Comparison of Health Care Costs Among Patients with Psoriasis Initiating Ixekizumab, Secukinumab, or Adalimumab

Andrew Blauvelt, MD, MBA; Nianwen Shi, PhD; Baojin Zhu, PhD; Russel Burge, PhD; William N. Malatestinic, PharmD, MBA; Chen-Yen Lin, PhD; Carolyn R. Lew, PhD; Nicole M. Zimmerman, MS; Orin M. Goldblum, MD; and Mwangi J. Murage, PhD, MPH

ABSTRACT

BACKGROUND: As more biologics become available for the treatment of psoriasis (PsO), there is a lack of direct comparisons of health care costs between patients who are treated by different medications, including ixekizumab (IXE), secukinumab (SEC), and adalimumab (ADA).

OBJECTIVE: To compare the real-world health care costs of patients with PsO initiating IXE with those of patients initiating either SEC or ADA.

METHODS: Patients diagnosed with PsO between July 1, 2015, and May 31, 2018, were identified from the IBM MarketScan commercial and Medicare databases. Two weighted patient sample sets were constructed based on drug claims between March 1, 2016, and May 31, 2018: IXE versus SEC and IXE versus ADA. Within each sample, the first claim of eligible drugs was set as the index date. Patients were aged ≥ 18 years and had ≥ 12 months of continuous eligibility before and after the index date. Patients with other indications for the index drug in the preperiod or with use of the index drug within 90 days before the index date were excluded. Inverse probability of treatment weighting (IPTW) was employed to balance cohorts. All-cause and PsO-related health care costs per member per month (PMPM) incurred during the 12-month follow-up period were assessed. Monthly PsO-related pharmacy costs were adjusted using drug discount rates published by the Institute for Clinical and Economic Review (ICER). Annual index drug costs were estimated by adjusting for medication possession ratio and ICER discount rates. All costs were weighted by IPTW.

RESULTS: Two study samples were identified: 357 IXE users were compared with 763 SEC users, and 388 IXE users were separately compared with 2,578 ADA users. Before weighting, IXE users were demographically and clinically similar to SEC users but were older and had worse health status than ADA users. Cohorts were balanced postweighting. After weighting, mean monthly all-cause health care costs were \$7,313 and \$6,477 ($P=0.002$) and mean PsO-related costs were \$6,303 and \$5,437 ($P<0.001$), for IXE and SEC users, respectively. Similarly, mean monthly all-cause health care costs were \$6,535 and \$5,557 ($P=0.026$) and mean PsO-related costs were \$5,792 and \$4,754 ($P=0.017$), for IXE and ADA users, respectively. After applying ICER adjustments, mean monthly PsO-related costs were comparable between groups: \$3,637/IXE versus \$3,443/SEC ($P=0.132$) and \$3,320/IXE versus \$3,287/ADA ($P=0.907$).

CONCLUSIONS: After adjusting for drug discount programs (through application of ICER discount rate), this real-world study estimated that average monthly PsO-related costs during the first year of treatment were similar between patients treated with IXE compared with those treated with SEC or ADA.

J Manag Care Spec Pharm. 2019;25(12):1366-76

Copyright © 2019, Academy of Managed Care Pharmacy. All rights reserved.

What is already known about this subject

- High drug acquisition costs are the primary driver of direct health care costs among patients with moderate to severe psoriasis (PsO).
- Cost-effectiveness has previously been calculated for the established biologics adalimumab (ADA) and secukinumab (SEC).

What this study adds

- After adjusting for drug discount programs, mean monthly PsO-related costs were similar between patients initiating ixekizumab (IXE) and patients initiating ADA and SEC.
- Study data do not support presumed differences in costs that are used to promote step therapy protocols for IXE, SEC, and ADA.

Psoriasis (PsO) is a chronic inflammatory disease that places a heavy physical and psychosocial burden on patients, which leads to high health care utilization and reduced work productivity.¹⁻³ The resulting economic burden in the United States was estimated in 2013 at \$51.7-\$63.2 billion in direct costs for PsO, \$36.4 billion in direct costs for comorbidities, and \$23.9-\$35.4 billion in indirect costs due to presenteeism, absenteeism, and unemployment.¹ At a per person level, health care costs are substantially higher for patients with moderate to severe disease compared with mild PsO, even when pharmacy costs are excluded.^{4,5}

Moderate to severe PsO is managed with systemic therapy, commonly with biologics that target tumor necrosis factor alpha (TNF- α) or interleukin (IL)-17A.^{6,7} Although real-world health care cost data exist for PsO patients on older TNF- α inhibitors, such as adalimumab (ADA),⁸ similar data do not exist for the newer IL-17A inhibitors, ixekizumab (IXE) and secukinumab (SEC), which were approved by the U.S. Food and Drug Administration in March 2016 and January 2015, respectively. To fill this gap, we compared the real-world health care costs of PsO patients initiating IXE to those of patients initiating either SEC or ADA.

Methods

Data Source

This analysis used administrative claims data, spanning the period from July 1, 2015, to May 31, 2018, from 3 IBM

Watson Health MarketScan Databases: the Commercial Claims and Encounters Database, the Medicare Supplemental and Coordination of Benefits Database, and the Early View Database. The Commercial database contains the inpatient, outpatient, and outpatient prescription drug claims of approximately 147.9 million employees and their dependents covered under both fee-for-service and managed care health plans between 1995 and 2017. The Medicare database contains the same information for approximately 10.6 million retirees with Medicare supplemental insurance paid for by employers between 1995 and 2017. The Early View database includes the same components as the Commercial and Medicare databases for the period from January to May 2018. All data were obtained using *International Classification of Diseases, Ninth/Tenth Revisions, Clinical Modification* (ICD-9-CM and ICD-10-CM) codes, Current Procedural Terminology, 4th edition codes, Healthcare Common Procedure Coding System codes, and National Drug Code numbers.

All database records are statistically deidentified and certified to be fully compliant with U.S. patient confidentiality requirements set forth in the Health Insurance Portability and Accountability Act of 1996. Because this study used only deidentified patient records and did not involve the collection, use, or transmittal of individually identifiable data, institutional review board approval to conduct this study was not necessary.

Patient Cohort

Patients with ≥ 1 inpatient or ≥ 2 outpatient claims ≥ 30 days apart for PsO (ICD-9-CM diagnoses: 696.1x or ICD-10-CM diagnoses: L40.0-L40.4, L40.8) between July 1, 2015, and May 31, 2018, were identified. Claims for diagnostic procedures were excluded. Two separate patient samples, those with ≥ 1 claim for IXE or SEC or those with ≥ 1 claim for IXE or ADA, were selected based on drug claims between March 1, 2016, and May 31, 2018, on or after a PsO diagnosis. Within the IXE-SEC sample, the first IXE or SEC claim set the index date and the index drug. Patients were classified as IXE or SEC users according to the index drug. Likewise, for the IXE-ADA sample, patients were assigned as IXE or ADA cohort based on the first claim for IXE or ADA. Because the 2 samples were selected independently, patients who had IXE only or switched from IXE to ADA or SEC during the index period were in both IXE cohorts in the 2 samples. The cohort assignment for patients who switched from SEC or ADA to IXE were determined within each comparison sample by the first drug the patients received.

All patients were required to be aged ≥ 18 years on the index date and have continuous enrollment with medical and pharmacy benefits for 12 months before (baseline period) and after the index date (follow-up period). Patients were excluded if they had the index drug within 90 days before the index

date or had a diagnosis during the pre-index period for any other indication approved at the time of the study for treatment with the index medication (psoriatic arthritis for IXE; psoriatic arthritis or ankylosing spondylitis for SEC; and psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, rheumatoid arthritis, Crohn disease, ulcerative colitis, hidradenitis suppurativa, or uveitis for ADA).

Covariates

Demographic characteristics, measured on the index date, included age, gender, geographic region, payer, and health plan type. Baseline clinical characteristics, measured in the 12-month baseline period, included Deyo-Charlson Comorbidity Index (DCCI); comorbid conditions (anxiety, coronary heart disease, depression, diabetes, hyperlipidemia, hypertension, obesity, osteoarthritis, other autoimmune disorders, peripheral vascular disease, and sleep apnea); and all-cause and PsO-related health care costs. Baseline PsO-related medication use was reported, including biologic use (ADA, brodalumab, certolizumab, etanercept, guselkumab, infliximab, IXE, SEC, or ustekinumab); nonbiologic systemic therapies (apremilast, acitretin, systemic steroids, cyclosporine, methotrexate, azathioprine, hydroxyurea, isotretinoin, leflunomide, methoxsalen, mycophenolate mofetil, sulfasalazine, or thioguanine); topical treatments; and phototherapy. The number of unique biologics used in the preperiod was also captured.

Treatment Costs

All-cause and PsO-related health care costs were estimated during the 12-month follow-up period. PsO-related costs were based on inpatient claims with a PsO diagnosis in the primary position, outpatient claims with a PsO diagnosis in any position, and medical and pharmacy claims indicative for PsO treatment listed in the Covariates section. Costs were reported for overall and by inpatient services, outpatient services (including emergency room visits), and outpatient pharmacy. Health care costs were based on paid amounts of adjudicated claims, including insurer and health plan payments, as well as patient cost-sharing in the form of copayment, deductible, and coinsurance. The costs for services provided under capitated arrangements were estimated using payment proxies that were computed based on paid claims at the procedure level using the MarketScan Commercial and Medicare supplemental databases. All dollar estimates were inflated to 2018 dollars using the medical care component of the Consumer Price Index.⁹ All costs were reported as per patient per month.

Statistical Analysis

To reduce observed confounding, inverse probability of treatment weighting (IPTW) was employed. Propensity scores, defined as the probability of being treated by IXE, were estimated via logistic regression models, using IXE versus SEC or

FIGURE 1 Patient Selection

IXE versus ADA as the dependent variable. Covariates included all demographic and clinical variables listed in the Covariates section along with the pre-index PsO-related costs. Weights were defined as $1/p$ for IXE patients and $1/(1-p)$ for SEC or ADA patients, with p defined as the estimated propensity score. Cohort balances were evaluated by standardized difference (StdDiff), where a StdDiff of ≤ 0.1 indicated a good balance. All cost data presented in this paper were weighted via IPTW.

Bivariate analyses were conducted for all variables. Categorical measures were reported as frequencies and percentages. Continuous measures were reported as means and standard deviations. For cost outcomes, the median, 25th, and 75th percentiles were also reported. Statistical significance was assessed for cost outcomes using chi-square tests for categorical variables, 2-sample t-tests for continuous variables, and Wilcoxon rank sum tests for comparing medians.

Weighted chi-square tests, t-tests, and Wilcoxon rank sum tests employing robust standard error were performed for post-weighting descriptive analyses.

Pharmacy Cost Adjustment

Pharmacy payment reported from insurance claims may not always nor consistently capture pharmacy rebates, patient assistance programs, and commissions to wholesalers. This may result in biased estimates in cost differences between treatment cohorts if 1 drug has a higher discount factor than another. To adjust for discounts not captured in claims, the Institute for Clinical and Economic Review (ICER) discount factors based on net price divided by wholesale acquisition cost (WAC) were applied to pharmacy costs (drug costs $\times$ [1–ICER discount factor]).¹⁰ Specifically, for index drugs, ICER discount factors of 0.44, 0.38, and 0.31 were applied to the costs of IXE, SEC, and ADA, respectively. For other medications identified

TABLE 1 Baseline Demographic and Clinical Characteristics Before and After Weighting, IXE Versus SEC

Baseline Patient Characteristics	Before Weighting			After Weighting		
	IXE	SEC	StdDiff ^a	IXE	SEC	StdDiff ^a
	n = 357			n = 763		
Age, years, mean (SD)	49.9 (11.7)	49.2 (12.0)	0.061	49.4 (12.1)	49.4 (11.9)	0
Male, %	54.1	51.1	0.059	52.8	52.3	0.010
Commercial payer, %	92.4	93.4	0.039	93.0	93.2	0.008
Insurance plan type, %			0.167			0.047
Comprehensive/indemnity	3.4	5.0		5.0	4.5	
HMO	5.9	7.6		7.1	7.1	
POS/POS with capitation	11.2	7.9		8.4	8.8	
PPO	59.7	58.1		58.4	58.7	
Other (e.g., CDHP, HDHP, EPO)	19.3	20.3		20.3	19.8	
Unknown	0.6	1.2		0.8	1.2	
Geographic region, %			0.216			0.073
Northeast	12.3	17.0		16.4	15.7	
North Central	17.6	17.6		18.0	17.7	
South	61.6	53.1		54.6	55.6	
West	8.4	12.1		11.0	10.8	
Unknown	0	0.3		0	0.2	
Deyo-Charlson Comorbidity Index score, mean (SD)	0.5 (1.2)	0.6 (1.2)	0.105	0.6 (1.3)	0.6 (1.2)	0.010
Comorbid conditions, %						
Anxiety	10.6	13.1	0.076	12.0	12.3	0.010
Coronary heart disease	5.9	4.8	0.046	5.2	5.3	0.003
Depression	13.4	11.4	0.062	12.2	12.3	0.004
Diabetes	15.4	19.5	0.109	16.9	18.0	0.030
Hyperlipidemia	33.1	29.5	0.077	30.2	30.6	0.009
Hypertension	39.5	40.2	0.015	38.8	39.7	0.019
Multiple sclerosis	0	0.4	0.089	0	0.4	0.092
Obesity	23.8	24.5	0.016	24.7	24.4	0.007
Osteoarthritis	10.4	11.3	0.029	11.2	11.1	0.004
Other autoimmune disorders	5.6	6.2	0.024	5.7	5.9	0.011
Peripheral vascular disease	0.8	2.6	N/A	1.7	2.0	N/A
Sleep apnea	9.5	11.1	0.053	9.9	10.6	0.022
PsO treatments						
Any biologics, %	66.4	70.2	0.083	70.0	69.3	0.014
Unique biologics, n, mean (SD)	0.7 (0.6)	0.8 (0.6)	0.135	0.8 (0.6)	0.8 (0.6)	0.028
Any systemic agents/targeted oral therapies, %	59.9	58.6	0.028	58.5	59.0	0.009
Any topical agents, %	75.9	76.5	0.015	76.6	76.5	0.002
Phototherapy or laser treatments, %	7.3	5.9	0.056	7.3	6.5	0.031
All-cause health care cost ^b , USD, mean (SD)	3,743 (3,824)	3,749 (4,155)	0.001	3,941 (4,121)	3,726 (4,336)	0.051
PsO-specific health care cost ^b , USD, mean (SD)	2,745 (2,330)	2,826 (2,585)	0.033	2,841 (2,286)	2,815 (2,746)	0.010

^aA standardized difference of less than 0.1 is considered well balanced.

^bReported per patient per month.

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; SEC = secukinumab; SD = standard deviation; StdDiff = standardized difference.

during the follow-up period, which were predominately biologics, the average ICER discount factors were obtained from all PsO-indicated biologics and applied: 0.30 for the IXE cohort and 0.31 for both the SEC and ADA cohorts. Total monthly adjusted PsO-related costs were obtained by combining monthly adjusted index drug costs, adjusted PsO-related pharmacy costs excluding index drugs, and PsO-related nonpharmacy costs.

Given the ICER discount rates were obtained from publication, we performed sensitivity analyses by estimating mean and median cost differences between cohorts after varying the discount rates for the index drugs by $\pm 5\%$.

Separately, we estimated year 1 costs for IXE, SEC, and ADA by applying 2 adjustments to the weighted index drug costs from claims during a 1-year follow-up period. First,

TABLE 2 Baseline Demographic and Clinical Characteristics Before and After Weighting, IXE Versus ADA

Baseline Patient Characteristics	Before Weighting			After Weighting		
	IXE	ADA	StdDiff ^a	IXE	ADA	StdDiff ^a
	n = 388			n = 2,578		
Age, years, mean (SD)	49.4 (11.3)	47.0 (12.7)	0.200	47.7 (12.5)	47.7 (12.9)	0.004
Male, %	55.4	56.1	0.013	56.2	56.5	0.006
Commercial payer, %	93.8	94.1	0.014	93.9	92.7	0.051
Insurance plan type, %			0.234			0.108
Comprehensive/indemnity	2.6	6.2		5.1	5.7	
HMO	6.7	7.1		6.3	6.9	
POS/POS with capitation	11.6	7.3		7.7	9.3	
PPO	59.0	57.3		60.1	56.6	
Other (e.g., CDHP, HDHP, EPO)	19.8	21.5		19.7	21.0	
Unknown	0.3	0.6		1.1	0.5	
Geographic region, %			0.155			0.087
Northeast	14.4	15.6		15.4	15.1	
North Central	16.5	20.7		19.3	19.8	
South	59.3	53.1		56.1	54.7	
West	9.8	10.4		9.2	10.1	
Unknown	0.0	0.3		0.0	0.3	
Deyo-Charlson Comorbidity Index score, mean (SD)	0.5 (1.2)	0.4 (1.0)	0.095	0.4 (1.1)	0.4 (1.0)	0.014
Comorbid conditions, %						
Anxiety	11.1	12.7	0.050	11.8	12.3	0.014
Coronary heart disease	6.7	4.2	0.109	3.9	4.4	0.027
Depression	13.4	10.4	0.094	12.2	10.6	0.049
Diabetes	18.6	13.5	0.139	14.5	15.2	0.021
Hyperlipidemia	34.3	29.0	0.113	31.5	29.2	0.051
Hypertension	39.2	33.1	0.127	33.7	33.4	0.008
Multiple sclerosis	0	0.1	N/A	0	0.1	N/A
Obesity	24.2	18.5	0.141	15.8	18.8	0.078
Osteoarthritis	9.5	8.9	0.021	9.1	8.9	0.008
Other autoimmune disorders	3.9	2.4	0.081	2.6	2.6	0.003
Peripheral vascular disease	1.0	1.4	0.030	1.1	1.3	0.016
Sleep apnea	13.1	8.5	0.149	8.9	9.0	0.005
PsO treatments						
Any biologics, %	69.1	41.5	0.578	43.8	46.0	0.044
Unique biologics, n, mean (SD)	0.8 (0.6)	0.4 (0.5)	0.658	5.0 (0.5)	0.5 (0.5)	0.038
Any systemic agents/targeted oral therapies, %	59.3	52.1	0.145	50.9	53.6	0.056
Any topical agents, %	75.3	71.8	0.078	72.5	72.6	0.003
Phototherapy or laser treatments, %	8.0	6.7	0.051	5.7	6.7	0.042
All-cause health care cost ^b , USD, mean (SD)	4,123 (3,871)	1,977 (2,483)	0.660	2,504 (3,406)	2,399 (2,988)	0.033
PsO-specific health care cost ^b , USD, mean (SD)	3,130 (2,568)	1,287 (1,551)	0.869	1,578 (1,836)	1,702 (2,308)	0.059

^aA standardized difference of less than 0.1 is considered well balanced.

^bReported per patient per month.

ADA = adalimumab; 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; SD = standard deviation; StdDiff = standardized difference.

the weighted index drug costs were divided by mean medication possession ratio (MPR) for each cohort to obtain the MPR-adjusted index drug cost, assuming the patients were fully adherent for 12 months. MPR was defined as the sum of days supply during the follow-up period divided by 365 days. Overlapping days supply between consecutive fills were appended. Second, the ICER discount factors (0.44/IXE,

0.38/SEC, and 0.31/ADA) were applied to the MPR-adjusted index drug costs (drug costs × [1 - ICER discount factor]) to obtain year 1 cost estimates for IXE, SEC, and ADA.

Results

A total of 357 IXE users and 763 SEC users met selection criteria for IXE-SEC comparisons. Separately, 388 IXE users

TABLE 3 Weighted All-Cause and PsO-Related Per Patient Per Month Health Care Costs, IXE Versus SEC and IXE Versus ADA

Cost Per Patient Per Month	IXE				SEC				P Value, Mean
	Mean (SD)		Median (Range ^a)		Mean (SD)		Median (Range ^a)		
All-cause costs, USD (SD)									
Total health care	7,313	(4,142)	6,680	(5,488-7,915)	6,477	(4,144)	5,827	(4,624-7,107)	0.002
Inpatient admissions	247	(1,426)	0	(0-0)	241	(1,280)	0	(0-0)	0.942
Outpatient services	611	(1,997)	166	(78-469)	614	(1,831)	211	(79-559)	0.981
Outpatient pharmacy	6,455	(3,226)	6,301	(5,015-7,190)	5,621	(3,408)	5,417	(4,213-6,244)	<0.001
PsO-related costs, USD (SD)									
Total health care	6,303	(3,191)	6,252	(4,994-7,122)	5,437	(3,367)	5,265	(4,080-6,071)	<0.001
Inpatient admissions	0	(0)	0	(0-0)	0	(0)	0	(0-0)	N/A
Outpatient services	40	(137)	21	(11-35)	54	(251)	22	(11-36)	0.221
Outpatient pharmacy	6,263	(3,184)	6,206	(4,960-7,098)	5,382	(3,370)	5,228	(4,032-6,034)	<0.001
Index drug costs, USD (SD)	5,613	(2,495)	5,826	(4,194-6,729)	4,626	(2,823)	4,723	(3,065-5,670)	<0.001
Cost Per Patient Per Month	IXE				ADA				P Value, Mean
	Mean (SD)		Median (Range ^a)		Mean (SD)		Median (Range ^a)		
All-cause costs, USD (SD)									
Total health care	6,535	(3,051)	6,206	(5,154-7,322)	5,557	(4,677)	4,914	(3,605-5,943)	0.026
Inpatient admissions	186	(986)	0	(0-0)	181	(1,651)	0	(0-0)	0.934
Outpatient services	418	(1,003)	154	(63-393)	467	(1,319)	172	(68-435)	0.366
Outpatient pharmacy	5,930	(2,646)	6,024	(4,730-6,744)	4,909	(4,167)	4,513	(3,226-5,436)	0.019
PsO-related costs, USD (SD)									
Total health care	5,792	(2,593)	5,902	(4,616-6,622)	4,754	(4,015)	4,400	(3,138-5,316)	0.017
Inpatient admissions	6	(139)	0	(0-0)	2	(65)	0	(0-0)	0.502
Outpatient services	34	(96)	20	(10-33)	57	(776)	19	(10-33)	0.135
Outpatient pharmacy	5,751	(2,584)	5,869	(4,597-6,581)	4,695	(3,965)	4,361	(3,093-5,271)	0.015
Index drug costs, USD (SD)	5,328	(2,382)	5,555	(3,924-6,412)	3,588	(1,884)	3,716	(2,180-4,842)	<0.001

^aReported range is the 25th percentile and the 75th percentile.

ADA = adalimumab; IXE = ixekizumab; N/A = not applicable; PsO = psoriasis; SEC = secukinumab; SD = standard deviation.

and 2,578 ADA users were included for IXE-ADA comparisons (Figure 1).

Before weighting, the IXE and SEC cohorts had similar baseline demographic and clinical profiles (Table 1). The mean age of IXE and SEC users was 49-50 years old, and 51%-54% were male. The baseline DCCI and total all-cause and PsO-related health care costs were comparable between the 2 cohorts. For IXE and SEC users, the most common comorbidities were hypertension (39.5% vs. 40.2%, StdDiff=0.015); hyperlipidemia (33.1% vs. 29.5%, StdDiff=0.077); and obesity (23.8% vs. 24.5%, StdDiff=0.029). Preperiod biologic use was similar between IXE (66%) and SEC (70%) users (StdDiff=0.083).

Before weighting, compared with ADA, IXE users were older and had worse baseline health status than ADA users, as demonstrated by higher baseline rates for comorbid conditions, including hypertension (39.2% vs. 33.1%, StdDiff=0.127); hyperlipidemia (34.3% vs. 29.0%, StdDiff=0.113); obesity (24.2% vs. 18.5%, StdDiff=0.141); diabetes (18.6% vs. 13.5%, StdDiff=0.139); and sleep apnea (13.1% vs. 8.5%, StdDiff=0.149; Table 2). IXE users had a higher rate of prior biologic use (69.1% vs. 41.5%, StdDiff=0.578); a higher number

of unique biologics used (0.8 ± 0.6 vs. 0.4 ± 0.5 , StdDiff=0.658); and a higher rate of systemic treatment use (59.3% vs. 52.1%, StdDiff=0.145) in the baseline period than ADA users. IXE users also incurred higher baseline total all-cause and PsO-related health care costs than ADA users. All baseline demographic and clinical characteristics were well balanced after weighting for both comparisons.

Health Care Costs, IXE Versus SEC

In the IXE-SEC comparison, the index monthly drug costs were $\$5,613 \pm \$2,495$ for IXE users and $\$4,626 \pm \$2,823$ for SEC users ($P < 0.001$; Table 3). Drug costs comprised 89% and 85% of PsO-related costs and 77% and 71% of all-cause costs for IXE and SEC users, respectively. In total, PsO-related monthly costs were $\$6,303 \pm \$3,191$ for IXE users and $\$5,437 \pm \$3,367$ for SEC users ($P < 0.001$), while the weighted mean monthly all-cause health care costs were $\$7,313 \pm \$4,142$ for IXE users and $\$6,477 \pm \$4,144$ for SEC users ($P = 0.002$). The differences in inpatient and outpatient costs were statistically insignificant and negligible. Examination based on median monthly costs showed similar patterns (Table 3).

TABLE 4 Adjusted PsO-Related Costs, IXE Versus SEC, IXE Versus ADA

Adjusted Cost Per Patient Per Month (Weighted)	Mean Cost Analysis				Median Cost Analysis			
	IXE	SEC	Diff	P Value	IXE	SEC	Diff	P Value
Index drug costs, USD	5,613	4,626	987	<0.001	5,826	4,723	1,103	<0.001
ICER discount rate	0.44	0.38			0.44	0.38		
ICER-adjusted index drug costs (A), USD	3,143	2,868	275		3,263	2,928	334	
PsO-related pharmacy costs, non-index drugs, USD	658	775	-117		11	22	-11	
ICER average discount rate (across biologics)	0.30	0.31			0.30	0.31		
ICER-adjusted PsO-related pharmacy costs, non-index drugs (B), USD	462	539	-77		8	16	-8	
Unadjusted inpatient and outpatient costs (C), USD	32	36	-4		21	21	0	
Total adjusted PsO-related costs (A+B+C), USD	3,637	3,443	195	0.132	3,546	3,311	235	0.002

Adjusted Cost Per Patient Per Month (Weighted)	Mean Cost Analysis				Median Cost Analysis			
	IXE	ADA	Diff	P Value	IXE	ADA	Diff	P Value
Index drug costs, USD	5,328	3,588	1,740	<0.001	5,555	3,716	\$839	<0.001
ICER discount rate	0.44	0.31			0.44	0.31		
ICER-adjusted index drug costs (A), USD	2,984	2,476	508		3,111	2,564	\$47	
PsO-related pharmacy costs, non-index drugs, USD	427	1,134	-707		4	20	-16	
ICER average discount rate (across biologics)	0.30	0.31			0.30	0.31		
ICER-adjusted PsO-related pharmacy costs, non-index drugs (B), USD	300	778	-478		3	14	-11	
Unadjusted inpatient and outpatient costs (C), USD	36	33	3		20	19	1	
Total adjusted PsO-related costs (A+B+C), USD	3,320	3,287	33	0.907	3,332	3,047	285	0.002

ADA=adalimumab; Diff=difference; ICER=Institute for Clinical and Economic Review; IXE=ixekizumab; PsO=psoriasis; SEC=secukinumab.

After applying ICER discounts, the adjusted mean monthly index drug costs were \$3,143 for IXE and \$2,868 for SEC, respectively. The adjusted mean monthly pharmacy costs excluding index drugs were \$462 for IXE and \$539 for SEC, respectively. Total adjusted mean monthly PsO-related costs were comparable between IXE and SEC (\$3,637 vs. \$3,443, $P=0.132$). Applying the same adjustment approach, the median monthly total adjusted PsO-related costs were \$3,546 for IXE and \$3,311 for SEC ($P=0.002$; Table 4). Sensitivity analyses showed the differences in mean adjusted PsO-related monthly costs ranged from no statistically significant differences between IXE and SEC to \$409 higher for IXE users when the discount rate was lowered by 5% for SEC and increased by 5% for IXE. Similar patterns were observed in median cost differences from same sensitivity analyses (Appendix A, available in online article).

The weighted mean MPR during 12-month follow-up was 0.70 for IXE and 0.67 for SEC. After MPR and ICER discount adjustments, year 1 mean costs of IXE and SEC were estimated to be \$53,883 and \$51,366, respectively.

Health Care Costs, IXE Versus ADA

In the IXE-ADA comparison, the monthly index drug costs were \$5,328±\$2,382 for IXE users and \$3,588±\$1,884 for ADA users ($P<0.001$; Table 3). Drug costs made up 92% and 75% of PsO-related costs and 82% and 65% of all-cause costs for IXE and ADA users, respectively. Higher index drug costs

for IXE users were partially offset by lower non-index drug pharmacy costs. In total, mean monthly PsO-related costs were \$5,792±\$2,593 for IXE users and \$4,754±\$4,015 for ADA users ($P=0.017$), while the weighted mean monthly all-cause health care costs were \$6,535±\$3,051 for IXE users and \$5,557±\$4,677 for ADA users ($P=0.026$).

After applying ICER discounts, the adjusted mean monthly index drug costs were \$2,984 for IXE and \$2,476 for ADA, respectively. The adjusted mean monthly pharmacy costs excluding index drugs were \$300 for IXE and \$778 for ADA, respectively. Total adjusted mean monthly PsO-related costs were comparable between IXE and ADA (\$3,320 vs. \$3,287, $P=0.907$). Applying the same adjustment approach, the median monthly total adjusted PsO-related costs were \$3,332 for IXE and \$3,047 for ADA ($P=0.002$; Table 4). Sensitivity analyses showed the differences in the mean adjusted PsO-related monthly costs remained statistically insignificant. Median cost differences from the same sensitivity analyses ranged from no statistically significant difference to \$466 higher for IXE users ($P<0.001$) when the discount rates were set at 95% of IXE base rate and 105% of ADA base rate (Appendix B, available in online article).

The weighted mean MPR during 12-month follow-up was 0.68 for IXE and 0.66 for ADA. Year 1 ICER-MPR-adjusted mean costs of IXE and ADA were estimated to be \$52,653 and \$45,013, respectively.

Discussion

In the recently updated British Association of Dermatologists guidelines for management of PsO, both SEC and ADA were suggested as potential first-line biologic agents.¹¹ By contrast, IXE is a newer biologic whose position within the PsO treatment algorithm has not been fully established. Understanding the real-world health care costs of patients initiating IXE compared with those initiating more established treatment options contributes to the comprehensive assessment of this newer treatment option. In this retrospective study based on real-world data, patients treated with IXE incurred \$836 and \$977 higher all-cause health care costs per patient per month in the first year after treatment initiation than those treated with SEC and ADA, respectively. The higher costs in the IXE cohort was primarily driven by the cost of index drug which is elevated in the first year due to the higher number of induction doses needed during initiation of IXE than SEC or ADA.¹⁰

In claims-based drug cost analysis, we report the paid amounts of adjudicated claims, including health plan payments and patient out-of-pocket costs. However, drug discount programs, which are commonly available for biologics and include rebates, patient assistance programs, and commissions to wholesalers,¹⁰ are not reliably captured in claims data.¹² Because the specifics of drug discount programs are generally confidential, we applied the discount estimates published in the 2018 ICER report.¹⁰ After applying the ICER adjustments to the index drug costs and other PsO medications, the difference in mean monthly index drug costs narrowed from 21% to 10% between IXE and SEC users, and from 48% to 21% between IXE and ADA users, respectively. Consequently, the mean monthly PsO-related cost differences decreased from 16% to 6% between IXE and SEC users and from 22% to 1% between IXE and ADA users, respectively. In summary, postadjustment mean monthly PsO-related costs were similar between patients initiating IXE and those initiating SEC or ADA.

The adjusted real-world index drug costs reported in this study are consistent with the estimates derived from sales reports and utilized in the ICER report.¹⁰ In the ICER report, the estimated annual cost of IXE was \$51,374 for the first year and \$37,686 for subsequent years, if patients were fully adherent and received a standard price discount. In our year 1 cost estimates for the index drugs, the adjusted annual mean drug cost for initiating IXE ranged from \$52,653 to \$53,883. The ICER estimated costs of SEC and ADA were \$49,624 and \$46,751 for the first year, whereas our analysis estimated the annual mean cost of year 1 for SEC and ADA at \$51,366 and \$45,013, respectively.

Previous studies have shown that direct health care costs for patients with moderate to severe PsO are substantial. In a study of patients taking biologics during 2010-2014, those who had moderate or severe disease had higher median annual all-cause total costs (\$37.7k [mild] vs. \$42.3k [moderate], \$49.3k [severe]),

and among these patients, pharmacy costs represented 73.8% to 89.9% of all-cause total costs.⁵ Foster et al. (2016) reported that biologic-treated patients without treatment failure incurred higher health care costs than those who had treatment failure. Higher costs were attributed to pharmacy costs, despite an offset in outpatient costs.¹³ In our study, the index drug alone represented 65%-89% of mean all-cause costs across the study drugs. The percentage would be higher if the costs of other biologics the patients switched to during the follow-up period were included. Nonpharmacy costs, such as inpatient and outpatient costs excluding office-administered medication, were less than \$40 per month for all comparison cohorts.

Because PsO is perceived as a non-life-threatening chronic disease, the primary focus of clinicians has been on mitigating the burden from reduced quality of life and losses in work productivity. Ninety-four percent of patients reported that PsO is a problem in their daily life, and 88% reported that it affects their overall emotional well-being.¹⁴ Across all measures, the negative effect of PsO on emotional and physical well-being was greater for patients with severe PsO than those with mild PsO. Among the 12% of PsO patients who were unemployed, 92% stated that PsO or psoriatic arthritis was the sole reason for not working, and among the 59% of patients working full- or part-time, 49% stated that they missed work due to PsO.

It has been shown that achieving a 90% or greater improvement in the Psoriasis Area and Severity Index (PASI) is associated with larger increases in quality of life scores compared with the lower 75% improvement threshold.^{15,16} The newer IL-17 inhibitors, such as IXE and SEC, have repeatedly shown superior efficacy at achieving 90% to 100% reduction in PASI score compared with older TNF- α inhibitors, such as ADA.¹⁰ A recent network meta-analysis demonstrated that when clear skin is the targeted outcome, IXE was the most cost-effective biologic therapy for treatment of moderate to severe PsO in the United States.¹⁷ As improved quality of life is a key outcome for PsO patients, economic assessments of the benefits of therapy would benefit from a nuanced approach to measuring the effect of clear skin.

Limitations

Interpretation of the study results should take into consideration several limitations. By relying on medical coding and prescription fills from administrative claims, this analysis was subject to data coding and data entry errors. The MarketScan Early View Database captures health care services incurred up to 45 days before data extraction completion and includes only fully adjudicated claims. As an estimate, about 97% of outpatient prescription claims, 74% of outpatient professional claims, and 65% of inpatient claims and outpatient facility claims in MarketScan are adjudicated at a 30-day lag. Consequently, health care costs were underestimated from claims incurred from January to May 2018. However, the

potential underestimation of the index drug costs was limited given all IXE and SEC prescriptions and the majority of ADA prescriptions were captured via outpatient pharmacy claims.

WAC does not accurately represent real drug transaction prices. As such, we attempted to overcome this issue by applying discounts from a comprehensive analysis performed by ICER. However, underestimation or overestimation may occur due to several reasons. First, some rebates and patient assistance programs may have been reflected in claims. Second, 2017 ICER discount factors were used to adjusted costs for 2016 through 2018. Third, an average ICER discount rate was applied to other medications that were mostly biologics. We did not apply the discounts at an individual drug level. Year 1 index drug costs were estimated based on MPR, which was built on the assumption that patients took medications as prescribed.

IPTW was employed to address observable imbalances between patient cohorts, yet not all relevant covariates, such as PsO severity, are captured in claims data. Pre-index biologic use, number of unique prior biologics, and PsO-related health care costs were included in the models as a proxy for severity, but residual unobservable differences may remain. In addition, the chosen databases are limited to only those individuals with commercial health coverage or private Medicare supplemental coverage. Consequently, the results of this analysis may not be generalizable to PsO patients with other types of insurance or without health insurance coverage.

Conclusions

This real-world study estimated that mean per patient per month PsO-related costs for the first year of treatment were comparable between patients treated with IXE or ADA and between patients treated with IXE or SEC after adjusting for ICER discounts. Costs of PsO management were predominately driven by pharmacy costs. Further examination of drug survival and patient quality of life will benefit comprehensive cost-effectiveness analyses between IXE, ADA, and SEC users.

Authors

ANDREW BLAUVELT, MD, MBA; Oregon Medical Research Center, Portland, Oregon. NIANWEN SHI, PhD; CAROLYN R. LEW, PhD; and NICOLE M. ZIMMERMAN, MS, IBM Watson Health, Cambridge, Massachusetts. BAOJIN ZHU, PhD; RUSSEL BURGE, PhD; WILLIAM N. MALATESTINIC, PharmD, MBA; CHEN-YEN LIN, PhD; ORIN M. GOLDBLUM, MD; and MWANGI J. MURAGE, PhD, MPH, Eli Lilly and Company, Indianapolis, Indiana.

AUTHOR CORRESPONDENCE: Mwangi J. Murage, PhD, MPH, Eli Lilly and Company, LTC – South, 1555 Harding St., Indianapolis, IN 46221. Tel.: 317.460.3619; E-mail: murage_mwangi_james@lilly.com.

DISCLOSURES

Funding for this study was provided to IBM Watson Health by Eli Lilly and Company. The analysis was conducted independently by IBM Watson Health. Eli Lilly and Company and IBM Watson Health collaborated on study design and interpretation of results. Shi, Lew, and Zimmerman were employed by IBM Watson Health and received funding from Eli Lilly and Company to conduct this study. Zhu, Burge, Malatestinic, Lin, Goldblum, and Murage were employed by Eli Lilly and Company while this study was conducted. Blauvelt has served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Akros, Allergan, Amgen, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dermavant, Dermira, Eli Lilly and Company, FLX Bio, Galderma, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Meiji, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Revance, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB Pharma, Valeant, and Vidac, and as a paid speaker for AbbVie, Regeneron, and Sanofi Genzyme.

A portion of these results were presented at the 2019 International Society for Pharmacoeconomics and Outcomes Research Annual Meeting; May 18-22, 2019; New Orleans, LA, and the 2019 Academy of Managed Care Pharmacy Annual Meeting; March 25-28, 2019; San Diego, CA.

ACKNOWLEDGMENTS

Medical writing services were provided by Jessamine Winer-Jones, PhD (IBM Watson Health), and these services were paid for by Eli Lilly and Company. Natalie N. Boytsov, PhD; Meghan E. Jones, MSPH; and Alan J. M. Brnabic, MSc (Eli Lilly and Company) provided expert review of the original protocol.

REFERENCES

1. Brezinski EA, Dhillon JS, Armstrong AW. Economic burden of psoriasis in the United States: a systematic review. *JAMA Dermatol*. 2015;151(6):651-58.
2. Kimball AB, Jacobson C, Weiss S, Vreeland MG, Wu Y. The psychosocial burden of psoriasis. *Am J Clin Dermatol*. 2005;6(6):383-92.
3. Langley RGB, Krueger GG, Griffiths CEM. Psoriasis: epidemiology, clinical features, and quality of life. *Ann Rheum Dis*. 2005;64(Suppl 2):ii18-ii23.
4. Yu AP, Tang J, Xie J, et al. Economic burden of psoriasis compared to the general population and stratified by disease severity. *Curr Med Res Opin*. 2009;25(10):2429-38.
5. Murage MJ, Anderson A, Oliveria SA, et al. Healthcare resource utilization and costs among psoriasis patients treated with biologics, overall and by disease severity. *J Med Econ*. 2018;21(8):745-54.
6. Campa M, Mansouri B, Warren R, Menter A. A review of biologic therapies targeting IL-23 and IL-17 for use in moderate-to-severe plaque psoriasis. *Dermatol Ther*. 2016;6(1):1-12.
7. Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2008;58(5):826-50.
8. Wu JJ, Guérin A, Gauthier G, Sundaram M. Healthcare resource utilization, healthcare costs and dose escalation in psoriasis patients initiated on ustekinumab versus adalimumab: a retrospective claim study. *J Dermatolog Treat*. 2017;28(4):290-8.
9. U.S. Department of Labor. Consumer Price Index. Archived detailed reports. 2018. Available at: <https://www.bls.gov/cpi/tables/detailed-reports/home.htm>. Accessed November 14, 2019.
10. Institute for Clinical and Economic Review. Targeted immunomodulators for the treatment of moderate-to-severe plaque psoriasis: effectiveness and value. August 3, 2019. Available at: https://icer-review.org/wp-content/uploads/2017/11/ICER_Psoriasis_Update_Final_Evidence_Report_10042018.pdf. Accessed October 28, 2019.

11. Smith CH, Jabbar-Lopez ZK, Yiu ZZ, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol*. 2017;177(3):628-36.
12. Motheral B, Brooks J, Clark MA, et al. A checklist for retrospective database studies—report of the ISPOR task force on retrospective databases. *Value Health*. 2003;6(2):90-97.
13. Foster SA, Zhu B, Guo J, et al. Patient characteristics, health care resource utilization, and costs associated with treatment-regimen failure with biologics in the treatment of psoriasis. *J Manag Care Spec Pharm*. 2016;22(4):396-405. Available at: <https://www.jmcp.org/doi/10.18553/jmcp.2016.22.4.396>.
14. Armstrong AW, Schupp C, Wu J, Bebo B. Quality of life and work productivity impairment among psoriasis patients: findings from the national psoriasis foundation survey data 2003-2011. *PLoS One*. 2012;7(12):e52935.
15. Puig L, Thom H, Mollon P, Tian H, Ramakrishna GS. Clear or almost clear skin improves the quality of life in patients with moderate-to-severe psoriasis: a systematic review and meta-analysis. *J Eur Acad Dermatol Venereol*. 2016;31(2):213-20.
16. Torii H, Sato N, Yoshinari T, Nakagawa H; Investigators JIS. Dramatic impact of a Psoriasis Area and Severity Index 90 response on the quality of life in patients with psoriasis: an analysis of Japanese clinical trials of infliximab. *J Dermatol*. 2012;39(3):253-59.
17. Al Sawah S, Foster SA, Burge R, et al. Cost per additional responder for ixekizumab and other FDA-approved biologics in moderate-to-severe plaque psoriasis. *J Med Econ*. 2017;20(12):1224-30.

APPENDIX A Sensitivity Analysis, Adjusted PsO-Related Cost Differences, IXE Versus SEC

Mean Cost Differences		ICER Discount Rate (SEC)		
		0.36	0.38	0.40
ICER Discount Rate (IXE) USD	0.42	237 (P=0.07)	323 (P=0.01)	409 (P=0.002)
	0.44	115 (P=0.38)	195 (P=0.13)	288 (P=0.02)
	0.46	-6 (P=0.96)	80 (P=0.53)	166 (P=0.19)
Median Cost Differences		0.36	0.38	0.40
ICER Discount Rate (IXE) USD	0.42	287 (P<0.001)	376 (P<0.001)	456 (P<0.001)
	0.44	156 (P=0.08)	235 (P=0.002)	326 (P<0.001)
	0.46	27 (P=0.88)	121 (P=0.23)	197 (P=0.009)

ICER=Institute for Clinical and Economic Review; IXE=ixekizumab; PsO=psoriasis; SEC=secukinumab.

APPENDIX B Sensitivity Analysis, Adjusted PsO-Related Cost Differences, IXE Versus ADA

Mean Cost Differences		ICER Discount Rate (ADA)		
		0.29	0.31	0.33
ICER Discount Rate (IXE) USD	0.418	93 (P=0.75)	148 (P=0.61)	203 (P=0.49)
	0.44	-21 (P=0.94)	34 (P=0.91)	89 (P=0.76)
	0.462	-135 (P=0.64)	-80 (P=0.78)	-25 (P=0.93)
Median Cost Differences		0.29	0.31	0.33
ICER Discount Rate (IXE) USD	0.418	351 (P=0.001)	406 (P<0.001)	466 (P<0.001)
	0.44	231 (P=0.02)	285 (P=0.002)	346 (P<0.001)
	0.462	101 (P=0.43)	158 (P=0.11)	216 (P=0.02)

ADA=adalimumab; ICER=Institute for Clinical and Economic Review; IXE=ixekizumab; PsO=psoriasis.