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Expert Review of Pharmacoeconomics & Outcomes Research

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ierp20

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To cite this article: Pieralessandro Lasalvia, Yaneth Gil-Rojas, Emmanuel Papadimitropoulos, Russel Burge & Diego Rosselli (2023) Estimate of the cost per responder for treatment with biological therapies of moderate-to-severe plaque psoriasis in Colombia for first-year and maintenance periods, Expert Review of Pharmacoeconomics & Outcomes Research, 23:5, 511-517, DOI: 10.1080/14737167.2023.2190514

To link to this article: https://doi.org/10.1080/14737167.2023.2190514

EXPERT REVIEW OF PHARMACOECONOMICS & OUTCOMES RESEARCH
2023, VOL. 23, NO. 5, 511–517
https://doi.org/10.1080/14737167.2023.2190514

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ORIGINAL RESEARCH

Estimate of the cost per responder for treatment with biological therapies of moderate-to-severe plaque psoriasis in Colombia for first-year and maintenance periods

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ABSTRACT

Introduction: Psoriasis is a chronic systemic inflammatory disease manifesting as erythematous and desquamative dermatoses.

Objectives: This study estimated the cost per responder (CPR) for the treatment of moderate-to-severe plaque psoriasis with biologic therapies approved by the Colombian regulatory agency.

Methods: This secondary study used a modeling based CPR estimation to evaluate psoriasis therapies in Colombia. We calculated CPR of achieving Psoriasis Area and Severity Index (PASI) scores of 75, 90, and 100 for biological treatments based on the number needed to treat (NNT), reported in previously published network meta-analyses. We calculated CPR for the first year and for the maintenance period. We ranked alternatives using the estimated CPR from each literature source using the Borda count method.

Results: Adalimumab, infliximab and etanercept were the least expensive alternatives. Ixekizumab, guselkumab and secukinumab were the treatments with the lowest NNT for PASI 75, 90, and 100. For both first year and maintenance periods, adalimumab, infliximab, guselkumab and ixekizumab had the lowest CPR. Sensitivity analyzes showed consistent results.

Conclusions: The application of CPR analysis of biologics to treat plaque psoriasis demonstrated that adalimumab, infliximab, guselkumab, and ixekizumab had the lowest CPR in the first year of treatment and during the maintenance period.

ARTICLE HISTORY
Received 11 October 2022
Accepted 9 March 2023

KEYWORDS
Biological therapies; Colombia; cost per responder; moderate-to-severe plaque psoriasis; number needed to treat; psoriasis

1. Introduction

Psoriasis is a chronic systemic immune-mediated inflammatory disease clinically manifesting with erythematous, scaly plaques. as erythematous and desquamative dermatoses. It has no cure and negatively affects the quality of life of those who suffer from it [1]. Psoriasis is characterized by localized or generalized, mostly symmetrical, sharply demarcated red plaques, usually covered with white or silver scales. These lesions cause itching, stinging, and pain on the affected areas [2]. Psoriasis is associated with several comorbidities such as arthritis, Crohn's disease, cardiovascular problems, depression, and nonalcoholic fatty liver disease; the most common form is plaque psoriasis which accounts for 90% of cases [2]. Development of psoriasis has also been associated with several lifestyle habits such as smoking and alcohol consumption [3,4]. Approximately 70% to 80% of patients with plaque psoriasis have a mild illness that can be adequately treated with topical therapy [1,2]. Moderate-to-severe plaque psoriasis is usually treated with systemic therapies. When patients do not respond or are intolerant, they are eligible for treatment with biological therapies, which have opened up new treatment possibilities and aim to prevent T cell proliferation or control of cytokines involved in the physiopathology of psoriasis [5]. It is also important to note that adherence and certain lifestyle habits such as substance abuse and diet composition can have an impact on treatment response and clinical outcomes [6,7]

Studies report the prevalence of psoriasis to range between 0.09% and 11.4% depending on population [1], with a consensus reporting the prevalence to be 2% to 4% in Western countries [8]. Age standardized incidence rates have been estimated at 57.8 per 100000 for a total of 4.6 million cases worldwide, with higher values in high (112.6) and medium (69.4) income countries [9].In Colombia, there are no studies on the prevalence or incidence of psoriasis, however, the Institute for Health Metrics and Evaluation estimates prevalence to be approximately 0.5% of the population, generating a loss of 22,046 disability-adjusted life years [10], making this disease a considerable health problem in the country.

Therapies with biological agents are expensive and, for middle-income countries with more acute resource constraints, it is necessary to establish their comparative effectiveness to make proper clinical and economic decisions about their use. The number needed to treat (NNT) and the cost per responder (CPR) are measures of comparative effectiveness that are both clinically and economically important and useful

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/14737167.2023.2190514

to inform the decision-making of both third-party payers and doctors offering an additional approach to traditional cost-effectiveness [11,12]. The NNT is a metric used to evaluate the impact of a treatment. It is defined as the number of individuals requiring treatment to produce, or avoid, an additional event compared to the events which would occur with the control treatment, usually placebo [13]. If the cost, C, of treating a patient with product X is C(X), then the total cost, CT, incurred to obtain (or avoid) an event, E, with X is given by CT(E) = C(X)×NNT. This is the CPR.

This paper estimates the CPR in the treatment of moderate-to-severe plaque psoriasis of the biological therapies adalimumab, etanercept, and infliximab (monoclonal antibodies against tumor necrosis factor-alpha [anti-TNF-α]), ixekizumab and secukinumab (monoclonal antibodies against pro-inflammatory cytokines interleukin [IL]-17), guselkumab (selective inhibitor of IL-23) and ustekinumab (monoclonal antibody against IL-12/23 proinflammatory cytokines) in Colombia from the NNT of patients who achieve 75%, 90%, and 100% reductions in the Psoriasis Area and Severity Index (PASI 75, PASI 90, and PASI 100, respectively) in the first year and in maintenance dosing following the first year, with each of these therapies.

2. Methods

This study is an economic modeling estimation of CPR for psoriasis for the following biological therapies in Colombia: adalimumab, etanercept, guselkumab, infliximab, ixekizumab, secukinumab, and ustekinumab. As such this is a secondary data use study.

2.1. Literature search

A literature search was conducted for evidence of the comparative effectiveness of these treatments in moderate to severe plaque psoriasis in adult patients from the secondary literature. For this, the MEDLINE database was consulted using the Ovid search engine (the search strategy is found in Supplementary Table 1). The initial inclusion criteria were published studies with systematic reviews of the literature and network meta-analysis (NMA) of the efficacy of adalimumab, etanercept, infliximab, ixekizumab, secukinumab, and ustekinumab in terms of PASI 75, PASI 90, and PASI 100 for patients with moderate to severe plaque psoriasis. All interventions were required to be evaluated in a single NMA.

Subsequently, a search strategy was developed using terms related to psoriasis, plaque psoriasis, specific therapies, and reviews, up to 5 years prior to November 2020 (see Supplementary Material). No geographical restrictions were applied to the search. Two independent reviewers carried out the selection of the title/summary and the revision of the full text according to the search strategy.

2.2. Calculation of NNT and CPR

Information on relative effects obtained from selected studies was extracted and translated to calculate NNT and CPR. Estimated response rates at each PASI response level were obtained by applying the relative risk of each therapy relative to placebo to the probability of achieving a given PASI level relative to placebo. This information was obtained directly from the selected studies using published data at the end of the first year.

The estimated placebo response rate corresponds to the absolute probability of achieving ≥75%, ≥90%, or 100% PASI relief of clinical features of psoriasis with placebo, based on the 'Single Technology Evaluation: Ixekizumab for the treatment of moderate to severe plaque psoriasis [ID904]' from the National Institute for Health and Care Excellence (NICE) [14]. For each treatment and for each selected study, the NNT was calculated as the inverse of the difference in PASI estimated response rates between biological treatment and placebo.

Confidence intervals (CI) for the NNT were obtained by inverting and exchanging the confidence limits for the absolute risk reduction (ARR). The ARR was calculated holding the level of response to placebo fixed. If the study directly reported NNTs, we extracted them along with their CIs or credibility intervals (CrI). The CPR was calculated for the mean value and the limits of the NNT interval. During the final phase of the review, we also decided to obtain information on guselkumab, since it had become a relevant alternative in Colombia. We did not modify the bibliographic search or the selected articles, but we proceeded to extract the relevant information in the selected reviews.

In relation to the estimation of costs, the costs of acquisition, administration, and monitoring of the medicines supplied were included and expressed in Colombian pesos (COP) as of 2020. The CPR was calculated for the following time periods: the first year (which includes the induction period plus maintenance dosing until completing the first full year on treatment) and the full maintenance period (each full year following the first year of therapy). Long-term data were obtained from meta-analyses using the 52-week efficacy results and these results were assumed to continue for all therapies in the maintenance period scenarios.

The prices of the medicines were obtained from official sources of information of the Drug Price Information System (known as SISMED) and from the price regulation memos of the Ministry of Health and Social Protection. According to the methodology of the Institute of Technological Evaluation in Health (IETS), the final price of medicines was estimated using the weighted average by market share of each of the pharmacological therapies evaluated in this study [15]. No distinction was made between name brand and biosimilars, but the prices were weighted in terms of market share. The prices of the therapies per unit are presented in Table 1. The dosage of each therapy was calculated based on the approved dosages established by the local regulatory agency for the different phases of product use (Supplementary Table 2).

Administration and monitoring costs were taken from the Tariff Manual of the Social Security Institute of the year 2001, with an increase of 30% in accordance with the methodology proposed by the IETS [15]. Cost of administration of drugs that are administered subcutaneously only applies for two sessions in the first year that correspond to the usual training period. Of the treatments considered in the analysis, infliximab is the only one with intravenous administration. For those administered subcutaneously and intravenously, a cost per session of COP $8,509 and COP $124,449, respectively, was considered. Detailed information on the monitoring costs is presented in Supplementary Table 3.

Table 1. Prices and total doses administered during treatment of biological therapies for moderate-to-severe plaque psoriasis in Colombia.

Alternative	Induction period (weeks)	Price per mg (COP)	Content (mg)	Price per MUC	Doses, first year (including week 52)	Doses, maintenance period
Adalimumab	16	$ 19,155	40	$ 766,212	28	26
Etanercept	12	$ 11,101	50	$ 555,035	64	52
Guselkumab	16	$ 56,363	100	$ 5,636,251	8	6
Infliximab[¥]	10	$ 7,595	100	$ 759,518	36	24
Ixekizumab	16	$ 32,304	80	$ 2,584,340	18	13
Secukinumab[β]	16	$ 9,495	150	$ 1,424,223	32	24
Ustekinumab	16	$ 187,875	45	$ 8,454,377	6	5

COP, Colombian pesos; MUC, minimum unit of content (e.g. vial, prefilled syringe).
[¥]Based on 80 kg-patient dosed 5 mg/kg at week 0, 2, 6, and every 8 weeks. Each infliximab dose is equivalent to 400 mg (4 x 100 mg vials).
[β]Secukinumab 300 mg as 2 × 150 mg mg/mL pens

Finally, we calculated the CPR for each treatment based on the published comparative efficacy data. We then ranked them by CPR across all studies using the Borda count method [16]. This ordering was carried out using the Borda method which allows different rankings to be aggregated into a single overall count. Consider a hypothetical scenario where two studies have ordered four therapeutic alternatives: A, B, C, and D in one study while, in the other study, the order is B, D, A, and C. In the Borda count, points are assigned for each therapy according to the number of alternatives under comparison (four in this case) and the order that each of the positions in the rankings occupy, so that the therapy that places first receives four points, the one that places second receives 3 points, and so on. The points obtained by each alternative in each order are added. The alternative that has the most points in total is placed first in the final overall order.

We performed sensitivity analyses for CPR considering the CrI or CI of the estimated NNT and the minimum and maximum prices of the treatments (Supplementary Table 4).

3. Results

3.1. Literature search

When applying inclusion criteria, we identified 3 studies that reported efficacy results at 52 weeks: Sawyer et al, 2019b [17], Yasmeen et al [18] and Armstrong et al 2018 [11]. They all performed Bayesian meta-analyses. In each study, we obtained comparative efficacy data related to PASI 75, 90, and 100. Most studies reported relative risks which we then transformed to NNT [16–21]. Armstrong et al 2018 [11] and Armstrong et al 2020 [22] directly reported NNT, which we extracted. And which we used to calculate NNT (Supplementary Table 5).

3.2. Calculation of NNT

The NNTs for PASI 75/90/100 at 52 weeks are shown in Table 2. Consistently, in all studies, ixekizumab, secukinumab, and guselkumab were more effective than ustekinumab for the PASI 75, PASI 90, and PASI 100 responses. Among anti-TNFs, infliximab was the most effective alternative at all levels of response. According to the study by Armstrong et al. 2020 [22], ixekizumab had the lowest NNT for PASI 75, 90, and 100 and the second lowest NNT according to Yasmeen et al. [18].

3.3. Calculation of CPR

Based on price, dosage, and cost information, in the first year of therapy (which includes costs of the induction and maintenance doses) adalimumab had the lowest cost of all treatments, followed by infliximab, etanercept, guselkumab, secukinumab, ixekizumab, and ustekinumab (Table 3).

Table 2. Estimated NNT with biological therapies to achieve PASI 75/90/100 in moderate-to-severe plaque psoriasis at 52 weeks.

		NNT – PASI 75			NNT – PASI 90			NNT – PASI 100		
Alternative	Study	Mean	LCrI	UCrI	Mean	LCrI	UCrI	Mean	LCrI	UCrI
Adalimumab	Sawyer et al 2019b	1.57	0.20	9.29	3.23	0.35	20.79	11.19	1.02	81.37
	Yasmeen et al 2020	1.97	0.58	5.99	4.05	1.11	13.00	13.08	3.25	45.83
	Armstrong et al 2020	1.56	1.49	1.64	2.35	2.16	2.57	6.10	5.29	7.09
Etanercept	Sawyer et al 2019b	1.91	0.31	9.99	4.26	0.65	23.26	16.65	2.34	98.04
	Yasmeen et al 2020	2.40	0.80	6.67	5.38	1.71	15.41	19.90	5.90	60.46
	Armstrong et al 2020	2.87	2.52	3.32	5.95	4.93	7.25	24.39	18.87	32.26
Guselkumab	Sawyer et al 2019b	–	–	–	–	–	–	–	–	–
	Yasmeen et al 2020	1.48	0.35	5.25	2.57	0.53	10.28	6.18	1.11	29.03
	Armstrong et al 2020	1.23	1.19	1.27	1.51	1.41	1.63	2.81	2.46	3.25
Infliximab	Sawyer et al 2019b	1.46	0.18	9.05	2.90	0.32	19.80	9.59	0.95	74.46
	Yasmeen et al 2020	1.82	0.51	5.75	3.59	0.92	12.17	10.88	2.46	40.68
	Armstrong et al 2020	1.33	1.27	1.40	1.78	1.62	1.96	3.79	3.21	4.50
Ixekizumab	Sawyer et al 2019b	1.22	0.12	8.65	2.18	0.19	17.99	6.18	0.45	62.07
	Yasmeen et al 2020	1.56	0.38	5.37	2.80	0.62	10.72	7.25	1.39	31.89
	Armstrong et al 2020	1.20	1.17	1.23	1.43	1.36	1.52	2.54	2.28	2.85
Secukinumab	Sawyer et al 2019b	1.25	0.13	8.72	2.28	0.20	18.32	6.65	0.50	64.47
	Yasmeen et al 2020	1.62	0.42	5.46	3.00	0.70	11.07	8.13	1.69	33.91
	Armstrong et al 2020	1.29	1.24	1.34	1.66	1.55	1.78	3.36	2.96	3.82
Ustekinumab	Sawyer et al 2019b	1.46	0.17	9.09	2.91	0.31	20.16	9.64	0.88	77.04
	Yasmeen et al 2020	1.89	0.54	5.91	3.81	1.00	12.74	11.94	2.79	43.98
	Armstrong et al 2020	1.55	1.48	1.64	2.34	2.14	2.56	6.02	5.21	6.99

NNT to achieve PASI 75/90/100 response among biological therapies relative to placebo, estimated with the relative effectiveness reported in 3 studies: Sawyer et al, Yasmeen et al and Armstrong et al. LCrI, lower credible interval; UCrI, upper credible interval; NNT, number needed to treat.

In the maintenance period in year 2 (the full year following the first year of therapy), the individual cost of each treatment was reduced due to fewer doses. Infliximab was the least expensive followed by adalimumab, etanercept, ixekizumab, guselkumab, secukinumab, and ustekinumab (Table 3).

In the first year (Table 4), the overall CPR ranking of biological therapies for the treatment of moderate-to-severe plaque psoriasis using the Borda count was as follows, from the lowest to highest CPR: adalimumab, infliximab, guselkumab, ixekizumab, secukinumab, etanercept, and ustekinumab to achieve PASI 75; and adalimumab, infliximab, ixekizumab, guselkumab, secukinumab, ustekinumab, and etanercept to achieve PASI 90. For PASI 100, the options that provided the lowest cost per responder were guselkumab, infliximab, adalimumab, and ixekizumab.

In the maintenance period (Table 5), the overall CPR ranking of biological therapies for the treatment of moderate-to-severe plaque psoriasis using the Borda count was as follows, from the lowest to highest CPR: infliximab, adalimumab, ixekizumab, guselkumab, secukinumab, etanercept, and ustekinumab to achieve PASI 75; and infliximab, adalimumab, ixekizumab, guselkumab, secukinumab, ustekinumab, and etanercept to achieve PASI 90. For PASI 100, the options that provided the lowest cost per responder were infliximab, ixekizumab, guselkumab, and adalimumab.

Table 3. Annual cost of biological therapies for treatment of moderate-to-severe plaque psoriasis for the first year and maintenance period.

	First Year – Costs (COP) (includes induction and maintenance doses)			
Alternative	Acquisition	Administration	Monitoring	Total
Adalimumab	21,453,934	17,017	277,738	21,748,689
Etanercept	35,522,216	17,017	284,388	35,823,621
Guselkumab	45,090,008	17,017	277,738	45,384,763
Infliximab	27,342,637	1,120,041	284,388	28,747,066
Ixekizumab	46,518,126	17,017	277,738	46,812,881
Secukinumab	45,575,141	17,017	277,738	45,869,896
Ustekinumab	50,726,262	17,017	277,738	51,021,017
	Maintenance period – Costs (COP)			
Alternative	Acquisition	Administration	Monitoring	Total
Adalimumab	19,921,510	0	69,826	19,991,336
Etanercept	28,861,801	0	69,826	28,931,627
Guselkumab	33,817,506	0	69,826	33,887,332
Infliximab	18,228,424	871,143	69,826	19,169,393
Ixekizumab	33,596,424	0	69,826	33,666,250
Secukinumab	34,181,356	0	69,826	34,251,182
Ustekinumab	42,271,885	0	69,826	42,341,711

COP, Colombian pesos.

Table 4. Cost per responder among biological therapies for moderate-to-severe plaque psoriasis in Colombia (First year).

	Sawyer et al. 2019b – 52 weeks			Yasmeen et al. 2020–52 weeks			Armstrong et al. 2020–52 weeks			
	Mean	LCrI	UCrI	Mean	LCrI	UCrI	Mean	LCrI	UCrI	Rank
CPR for PASI 75 – First year										
Adalimumab	$ 34.3	$ 4.3	$ 202.1	$ 42.8	$ 12.7	$ 130.3	$ 33.8	$ 32.4	$ 35.7	1
Etanercept	$ 68.4	$ 11.3	$ 357.8	$ 85.9	$ 28.8	$ 238.9	$ 102.8	$ 90.3	$ 118.9	6
Guselkumab	-	-	-	$ 67.3	$ 15.8	$ 238.4	$ 55.8	$ 54.0	$ 57.6	3
Infliximab	$ 42.0	$ 5.3	$ 260.3	$ 52.4	$ 14.7	$ 165.3	$ 38.2	$ 36.5	$ 40.2	2
Ixekizumab	$ 56.9	$ 5.7	$ 404.9	$ 73.1	$ 18.0	$ 251.5	$ 56.2	$ 54.8	$ 57.6	4
Secukinumab	$ 57.3	$ 5.8	$ 400.0	$ 74.4	$ 19.2	$ 250.2	$ 59.2	$ 56.9	$ 61.5	5
Ustekinumab	$ 74.7	$ 8.9	$ 463.9	$ 96.5	$ 27.4	$ 301.5	$ 79.1	$ 75.5	$ 83.7	7
CPR for PASI 90 – First year										
Adalimumab	$ 70.2	$ 7.7	$ 452.2	$ 88.0	$ 24.2	$ 282.8	$ 51.1	$ 47.0	$ 55.9	1
Etanercept	$ 152.5	$ 23.4	$ 833.1	$ 192.6	$ 61.2	$ 552.0	$ 213.2	$ 176.6	$ 259.7	7
Guselkumab				$ 116.5	$ 24.1	$ 466.4	$ 68.5	$ 64.0	$ 74.0	4
Infliximab	$ 83.3	$ 9.3	$ 569.2	$ 103.3	$ 26.3	$ 349.7	$ 51.2	$ 46.6	$ 56.3	2
Ixekizumab	$ 101.9	$ 8.8	$ 842.0	$ 131.3	$ 28.9	$ 501.7	$ 66.9	$ 63.7	$ 71.2	3
Secukinumab	$ 104.7	$ 9.1	$ 840.1	$ 137.5	$ 32.0	$ 508.0	$ 76.1	$ 71.1	$ 81.6	5
Ustekinumab	$ 148.2	$ 15.7	$ 1,028.6	$ 194.6	$ 50.8	$ 649.9	$ 119.4	$ 109.2	$ 130.6	6
CPR for PASI 100 – First year										
Adalimumab	$ 243.3	$ 22.3	$ 1,769.6	$ 284.4	$ 70.6	$ 996.7	$ 132.7	$ 115.1	$ 154.2	3
Etanercept	$ 596.4	$ 83.9	$ 3,512.1	$ 712.8	$ 211.3	$ 2,165.9	$ 873.7	$ 676.0	$ 1,155.7	7
Guselkumab	-	-	-	$ 280.5	$ 50.2	$ 1,317.4	$ 127.5	$ 111.6	$ 147.5	1
Infliximab	$ 275.6	$ 27.3	$ 2,140.5	$ 312.7	$ 70.7	$ 1,169.5	$ 109.0	$ 92.3	$ 129.4	1
Ixekizumab	$ 289.5	$ 21.2	$ 2,905.8	$ 339.4	$ 65.1	$ 1,492.8	$ 118.9	$ 106.7	$ 133.4	4
Secukinumab	$ 305.2	$ 22.9	$ 2,957.4	$ 372.7	$ 77.4	$ 1,555.4	$ 154.1	$ 135.8	$ 175.2	5
Ustekinumab	$ 492.0	$ 45.1	$ 3,930.7	$ 609.3	$ 142.5	$ 2,243.7	$ 307.1	$ 265.8	$ 356.6	6

CPR, cost per responder; LCrI, lower credible interval; UCrI, upper credible interval.

Table 5. Cost per responder among biological therapies for moderate-to-severe plaque psoriasis in Colombia (Maintenance period).

	Sawyer et al. 2019b – 52 weeks			Yasmeen et al. 2020–52 weeks			Armstrong et al. 2020–52 weeks			Maintenance period
	Mean	LCrI	UCrI	Mean	LCrI	UCrI	Mean	LCrI	UCrI	Rank
CPR for PASI 75 – Maintenance period										
Adalimumab	$ 31.5	$ 4.0	$ 185.7	$ 39.3	$ 11.7	$ 119.8	$ 31.1	$ 29.8	$ 32.8	2
Etanercept	$ 55.3	$ 9.1	$ 289.0	$ 69.4	$ 23.2	$ 193.0	$ 83.0	$ 72.9	$ 96.1	6
Guselkumab	- – -			$ 50.3	$ 11.8	$ 178.0	$ 41.7	$ 40.3	$ 43.0	4
Infliximab	$ 28.0	$ 3.5	$ 173.6	$ 34.9	$ 9.8	$ 110.2	$ 25.5	$ 24.3	$ 26.8	1
Ixekizumab	$ 40.9	$ 4.1	$ 291.2	$ 52.6	$ 13.0	$ 180.9	$ 40.4	$ 39.4	$ 41.4	3
Secukinumab	$ 42.8	$ 4.3	$ 298.7	$ 55.6	$ 14.3	$ 186.9	$ 44.2	$ 42.5	$ 45.9	5
Ustekinumab	$ 62.0	$ 7.4	$ 385.0	$ 80.1	$ 22.7	$ 250.2	$ 65.6	$ 62.7	$ 69.4	7
CPR for PASI 90 – Maintenance period										
Adalimumab	$ 64.5	$ 7.1	$ 415.6	$ 80.9	$ 22.2	$ 260.0	$ 47.0	$ 43.2	$ 51.4	2
Etanercept	$ 123.2	$ 18.9	$ 672.8	$ 155.5	$ 49.4	$ 445.8	$ 172.1	$ 142.6	$ 209.8	7
Guselkumab	-	–	–	$ 87.0	$ 18.0	$ 348.3	$ 51.2	$ 47.8	$ 55.2	4
Infliximab	$ 55.5	$ 6.2	$ 379.6	$ 68.9	$ 17.6	$ 233.2	$ 34.1	$ 31.1	$ 37.6	1
Ixekizumab	$ 73.3	$ 6.3	$ 605.5	$ 94.4	$ 20.8	$ 360.8	$ 48.1	$ 45.8	$ 51.2	3
Secukinumab	$ 78.2	$ 6.8	$ 627.3	$ 102.7	$ 23.9	$ 379.3	$ 56.9	$ 53.1	$ 61.0	5
Ustekinumab	$ 123.0	$ 13.0	$ 853.7	$ 161.5	$ 42.1	$ 539.4	$ 99.1	$ 90.6	$ 108.4	6
CPR for PASI 100 – Maintenance period										
Adalimumab	$ 223.7	$ 20.5	$ 1,626.6	$ 261.5	$ 64.9	$ 916.2	$ 121.9	$ 105.8	$ 141.7	4
Etanercept	$ 481.6	$ 67.7	$ 2,836.4	$ 575.6	$ 170.7	$ 1,749.2	$ 705.6	$ 545.9	$ 933.3	7
Guselkumab	-	–	–	$ 209.5	$ 37.5	$ 983.7	$ 95.2	$ 83.4	$ 110.1	3
Infliximab	$ 183.8	$ 18.2	$ 1,427.4	$ 208.5	$ 47.1	$ 779.9	$ 72.7	$ 61.5	$ 86.3	1
Ixekizumab	$ 208.2	$ 15.2	$ 2,089.8	$ 244.1	$ 46.8	$ 1,073.5	$ 85.5	$ 76.8	$ 95.9	2
Secukinumab	$ 227.9	$ 17.1	$ 2,208.3	$ 278.3	$ 57.8	$ 1,161.5	$ 115.1	$ 101.4	$ 130.8	5
Ustekinumab	$ 408.3	$ 37.4	$ 3,262.1	$ 505.6	$ 118.3	$ 1,862.0	$ 254.9	$ 220.6	$ 296.0	6

CPR, cost per responder; LCrI, lower credible interval; UCrI, upper credible interval.

When considering minimal drug prices, most results were consistent with the base case (Supplementary Table 6). For first year results, the only exceptions were found with PASI 75 (ixekizumab changed rank to third and guselkumab to fourth) and PASI 90 (ustekinumab changed rank to seventh and etanercept to sixth). For the maintenance period, the only exception was found with PASI 90 (ustekinumab changed rank to seventh and etanercept to sixth).

When considering maximum drug prices, most results were consistent with the base case (Supplementary Table 7). For first year results, the only exceptions were found with PASI 75 (ixekizumab changed rank to third and guselkumab to fourth) and PASI 90 (ustekinumab changed rank to seventh and etanercept to sixth). For maintenance, the only exception was found with PASI 90 (ustekinumab changed rank to seventh and etanercept to sixth).

4. Discussion

The current study shows that the treatment options with the lowest CPR during the first year were adalimumab, infliximab, guselkumab, and ixekizumab. We demonstrate that ixekizumab had consistently lower CPR in the maintenance period and outperformed guselkumab.

Based on the percentage of patients who achieved a 75%, 90%, and 100% reduction in PASI compared to baseline, all biologic therapies are significantly more effective than placebo. Furthermore, the NNT for each biologic in the different studies implies that those anti-IL-17 and anti-IL-23 therapies currently available in Colombia are more effective than anti-IL-12/23 therapies, which in turn outperform anti-TNF-α. The main exception to this finding was for infliximab, which provides similar or better results compared to ustekinumab. Individually, in all analyses the efficacy of ixekizumab and guselkumab was superior to that of the other treatments in achieving both PASI 75, PASI 90, and PASI 100.

At an individual level, therapies with lower CPR were linked to lower prices, costs, and dosing regimens with a lower frequency of administration. Adalimumab is the least expensive technology in both the first year and maintenance year and is thus associated with a lower CPR to achieve PASI 75 responses. Recently, PASI 90 and PASI 100 responses have become feasible treatment goals, and there is growing expectation among dermatologists about more effective and rapid therapies for the treatment of moderate-to-severe plaque psoriasis [23,24]. Ixekizumab is therefore emerging as a viable option in the Colombian market. However, CPR estimates are susceptible to changes in the market prices of therapies. Differences between first year and maintenance year results are produced by variation in how many doses are received during the induction period for each technology.

There are other similar studies in the literature. A study from the United State [11] shows that the treatments with the best CPR for PASI 75 and PASI 90 are infliximab, secukinumab, adalimumab, and ixekizumab. Another study from the United States found that the medications with the best CPR estimates were ustekinumab for PASI 75 and secukinumab and ixekizumab for PASI 90 [25]. In another study that considered head-to-head data from the phase 3 clinical studies of ixekizumab versus etanercept (UNCOVER 2 and UNCOVER 3), ixekizumab had a better CPR compared to etanercept in PASI 75, PASI 90, and PASI 100 [26]. The main limitation in comparing these results with those in the present study derives from differences in the sources of effectiveness and the costs of medicines, which can vary significantly between different countries. These differences arise from specificities of each country in terms of healthcare resource reimbursement, market dynamics and price regulation mechanism. Considering the importance that these costs have on final results, it becomes difficult to directly compare efficiency measures directly.

The main strength of this study is that the efficacy data were obtained from recent systematic reviews of the literature with meta-analyses, conducted using valid and accepted methods. However, the research on comparative effectiveness in plaque psoriasis is progressing rapidly with new clinical evidence being generated on existing therapies as well as those under development. CPR estimations are dependent on local costs. As such having a Colombian-specific estimation can be valuable since extrapolation from international studies can be difficult.

There are several limitations to consider. The first is related to NNT consistency. When considering the maintenance year period, NNT showed some differences between studies. Results were more similar when considering PASI 75 and bigger differences were estimated for PASI 90 and PASI 100. Data from Armstrong et al. 2020 [22] showed consistently narrower CrI than the other references. Both Yasmeen et al [18] and Armstrong et al. [22] developed a Bayesian multinomial probability model for PASI responses but the rank obtained for the NNT was different. In the model by Yasmeen et al, guselkumab was the option with the lowest NNT while in the model by Armstrong et al, it was ixekizumab. These differences occurred even when considering that they were all Bayesian meta-analyses. Possible explanations include characteristics of each meta-analysis (differences in model specification, primary study selection, details about data extraction from primary studies, handling of heterogeneity within primary studies) and differences in how we calculated NNT from extracted data (some were estimated from baseline risk and relative risks, while others were directly extracted from the meta-analyses). It is important to note that even when point estimates varied, most of the CrI/CI overlapped for each individual treatment across meta-analyses. Our results show a variety of point estimates and intervals for CPR, where both the inconsistency between studies and the precision for each one lead to a wide range of CPR. It is also important to note that the characteristics of the primary studies (population characteristics, study length, timing of outcome assessment) could also add heterogeneity in the estimations.

A further limitation is related to the baseline risk considered for the calculation of NNT. The placebo response rates vary considerably between individual clinical studies in plaque psoriasis because of differences in factors such as study design, eligibility criteria, duration or severity of the disease, and previous treatments that patients have receive [11,14,19,21,27,28]. This has two effects on our study. The first is related to the issue that primary studies with different baseline risks may produce different effect estimates for each intervention. When these data are pooled and analyzed in a network meta-analysis, it becomes a potential source of heterogeneity. In the most extreme cases, this may lead to violations in fundamental transitivity assumptions for network meta-analysis validity. The second issue stems from the fact that we are using baseline risk to estimate NNT from relative risks. Selection of different baseline risks leads to widely different NNT estimations. The rationale was to consider a parameter that has already been integrated into a health technology assessment from a reputable institution, rather than arbitrarily selecting one in this study.

Another limitation is that these NMAs only consider primary endpoint visits and not all visits. Thus, the benefits of faster response are not considered. Analyses that have examined cumulative benefits (area under the curve) may show different (better) CPR in terms of a cumulative benefit [29,30].

Other limitations stem from the simplifications and assumptions that are required in the model, such as an average weight for the whole cohort, that could impact weight-dependent drugs such as infliximab, and the lack of dose changes over time.

As a point of future research, it is interesting to mention the potential value of precision medicine for psoriasis patients and the efficiency of available treatments. On one hand, it would be possible to maximize positive results by preventing disease progression in a targeted way. On the other hand, it could also be possible to avoid or decrease unresponsiveness to treatments, reducing expenditure on futile treatments and time for impacting the disease.

Given the chronic nature of psoriasis and the importance of long-term effectiveness in a real-world clinical environment, it will be necessary to evaluate the relative effectiveness of therapies in the long term and the impact that this would have on the NNTs as well as the associated costs, offering a better understanding of the comparative effectiveness of biological therapies.

5. Conclusions

Comparative efficacy data on biologic therapies for psoriasis from published NMAs and Colombian biologic costs were used to calculate the cost per responder for each biologic treatment. When considering the first year and second year maintenance period, the treatment options that provide the lowest cost per responder were adalimumab, infliximab, ixekizumab, and guselkumab. Our study results may provide important comparative cost-efficiency information to physicians and third-party payers in Colombia.

Funding

NeuroEconomix received funding from Eli Lilly and Cmopany for this study.

Declaration of interest

P Lasalvia and Y Gil-Rojas were employees of NeuroEconomix. E Papadimitropoulos and R Burge were employees of Eli Lilly and Company when this research was conducted. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Author contributions

P Lasalvia and Y Gil-Rojas contributed to the conception of study cost estimation, data analysis, and drafting of the manuscript and final manuscript review. E Papadimitropoulos, R Burge and D Rosselli contributed to the conception of the study and final revision of the manuscript. All authors read and approved the final version of the manuscript to be published.

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