reason, cost-effectiveness analysis and budget impact analysis play a crucial role in assessing the economic impact of new health technologies in light of their clinical benefit. Our findings suggest that lebrikizumab

Table 6 Budget impact sensitivity analysis

	Year 1	Year 2	Year 3	Overall
Sensitivity analysis 1[a]				
Total cost in the scenario with lebrikizumab	130,357,369	163,485,262	203,616,324	497,458,956
Total cost in the scenario without lebrikizumab	129,671,131	164,800,471	205,285,589	499,757,191
Budget impact	686,238	− 1,315,209	− 1,669,264	− 2,298,235
Sensitivity analysis 2[a]				
Total cost in the scenario with lebrikizumab	130,100,393	163,809,751	204,818,234	498,728,378
Total cost in the scenario without lebrikizumab	129,671,131	164,800,471	205,285,589	499,757,191
Budget impact	429,262	− 990,720	− 467,355	− 1,028,813
Sensitivity analysis 3[a]				
Total cost in the scenario with lebrikizumab	130,001,037	164,384,692	205,209,633	499,595,362
Total cost in the scenario without lebrikizumab	129,671,131	164,800,471	205,285,589	499,757,191
Budget impact	329,906	− 415,779	− 75,955	− 161,829

Costs are reported in euros (€)

[a]Sensitivity analysis 1, 2, and 3 assumed a reduction of lebrikizumab market penetration of 25%, 50%, and 75% compared with the base case analysis

represents a valuable therapeutic alternative to dupilumab and tralokinumab in the treatment of patients with severe AD. These results indicate that the availability of lebrikizumab may help reduce the clinical and economic burden of the disease. In particular, lebrikizumab was associated with cost savings of approximately €3.3 million, mainly due to reduced drug acquisition costs, lower adverse events management costs, and decreased disease management expenses.

A recent meta-analysis confirmed the efficacy of lebrikizumab for patients with moderate-to-severe AD. The use of lebrikizumab was associated with improvement across multiple clinical efficacy measures, including EASI, SCORAD, IGA, BSA, P-NRS, or P-VAS, sleep-loss score, DLQI, and POEM. The authors also reported significant improvements in signs and symptoms of the disease, quality of life (QoL), and a favorable safety profile of lebrikizumab [40–42]. Drucker and colleagues highlighted the efficacy of lebrikizumab, which can be considered similar to dupilumab, as new treatment for patients with AD [41, 42].

While previous studies have examined the budget impact of various AD treatments, no studies have specifically evaluated the budget impact of lebrikizumab in patients with severe AD [43–45]. For lebrikizumab, the body of available evidence comprised only of few cost-effectiveness analyses. For example, a recent NICE evaluation revealed that lebrikizumab is cost-effective compared to other biologics (dupilumab or tralokinumab) for treating moderate-to-severe AD [34]. Similarly, an Austrian cost-effectiveness analysis, using a lifetime horizon, demonstrated a cost saving of €2409 when using lebrikizumab instead of dupilumab for moderate-to-severe AD [46]. The limited availability of economic data on lebrikizumab highlights the need for further cost-effectiveness and budget impact studies to comprehensively assess its economic value in treating patients with moderate-to-severe AD.

Severe AD imposes a substantial financial burden on the healthcare system due to high treatment costs and the need for specialist dermatologist consultations, which increased with disease severity and uncontrolled symptoms.

The disease is also associated with an increased burden for society in terms of lost work productivity and absenteeism [23]. A literature review estimated that the economic impact of moderate-to-severe AD in Europe is approximately €30 billion, which includes costs due to sick leave and productivity loss (€15.2 billion), direct medical costs (€10.1 billion), and patient/family personal costs (€4.7 billion) [23]. However, the analysis did not include more recent treatments which have an important economic burden in the management of patients with severe AD. Furthermore, the condition significantly impacts not only monetary costs but also intangible costs, profoundly affecting the QoL of patients. These patients often experience sleep disturbances, pain and discomfort, emotional and well-being disorders, as well as relationship and self-esteem issues [22, 23, 25]. Given the economic and humanistic impact of this condition, it is essential to ensure the availability of cost-effective treatments that minimize financial strain on the Italian NHS. Our findings provide valuable economic evidence supporting the use of lebrikizumab as a new treatment for patients with severe AD. The availability of cost-saving therapies is crucial to optimize healthcare resource allocation, particularly in resource-limited healthcare systems.

Despite promising clinical trial results and positive results of pharmacoeconomics analyses, the real-world adoption of lebrikizumab may face several challenges. For instance, clinical beliefs might impact treatment adoption. In this context, unfamiliarity with guidelines, insufficient training, and lack of knowledge and experience might limit the use of new biologics in clinical practice [47–49].

This study has several strengths. First, we developed a budget impact model that fully accounts for the characteristics of the Italian health system and clinical practice. Second, epidemiology, resource utilization for disease management, as well as AEs management and cost data were validated by Italian clinical experts. As for other budget impact analyses, all costs related to health events were estimated using micro-costing methods, which included the identification of healthcare resources, quantification, utilization rates, and unit costs. This approach ensures robust estimates of cost parameters at the local level [44].

As with all modelling analyses, this analysis has limitations which should be considered when interpreting the results. First, the budget impact analysis was based on projected utilization rates of lebrikizumab, as outlined in the scenario analyses; however, the findings may not be generalizable to populations with different adoption rates of the drug. Second, the analysis was restricted to monoclonal antibodies used for treating patients with severe AD. JAK inhibitors were not included in the analysis because they are oral agents with a different mechanism of action. Our analysis specifically focused on monoclonal antibodies. Furthermore, the safety profile of JAK inhibitors limits their use in patients with AD. Specifically, some authors suggest their use in patients with contraindications to or inadequate response to biologics [50–52], and regulatory agencies recommend their use with caution in patients at risk of venous thromboembolism (VTE), cancer, or major cardiovascular problem [53, 54].

Therefore, it is possible that including JAK inhibitors in the analysis could result in a different economic impact. In addition, we used the Italian NHS perspective by considering only direct medical costs associated with disease management, excluding patients' incurred costs or potential saving from accessing lebrikizumab. Similarly, for the management of adverse events, the costs incurred by the Italian NHS as suggested by clinical experts were considered. However, alternative approaches to AE management may result in a different budget impact. To account for potential variation in AE management costs, a one-way sensitivity analysis was performed. Finally, the numbers of clinical visits for responders and non-responders were derived from clinical expert opinion on disease management in Italy. Consequently, different therapeutic pathways might influence the economic estimations.

CONCLUSION

The introduction of lebrikizumab in Italy could reduce the overall costs for patients with severe AD, who can be treated with biologic agents, in line with AIFA reimbursement criteria. Lebrikizumab is associated with improved patient management and cost saving for the Italian NHS. This data could serve as valuable information for healthcare decision makers to optimize the value derived from the treatment and management of patients with severe AD. This is particularly important considering the significant impact the disease has on patients' QoL. Given the limited real-world data available on efficacy, safety, and economic impact of lebrikizumab, further studies are needed to confirm or refine the findings from this analysis.

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Data Availability. The budget impact model structure and the data sources analyzed during the current study are available from the corresponding author on reasonable request. All data used to construct the model from both primary and secondary sources has also been presented within this manuscript.

Declarations

Conflicts of Interest. Ippazio Cosimo Antonazzo and Roberto Langella declare no conflicts of interest. Cataldo Patruno received grants and personal fees from AbbVie, Almirall, Amgen, Eli Lilly, Galderma, La Roche-Posay, Leo Pharma, Novartis, Pfizer, Pierre Fabre, Sanofi. Giampiero Girolomoni has received personal fees from AbbVie, Almirall, Amgen, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli-Lilly, Leo Pharma, Merck Serono, Novartis, Pfizer, Pierre Fabre, Samsung bioepis and Sanofi. Veronica Ottobrino is employed at Almirall S.p.A. Lorenzo Giovanni Mantovani has received grants and personal fees from Bayer AG, Boehringer Ingelheim, Pfizer and Daiichi-Sankyo. Paolo Angelo Cortesi has received a research grant from Baxalta, now part of Shire, and speaking honoraria from Pfizer and Roche.

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