



# Healthcare Costs Among Patients with Psoriasis Treated with Ixekizumab Versus Secukinumab in Real-World Settings Over 24 Months

Andrew Blauvelt<sup>1</sup> · Nianwen Shi<sup>2</sup> · Russel Burge<sup>3,4</sup> · Bilal Atiya<sup>3</sup> · Baojin Zhu<sup>3</sup> · Najwa Somani<sup>3</sup> · Terri Ridenour<sup>3</sup> · Carolyn R. Lew<sup>2</sup> · Nicole M. Zimmerman<sup>2</sup> · Mwangi J. Murage<sup>3</sup>

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## Abstract

**Objective** The aim of this study was to compare healthcare costs between ixekizumab (IXE)-treated and secukinumab (SEC)-treated patients with psoriasis over a 24-month follow-up period in the United States.

**Methods** Patients with psoriasis diagnosis were identified from IBM Watson Health MarketScan<sup>®</sup> Research Databases; those with one or more claim for index drug (IXE or SEC) between March 1, 2016 and October 31, 2019 were included. Included patients were  $\geq 18$  years old and had continuous enrollment with medical and pharmacy benefits  $\geq 6$  months before and  $\geq 24$  months after index date. Patients were classified as IXE or SEC users based on drug received at index. Per patient per month (PPPM) all-cause, psoriasis-related, and index drug costs for IXE and SEC users were estimated over 24 months of follow-up. Institute for Clinical and Economic Review (ICER) discount factors were applied to adjust pharmacy costs. Index drug costs were additionally adjusted for adherence. Inverse probability of treatment weighting was used to address cohort imbalances. Chi-square/*t* tests were used to compare IXE versus SEC users; *p* value  $< 0.05$  was considered statistically significant.

**Results** Overall, 1461 patients (IXE users,  $n = 471$ ; SEC users,  $n = 990$ ) were included. IXE versus SEC users had higher weighted PPPM all-cause, psoriasis-related, and index drug costs ( $p \leq 0.001$ ). IXE versus SEC users had comparable ICER-adjusted mean PPPM all-cause costs (US\$4172  $\pm$  3349 vs US\$3978  $\pm$  2619;  $p = 0.227$ ) and psoriasis-related costs (US\$2950  $\pm$  1332 vs US\$2899  $\pm$  1152;  $p = 0.447$ ). After applying ICER and adherence adjustments, index drug costs were similar between IXE and SEC users (US\$3794  $\pm$  1822 vs US\$3766  $\pm$  1973;  $p = 0.795$ ).

**Conclusions** All-cause and psoriasis-related costs were comparable between IXE and SEC users after ICER adjustments; index drug costs were similar after ICER and adherence adjustments.

## 1 Introduction

Psoriasis is a chronic inflammatory skin disease that affects 7.4 million adults in the United States (US) [1]. The disease substantially impairs patient quality of life and work

✉ Mwangi J. Murage  
murage\_mwangi\_james@lilly.com

<sup>1</sup> Oregon Medical Research Center, Portland, OR, USA

<sup>2</sup> IBM Watson Health, Cambridge, MA, USA

<sup>3</sup> Value, Evidence, and Outcomes (VEO), Eli Lilly and Company, LCT-South Building 171-2, Drop Code 5221, 1555 Harding St., Indianapolis, IN 46221, USA

<sup>4</sup> University of Cincinnati, Cincinnati, OH, USA

### Key Points for Decision Makers

This study compared longer-term (24 months) treatment costs of ixekizumab and secukinumab among psoriasis patients.

Real-world treatment costs of biologics for psoriasis are affected by discounts and medication adherence; hence, both factors should be considered when comparing costs across treatment groups.

All-cause and psoriasis-related costs were comparable between ixekizumab and secukinumab users after adjusting by discount factors published by the Institute for Clinical and Economic Review (ICER).

productivity [2], and imposes a significant economic burden [3]. Psoriasis is also commonly associated with multiple comorbidities [4] that incur incremental direct healthcare costs and indirect costs due to productivity loss [5]. The economic burden of psoriasis in the US in 2013 was estimated to be US\$112 billion and increased with disease severity; of this, approximately US\$51.7 billion was attributable to direct costs [6]. Utilization of pharmaceuticals, including highly efficacious biologic therapies, is the primary driving component of overall healthcare costs in psoriasis [7].

Recommended treatments for psoriasis include topical therapies, phototherapy, non-biologic systemic agents, and biologic therapies [8, 9]. Treatments for moderate-to-severe psoriasis have evolved over recent decades with the introduction of targeted biologic therapies [10]. Ixekizumab (IXE) and secukinumab (SEC) are monoclonal antibodies that target interleukin 17A (IL-17A), a key cytokine in psoriasis pathogenesis, and are approved for the treatment of psoriasis [11, 12]. IXE and SEC have shown high levels of efficacy in clinical trials, but data on their direct comparison of healthcare costs are limited. In a prior real-world study, psoriasis-related costs between IXE and SEC users were reported to be similar after adjusting for nationally representative price discounts published by the Institute for Clinical and Economic Review (ICER) [13]. While the study provided evidence on the comparison of costs of both IL-17A inhibitors (IXE vs SEC) for a follow-up period of 12 months, longer term follow-up costs were not examined. Long-term costs are important to assess given that psoriasis is a chronic condition often requiring life-long treatment. Also, IXE has been approved for over 2 years, hence a 24-month follow-up study is essential. Using a methodology similar to the Blauvelt et al. study [13], here we compared real-world healthcare costs of IXE and SEC in treating psoriasis during a 24-month follow-up period.

## 2 Methods

### 2.1 Study Design and Data Source

This retrospective observational study utilized health insurance claims data to characterize adult patients with psoriasis in the US who were treated with IXE or SEC with respect to healthcare cost comparisons. The study period was from March 1, 2015 to October 31, 2019 and included a 6-month pre-index period and a 24-month post-index period (Online resource Fig. S1, see electronic supplementary material [ESM]).

Data were extracted from three IBM Watson Health® MarketScan® Research Databases: MarketScan Commercial Database, MarketScan Medicare Supplemental Database, and MarketScan Monthly Early View Database. All three databases provide detailed information on healthcare

utilization and medication use over time. The MarketScan Commercial Database contains the standardized inpatient, outpatient, pharmaceutical, and health plan enrollment data of employees and their dependents who are covered by employer-sponsored private health insurance in the US. The Medicare Supplemental Database contains the same information for retirees with Medicare supplemental insurance paid for by employers. The MarketScan Monthly Early View Database also includes these same components; however, monthly releases of this database capture healthcare services incurred as late as approximately 60 days before data release.

All database records used in the study are de-identified and fully compliant with the US Health Insurance Portability and Accountability Act of 1996. This study was exempted from Institutional Review Board approval as it did not involve collection, use, or transmittal of individually identifiable data.

### 2.2 Patient Selection

Patients with at least one inpatient or two non-diagnostic outpatient claims ( $\geq 30$  days apart) for psoriasis (International Classification of Diseases, Ninth/Tenth Revisions, Clinical Modification: ICD-9-CM diagnosis code 696.1x or ICD-10-CM diagnosis codes L40.0–L40.4 or L40.8–L40.9) between March 1, 2015 and October 31, 2019 were identified. Patients with one or more claim for the index drug (IXE or SEC) between March 1, 2016 and October 31, 2019 on or after a psoriasis diagnosis were included. The date of the first IXE or SEC claim was the index date and patients were classified as IXE or SEC users, based on the drug received at index.

Patients were required to be  $\geq 18$  years of age at the index date and have continuous enrollment with medical and pharmacy benefits  $\geq 6$  months before and  $\geq 24$  months starting from the index date. Patients were excluded if they had diagnoses of non-psoriasis indications in the pre-index period for which the index drugs were approved (psoriatic arthritis for IXE/SEC; ankylosing spondylitis for SEC). Those with index drug claims within 90 days before the index date were also excluded.

### 2.3 Healthcare Costs (Unadjusted)

All-cause direct healthcare costs, psoriasis-related direct healthcare costs, and index drug costs for IXE and SEC users were estimated over a 24-month follow-up. Psoriasis-related costs were defined as costs recorded on inpatient claims with a primary diagnosis for psoriasis or outpatient claims with a psoriasis diagnosis in any position, or for medication treatment specifically for psoriasis. Costs were reported for total as well as for inpatient services, outpatient services, and outpatient pharmacy. Healthcare costs were based on paid

amounts of adjudicated claims, including insurer and health plan payments as well as patient cost-sharing (co-payment, deductible, and coinsurance). Costs for services provided under capitated arrangements were estimated using payment proxies based on paid claims at the procedure level using the MarketScan Commercial and Medicare Supplemental Databases. All dollar estimates were adjusted to 2019 dollars using the Medical Care Component of the Consumer Price Index. All costs were reported as per patient per month (PPPM).

## 2.4 Healthcare Cost Adjustments: ICER-Adjusted and ICER-Adherence-Adjusted Costs

Healthcare costs reported from insurance claims may not consistently capture discounts like pharmacy rebates, patient assistance programs, and commissions to wholesale. Thus, published (2018) ICER discount factors (based on net price divided by wholesale acquisition cost) were applied to index drugs (IXE and SEC) and other psoriasis biologic drug costs to adjust pharmacy costs (i.e., drug costs  $\times$  [1-ICER discount factor]) in order to obtain the adjusted all-cause and adjusted psoriasis-related costs. ICER discount rates of 0.44 and 0.38 were applied to IXE and SEC, respectively [14]. For other biologics, ICER discount factors were applied as follows: 0.31/adalimumab, 0.20/brodalumab, 0.36/certolizumab, 0.31/etanercept, 0.33/guselkumab, 0.22/infliximab, and 0.27/ustekinumab. Adjusted all-cause and adjusted psoriasis-related costs were obtained by combining the following: (1) index drug costs adjusted by ICER discount factors (ICER-adjusted); (2) ICER-adjusted other psoriasis-related biologic costs; and (3) all-cause or psoriasis-related healthcare costs, excluding psoriasis-specific biologics costs. Quarterly ICER-adjusted all-cause costs, psoriasis-related costs, and index drug costs during the follow-up period were also reported. We further performed sensitivity analyses by varying the index drug discount rates by  $\pm 5\%$ , estimating mean cost differences in ICER-adjusted all-cause costs and psoriasis-related costs.

Post-period index drug costs are impacted by treatment adherence as higher adherence leads to greater consumption of medication. Thus, for ICER-adjusted index drug costs, additional adjustment by adherence was performed (by dividing the ICER-adjusted index drug costs by treatment adherence for each cohort) to obtain ICER-adherence-adjusted index drug costs. The adjusted costs represent the index drug costs when the patients are fully adherent to treatment over a 24-month period. Adherence, measured as the proportion of days covered (PDC), was defined as the number of days with medication on hand during the 24-month follow-up period for each cohort divided by 730. When two prescriptions had overlapping days' supply, to avoid double counting, the start date of the second script was adjusted to the date after the end of the prior script.

## 2.5 Covariates

Demographic characteristics were measured at index date and included age, gender, geographic region, payer, and health plan type. Clinical characteristics were measured in the pre-index period and included Deyo Charlson Comorbidity Index (DCCI) and comorbid diseases (anxiety, coronary heart disease, depression, diabetes mellitus, hyperlipidemia, hypertension, obesity, osteoarthritis, other autoimmune disorders, and sleep apnea). Pre-period psoriasis-related medication use such as biologic use (adalimumab, brodalumab, certolizumab, etanercept, guselkumab, infliximab, IXE, SEC, or ustekinumab); systemic agents/targeted oral therapies (apremilast, acitretin, systemic steroids, cyclosporine, methotrexate, azathioprine, hydroxyurea, isotretinoin, leflunomide, methoxsalen, mycophenolate mofetil, sulfasalazine, or thioguanine); topical treatments; and phototherapy were also included. Other covariates were pre-period psoriasis-related costs and comorbidity-related costs.

## 2.6 Statistical Analyses

Descriptive statistics were reported for the comparison of IXE versus SEC; categorical variables were presented as percentages and continuous variables were summarized by means and standard deviations. To address cohort imbalances, inverse probability of treatment weighting (IPTW) was calculated from a logistic regression model with IXE versus SEC as the dependent variable. Covariates in IPTW included all variables listed in the *Covariates* section. Standardized difference (Std Diff)  $\leq 10$  between the cohorts indicated a good balance. All cost data reported were weighted via IPTW.

Statistical tests of significance for comparison of weighted values were as follows: weighted *t* tests (for continuous variables); weighted Chi-square tests (for binary or categorical variables). An a priori *p* value of  $<0.05$  was considered statistically significant. All descriptive analyses were conducted using WPS Analytics, version 4.02 (World Programming, United Kingdom). IPTW model was generated with R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

## 3 Results

### 3.1 Demographics and Clinical Characteristics

Among the 261,539 patients diagnosed with psoriasis, 1461 patients (IXE users,  $n = 471$ ; SEC users,  $n = 990$ ) were included in the study (Fig. 1). Demographic and clinical characteristics are summarized in Table 1. Before weighting, most of the baseline demographics and clinical

characteristics were similar between IXE and SEC groups. The mean age was 48.1 years in the IXE group and 48.2 years in the SEC group; 55.0% and 52.7% were male in the IXE and SEC groups, respectively. Most patients were commercially insured in both groups.

Before weighting, the pre-index DCCI was comparable between IXE and SEC users (0.3 vs 0.4, Std Diff 9.6). For IXE and SEC users, the most common comorbidities were hypertension (25.1% vs 28.2%, Std Diff 7.1), hyperlipidemia (21.0% vs 20.4%, Std Diff 1.5), and obesity (16.8% vs 17.2%, Std Diff 1.1). Pre-index biologic use was similar between IXE and SEC users (55.4% vs 54.7%, Std Diff 1.3). Both pre-index all-cause costs (US\$3352 vs US\$3201, Std Diff 4.5) and psoriasis-related healthcare costs (US\$2434 vs US\$2300, Std Diff 6.0) were comparable between the two groups. All baseline demographic and

clinical characteristics were well balanced after weighting between the IXE and SEC groups.

### 3.2 Unadjusted Healthcare Costs

After weighting, mean  $\pm$  SD PPPM all-cause healthcare costs during the 24-month follow-up period were higher in IXE users (US\$6183  $\pm$  US\$3614) than SEC users (US\$5612  $\pm$  US\$2926;  $p = 0.001$ ) with an average duration of treatment of 453 days among IXE users and 420 days among SEC users. Healthcare plan cost was the major contributor towards higher cost among IXE users (US\$5875  $\pm$  US\$3591) than SEC users (US\$5335  $\pm$  US\$2897;  $p = 0.002$ ); patient out-of-pocket expense was similar among IXE (US\$308  $\pm$  US\$364) and SEC (US\$276  $\pm$  US\$314) users. Psoriasis-related costs were higher in IXE

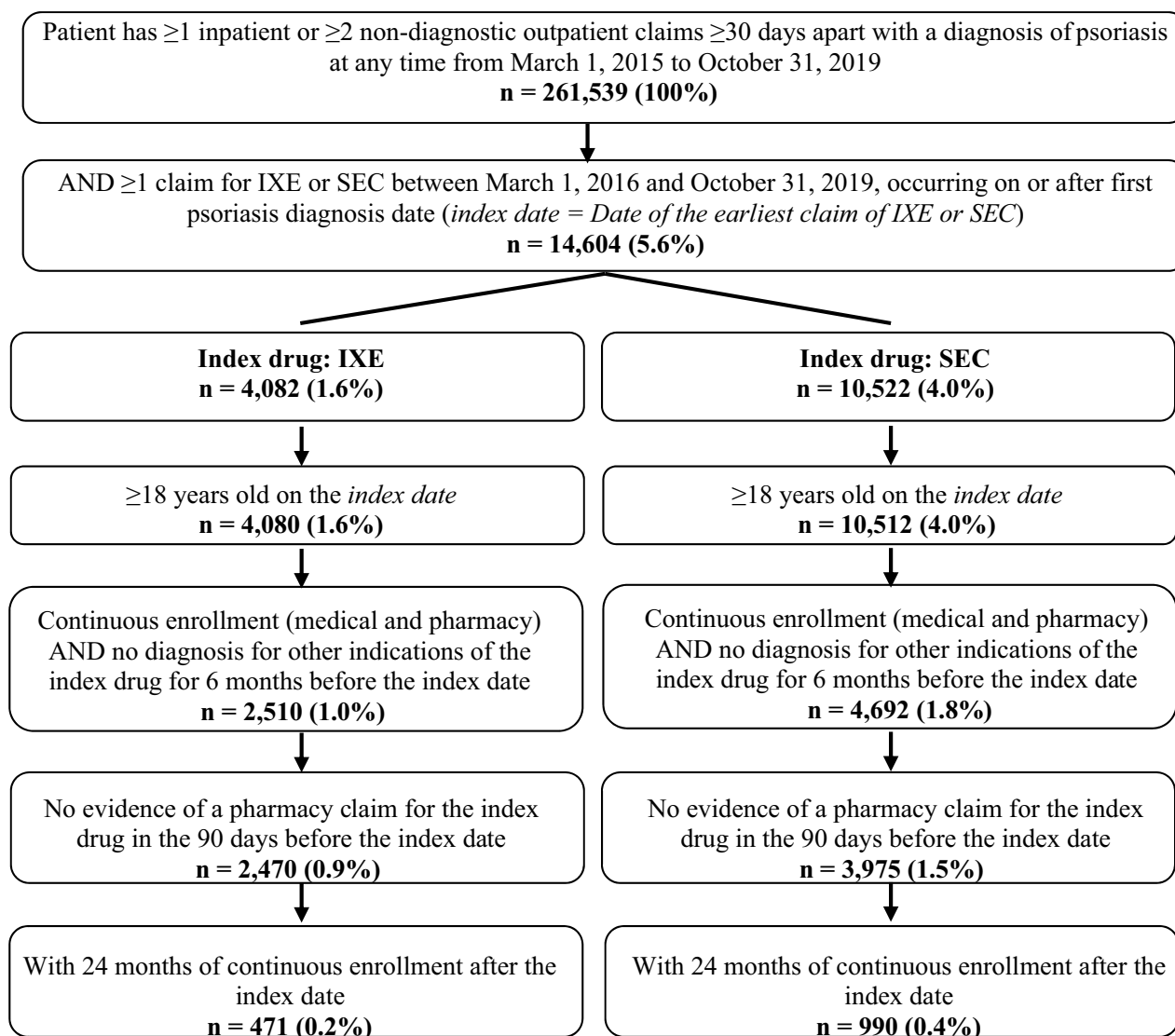


Fig. 1 Patient attrition flow chart. IXE ixekizumab, SEC secukinumab

**Table 1** Baseline demographic (demographic characteristics were measured on the index date) and clinical (clinical characteristics were measured during the 6-month pre-index period) characteristics before and after weighting

Variable	Before weighting			After weighting		
	IXE ( <i>n</i> = 471)	SEC ( <i>n</i> = 990)	Std. diff. <sup>a</sup>	IXE	SEC	Std. diff. <sup>a</sup>
Age, mean (SD)	48.1 (10.8)	48.2 (11.4)	0.7	48.0 (11.1)	48.1 (11.3)	0.9
Gender, (male), %	55.0	52.7	4.5	53.8	53.5	0.6
<i>Primary payer, %</i>						
Commercial	96.8	95.9	5.1	96.4	96.2	1.0
Medicare	3.2	4.1		3.6	3.8	
<i>Plan type, %</i>						
Comprehensive/indemnity	2.1	3.3	21.9	2.7	2.9	8.7
EPO/PPO	62.2	57.4		60.1	58.7	
POS/POS with capitation	4.2	4.9		4.4	4.7	
HMO	7.9	13.1		11.3	11.4	
CDHP, HDHP	22.9	19.8		20.8	20.8	
Other/unknown	0.6	1.4		0.6	1.5	
<i>Region, %</i>						
Northeast	16.3	17.6	9.9	17.0	17.1	2.6
North Central	22.3	21.2		21.6	21.6	
South	50.5	47.6		49.0	48.6	
West	10.6	13.4		12.0	12.5	
Unknown	0.2	0.2		0.3	0.2	
Pre-index Deyo Charlson Comorbidity Index (mean, SD)	0.3 (0.9)	0.4 (1.0)	9.6	0.4 (1.0)	0.4 (0.9)	0.5
<i>Pre-index comorbidities, %</i>						
Anxiety	6.4	9.1	10.2	7.8	8.2	1.4
Coronary heart disease	1.9	4.0	12.6	2.9	3.3	2.3
Depression	6.6	7.5	3.5	7.1	7.2	0.1
Diabetes	14.4	14.6	0.6	14.1	14.5	1.3
Hyperlipidemia	21.0	20.4	1.5	19.8	20.5	1.7
Hypertension	25.1	28.2	7.1	26.5	27.0	1.2
Obesity	16.8	17.2	1.1	16.9	17.1	0.5
Other autoimmune disorders	3.6	4.2	3.3	3.8	4.0	1.0
Sleep apnea	9.1	8.9	0.8	9.0	9.0	0.2
<i>Pre-index treatments, %</i>						
Biologics	55.4	54.7	1.3	54.9	54.9	0.0
Systemic agents/targeted oral therapies	41.2	42.2	2.1	41.8	41.9	0.2
Topical agents	59.4	60.3	1.7	59.4	59.9	1.0
Phototherapy or laser treatments	4.2	2.8	n/a	3.5	3.3	n/a
Pre-index all-cause healthcare costs <sup>b</sup> , USD (mean, SD)	3352 (3371)	3201 (3299)	4.5	3343 (3408)	3173 (3192)	5.1
Pre-index psoriasis-related healthcare costs <sup>b</sup> , USD (mean, SD)	2434 (2272)	2300 (2161)	6.0	2394 (2275)	2315 (2164)	3.6

CDHP consumer-driven health plan, EPO exclusive provider organization, HDHP high deductible health plan, HMO health maintenance organization, IXE ixekizumab, POS point of service, PPO preferred provider organization, PPPM per patient per month, SD standard deviation, SEC secukinumab, Std. diff. standardized difference, USD United States dollars

<sup>a</sup>A standardized difference of  $\leq 10$  is considered well balanced

<sup>b</sup>Reported PPPM

users (US\$4961  $\pm$  US\$1989) than SEC users (US\$4532  $\pm$  US\$1772;  $p < 0.001$ ) (Figs. 2, 3). Outpatient pharmacy costs comprised 82.9% and 84.2% of all-cause costs and 97.9% and 98.3% of psoriasis-related costs for IXE and

SEC users, respectively (Fig. 2). The monthly index drug costs were higher in IXE users than SEC users (US\$3990  $\pm$  US\$1917 vs US\$3394  $\pm$  US\$1778;  $p < 0.001$ ) (Fig. 4).

### 3.3 ICER-Adjusted All-Cause and Psoriasis-Related Costs

After ICER adjustment, mean PPPM all-cause costs (US\$4172 ± US\$3349 vs US\$3978 ± US\$2619; *p* = 0.227) and psoriasis-related costs (US\$2950 ± US\$1332 vs US\$2899 ± US\$1152; *p* = 0.447) were comparable between IXE and SEC users (Fig. 3).

ICER-adjusted mean all-cause healthcare costs accrued by IXE and SEC users declined after the first quarter and did not fluctuate considerably in the subsequent quarters (Online resource Fig. S2, see ESM). A similar pattern was observed with ICER-adjusted psoriasis-related and index drug costs (Online resource Fig. S3 and Fig. S4, see ESM).

In the sensitivity analyses, by varying the ICER discount factors by ±5%, no significant differences in mean all-cause ICER-adjusted costs were observed between IXE and SEC users. For psoriasis-related costs, highest IXE and lowest SEC ICER discounts (0.46 vs 0.36, respectively) resulted in −US\$84 (*p* value: non-significant) for IXE versus SEC, while lowest IXE and highest SEC ICER discounts (0.42 vs 0.40, respectively) led to +US\$188 (*p* < 0.05) for IXE versus SEC (Online resource Table S1, see ESM).

### 3.4 ICER- and Adherence-Adjusted Index Drug Costs

ICER-adjusted mean PPPM index drug costs were higher for IXE users (US\$2235 ± US\$1073) than SEC users (US\$2104 ± US\$1103; *p* = 0.033, Fig. 4). Mean adherence during follow-up was similar for IXE versus SEC

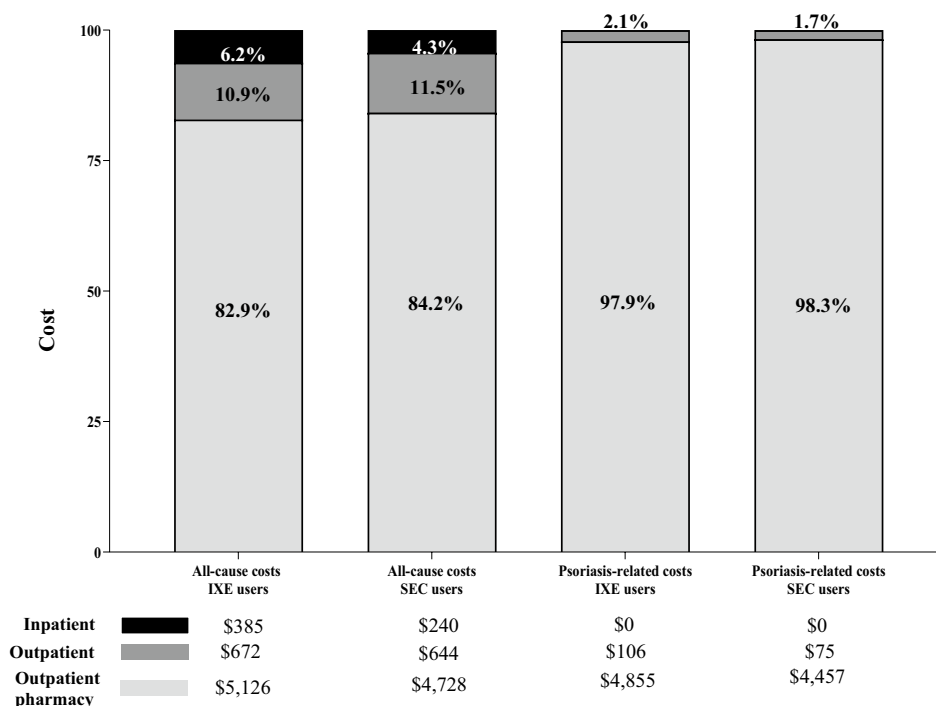
(PDC, 0.58 vs 0.55; *p* = 0.092). However, more IXE users than SEC users (39.1% vs 31.6%; *p* = 0.005) were highly adherent (PDC ≥ 80%). After applying ICER and adherence adjustments, mean PPPM index drug costs were similar between IXE and SEC users (US\$3794 ± US\$1822 vs US\$3766 ± US\$1973; *p* = 0.795, Fig. 4).

## 4 Discussion

In this retrospective claims-based study, we compared healthcare costs of patients with psoriasis treated with IXE or SEC over a 24-month follow-up period. Although the mean unadjusted PPPM all-cause, psoriasis-related, and index drug costs were higher for IXE users than SEC users, these costs were similar after adjusting for payer discounts and adherence to drug.

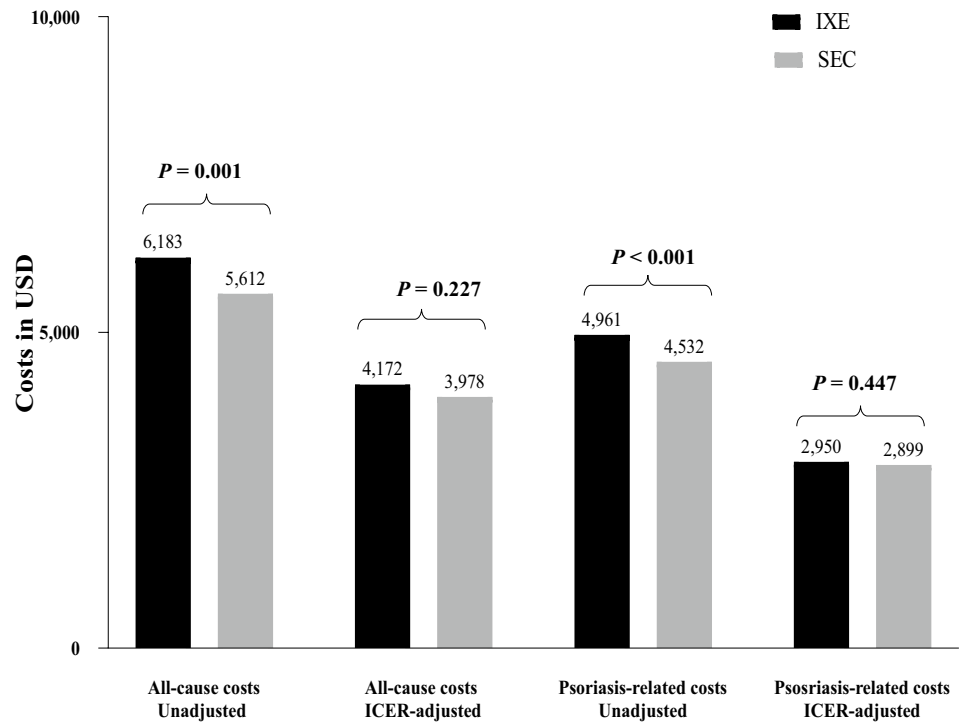
The unadjusted PPPM all-cause, psoriasis-related, and index drug costs for both IXE and SEC users reported in the current study with a 24-month follow-up period were lower than that reported in a previous study by Blauvelt et al. with a 12-month follow-up period [13]. In the previous study, the unadjusted PPPM costs for IXE versus SEC users, respectively, were as follows: all-cause costs, US\$7313 versus US\$6477; psoriasis-related costs, US\$6303 versus US\$5437; and index drug costs, US\$5613 versus US\$4626 [13]. However, the trend was similar to the current study, with the unadjusted costs being higher in IXE users than SEC users. Similarly, another study with a variable follow-up period (average: 7.5 months) reported higher unadjusted

**Fig. 2** Stratified weighted all-cause and psoriasis-related healthcare costs (PPPM): unadjusted. Cost is calculated in USD. Total all-cause costs (mean ± SD): IXE users = US\$6183 ± 3614 and SEC users = US\$5612 ± 2926. Psoriasis-related costs: IXE users = US\$4961 ± 1989 and SEC users = US\$4532 ± 1772. IXE ixekizumab, PPPM per patient per month, SD standard deviation, SEC secukinumab, USD United States dollars

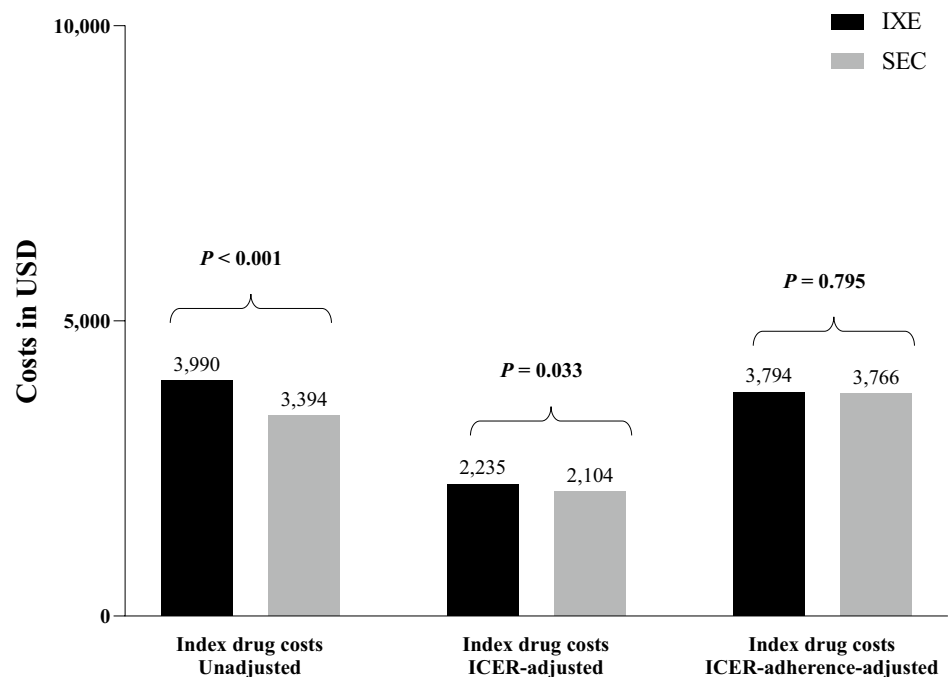




**Fig. 3** Weighted all-cause and psoriasis-related healthcare costs (PPPM): unadjusted and ICER-adjusted. Cost is calculated in USD. *P*-Values are from t-test for continuous variables. ICER Institute for Clinical and Economic Review, IXE ixekizumab, PPPM per patient per month, SEC secukinumab, USD United States dollars



**Fig. 4** Weighted index drug costs (PPPM): unadjusted, ICER-adjusted and ICER-adherence-adjusted. Cost is calculated in USD. *p* values are from t-test for continuous variables. ICER Institute for Clinical and Economic Review, IXE ixekizumab, PPPM per patient per month, SEC secukinumab, USD United States dollars



PPPM all-cause costs (US\$8371) and psoriasis-related costs (US\$7612) for IXE users [15] compared with the current study (all-cause: US\$6183; psoriasis-related: US\$4961). The lower unadjusted index drug, psoriasis-related, and all-cause costs in the current study (vs previous studies [13, 15]) could be attributed to the longer follow-up period or

other factors like different treatment adherence level. The 2018 ICER report on targeted immunomodulators for the treatment of moderate-to-severe psoriasis also suggested a similar trend of average costs decline for IXE (year 1: US\$51,374 vs year 2+: US\$37,685) [14]. Specifically, the shorter time frames in other studies could have led to higher

average costs per patient due to the ‘front loading’ of the dosing (induction period). The average costs decline over time as more observed therapies occur under the maintenance dosing (every 4 weeks).

Similar to previous reports on psoriasis costs, pharmacy cost in the current study was the preponderant healthcare cost that accounted for > 80% of all-cause and > 95% of psoriasis-related costs, regardless of the treatment [7, 13, 15]. In a claims-based study in patients with psoriasis using IXE, a majority of the pharmacy costs were reported to be covered by health plans, with < 4% of costs being borne by patients as out-of-pocket expenses [15]. This reduces the economic burden on patients, which is an important factor considering the high cost of the biologics compared with traditional systemic medications [6].

Costs recorded on insurance claims may not always account for discounts (e.g., pharmacy rebates, patient assistance programs, commissions to wholesale) and may overestimate pharmacy costs. This may also lead to biased estimates of cost difference between drugs if the discount factors are not similar. Thus, it is important to adjust pharmacy costs to account for discounts not captured in claims. Since the information on drug discounts are usually confidential, we used the discount factors published by ICER. In the current study, after applying ICER adjustments to the index drug costs, the difference in mean monthly index drug costs between IXE and SEC users declined from US\$596 (US\$3990 vs US\$3394) to US\$131 (US\$2235 vs US\$2104). The mean PPPM all-cause costs were comparable between IXE and SEC users after applying ICER adjustments. Furthermore, ICER-adjusted mean PPPM psoriasis-related costs in our study were comparable between IXE and SEC users (US\$2950 vs US\$2899;  $p = 0.447$ ), similar to the findings from a previous study over a 12-month follow-up (US\$3637 vs US\$3443;  $p = 0.132$ ) [13]. These data, showing comparable healthcare costs between IXE and SEC users, could help guide clinicians regarding the choice of biologic therapy.

ICER-adjusted healthcare costs for IXE and SEC users were high in the first quarter of the follow-up period, likely due to the higher number of doses required in the induction period as mentioned previously. The costs dropped substantially after the first 3 months and did not fluctuate considerably. The difference in ICER-adjusted index drug costs incurred by IXE and SEC users declined from US\$655 in the first quarter (US\$6097 vs US\$5442) to US\$86 in the second quarter (US\$2208 vs US\$2122). Furthermore, in the current study, sensitivity analyses generally agreed with the main analysis that the ICER-adjusted all-cause and psoriasis-related costs were similar between IXE and SEC.

In real-world settings, adherence plays an important role in comparing cost effectiveness of interventions [16]. Adherence to medications in psoriasis is poor [17, 18]. Costs are impacted by adherence as higher adherence leads to greater

consumption of medication; it is thus important to adjust for adherence while comparing costs of interventions. In line with a previous report with a follow-up period of 14–16 months, more IXE users than SEC users were highly adherent (PDC  $\geq 80\%$ ) in our study [19]. After adjusting for both ICER discounts and adherence, differences in mean index drug costs PPPM between IXE and SEC users declined from US\$596 (US\$3990 vs US\$3394) to US\$28 (US\$3794 vs US\$3766). This highlights the added benefits of higher treatment adherence among IXE users as both treatments are equally expensive and no significant differences in ICER-adjusted all-cause and psoriasis-related costs between IXE and SEC were observed [20, 21].

Biologic therapies have shifted the treatment paradigm of psoriasis; however, some patients receiving biologics have an inadequate response to therapy or loss of efficacy over time [22]. Given the similar costs observed between IXE and SEC after ICER and adherence adjustments, other outcomes (benefits) are important to understand the relative value of these therapies. Some measures include quality-adjusted life-years (QALYs), patient-reported outcomes (e.g., itch, Dermatology Quality Life Index), and cumulative time in better skin clearance levels (e.g., Psoriasis Area and Severity Index [PASI] 75, PASI 90). The ICER 2018 report projected that over 10 years, the total cost of treatment with IXE versus SEC would be US\$311,000 versus US\$305,000, with total QALYs being 7.42 versus 7.34, respectively, and the time spent in PASI 90+ health state being 70.9 months versus 63.5 months, respectively [14]. A number of studies have compared the cost effectiveness of biologics available for psoriasis treatment [22, 23]. A recent cost-effectiveness analysis reported that IXE provided more QALYs at lower costs than SEC for treating patients with psoriasis in Spain [22]. In addition, a recent network meta-analysis evaluating the cost efficacy of US Food and Drug Administration-approved biologics (IXE, SEC, ustekinumab, adalimumab, and etanercept) reported that IXE was the most cost-effective biologic in the US to achieve complete resolution (PASI 100) [23].

In summary, our current study and prior publication [13] add real-world evidence that there were no significant differences in general healthcare costs, psoriasis-related costs, and costs of IXE versus SEC between patients treated with IXE and SEC over 12 and 24 months. These findings will be important for clinicians to understand the cost effectiveness of approved biologics for the treatment of moderate-to-severe psoriasis.

#### 4.1 Limitations

Some limitations should be considered when interpreting the data from this study. Firstly, there was potential for



inaccurate coding or omissions and lack of clinical details from the medical claims that may have influenced the treatment used. Secondly, claims data may not accurately capture real drug transaction prices such as discounts and patient assistance programs. This was rectified to some extent by applying discounts from a comprehensive analysis performed by ICER. Underestimation or overestimation, however, may occur due to several reasons. 2018 ICER discount factors were used to adjust costs for 2016–2019. Adjustment by ICER discount factors may lead to double-discounting if these discounts are captured in claims payments. Thirdly, IPTW was employed to address observable imbalances between patient cohorts, yet not all relevant covariates, such as psoriasis severity, are captured in claims data. Fourthly, while the Early View Database (used to capture the most recent utilization of study drugs) contains fully adjudicated claims, the medical component of care for some patients may not have been complete as some claims (especially inpatient) take longer to be paid; consequently, healthcare costs were underestimated. Finally, results may not be generalizable to those without commercial or private Medicare supplemental coverage.

## 5 Conclusions

Based on real-world data, this retrospective analysis showed that all-cause, psoriasis-related, and index drug costs were higher in IXE users than SEC users before ICER adjustments. However, after applying ICER adjustments, all-cause and psoriasis-related costs were comparable between IXE and SEC users over 24 months. Index drug costs were similar between IXE and SEC users over 24 months after taking ICER discounts and treatment adherence into consideration. These results may inform clinicians when making decisions regarding biologic treatment for their patients with psoriasis. Future studies assessing healthcare costs, psoriasis-related costs, and implications of treatment patterns among subgroups of psoriasis patients, including those with challenging-to-treat body areas, are required to understand cost experiences of different psoriasis manifestations.

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## Declarations

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**Conflict of interest** Andrew Blauvelt has served as a scientific adviser/ received honoraria from AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, EcoR1, Eli Lilly and Company, Evomune, Forte, Galderma, Incyte, Janssen, Landos, Leo, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, UCB Pharma, and Vibliome; has acted as a clinical study investigator/institution has received clinical study funds from AbbVie, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte, Janssen, Leo, Novartis, Pfizer, Regeneron, Sun Pharma, and UCB Pharma. Nianwen Shi, Carolyn R. Lew, and Nicole M. Zimmerman are employees of IBM Watson Health, which was compensated by Eli Lilly and Company for conducting this research. Russel Burge, Bilal Atiya, Baojin Zhu, Najwa Somani, Terri Ridenour, and Mwangi Murage are full-time employees and/or minor stockholders of Eli Lilly and Company.

**Data availability** The datasets and codes used for the analyses in the current study are not publicly available due to proprietary reasons. However, IBM MarketScan<sup>®</sup> Research Databases from IBM Watson Health, USA, are available with a licensing fee.

**Author contributions** Nianwen Shi, Russel Burge, Terri Ridenour, and Mwangi Murage contributed to the study conception or design. All authors contributed to acquisition, analysis, or interpretation of data. All authors critically revised the manuscript for important intellectual content. All authors provided final approval of the version to be published and agree to be accountable for all aspects of the work.

**Ethics approval** All database records used in the study are de-identified and fully compliant with the US Health Insurance Portability and Accountability Act of 1996. This study was exempted from Institutional Review Board approval as it did not involve collection, use, or transmittal of individually identifiable data.

**Consent to participate** Not applicable.

**Consent for publication** Not applicable.

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