

Psoriatic Arthritis Treatment Patterns and Costs Among Pharmacologic Treatment–Naïve Patients

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Psoriatic arthritis (PsA) is a heterogeneous inflammatory disease. Clinical manifestations of PsA include peripheral arthritis, axial disease, dactylitis, enthesitis, and psoriatic skin and nail disease.¹ In addition to having an increased risk of severe disability and increased mortality,² patients with PsA experience significant psychosocial burdens and diminished health-related quality of life.³ Early diagnosis of PsA and effective treatment are therefore key to improving quality of life and slowing the progression of disease. PsA has an estimated incidence of 0.06% to 0.25% in the United States and up to 41% in patients with psoriasis.⁴

A number of treatment options are available for patients with PsA. Historically, active PsA has been treated with oral small molecules (OSMs) such as methotrexate, which are still recommended, albeit after use of a tumor necrosis factor inhibitor (TNFi),⁵ for the treatment of peripheral arthritis of PsA.^{6,7} Biologic therapies were first approved for PsA in 2002.⁸ Biologic therapies now approved for PsA include the TNFis: ustekinumab (an interleukin [IL]–12/23 inhibitor), secukinumab and ixekizumab (IL-17a inhibitors), and abatacept (a selective T-cell costimulation modulator). Newer oral therapies such as tofacitinib (Janus kinase [JAK] inhibitor) and apremilast (phosphodiesterase-4 [PDE4] inhibitor) have also been approved. Partly because of the increase in the number of available therapies, treatment guidelines have been updated to reflect the improved efficacy and safety of these newer medications on the market. For instance, the American College of Rheumatology (ACR)/National Psoriasis Foundation 2018 treatment guidelines recommend, based on the available body of evidence, that treatment-naïve patients with PsA use a TNFi over an OSM (including apremilast).⁵

It is well known that biologic medications are costlier than OSMs such as methotrexate and sulfasalazine,⁹ which is a concern for payers, clinicians, and patients. Nevertheless, the disease-modifying properties of biologics may translate into longer-term savings and better outcomes for patients as the disease becomes controlled over time. Thus, although a therapy may be expensive, it may be cost saving in the long term, and real-world data are needed to address this question. To our knowledge, few studies have looked at the use of all available therapies for the treatment-naïve PsA population.

ABSTRACT

OBJECTIVES: Pharmacologic treatment for psoriatic arthritis (PsA) includes traditional oral small molecules (OSMs), tumor necrosis factor inhibitors (TNFis), and newer oral therapies such as a phosphodiesterase-4 (PDE4) inhibitor and a Janus kinase inhibitor. We aimed to describe treatment patterns and health care costs for treatment-naïve patients with active PsA initiating pharmacologic treatment.

STUDY DESIGN: This was an observational, retrospective study.

METHODS: We assessed treatment patterns and health care costs from the IBM MarketScan Research databases. We calculated costs during the 12-month follow-up period for inpatient and outpatient medical health care, including outpatient prescription costs.

RESULTS: A total of 3491 patients were identified for the study. Incident therapies included OSMs methotrexate (58.3%), sulfasalazine (9.8%), hydroxychloroquine (2.3%), and other OSMs (1.9%); TNFis adalimumab (12.3%), etanercept (8.6%), infliximab (1.9%), and other TNFis (1.4%); and the PDE4 inhibitor apremilast (2.6%). Persistence ranged from 15.2% to 34.6% with OSM monotherapy and from 42.9% to 58.2% with TNFi monotherapy. Percentage of patients with a gap of at least 60 days in therapy ranged from 42.9% to 48.5% with OSMs and from 17.9% to 29.9% with TNFis. Mean first-line unadjusted per-patient per-month total health care costs for OSMs ranged from \$1029 to \$1456 and mean total health care costs ranged from \$19,173 to \$25,013. Mean unadjusted per-patient per-month total health care costs for TNFis ranged from \$4203 to \$7063 and mean total health care costs ranged from \$45,635 to \$60,933.

CONCLUSIONS: Although patients using OSMs had generally lower total health care costs, they also had the highest rates of treatment modifications such as low persistence and medication gaps of at least 60 days.

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A recent study that assessed treatment-naïve patients with PsA focused on only 1 class of medications and did not capture the full spectrum of medication use and health care costs.⁹ Further, little is known about initial treatment patterns across all medications in PsA, particularly whether therapies are initiated as monotherapy or in combination with other drugs. Real-world evidence on medication use by these patients may help payers understand the true costs of therapy and health care. In this study, we evaluated treatment patterns and costs during a period when several new medications became commercially available (2009-2017). We aimed to address costs over the first year of treatment among patients with PsA initiating their first therapy and to examine treatment patterns in that first year.

METHODS

Data Source and Study Design

This was an observational retrospective analysis of deidentified claims data from the IBM MarketScan Commercial and Medicare Supplemental Databases. These databases provide access to medical and prescription drug claims for privately insured individuals, including individuals 65 years and older with Medicare supplemental coverage.

The study period spanned January 1, 2009, through June 30, 2017. We defined the first PsA diagnosis date as the diagnostic index date. The treatment index date was the date of first claim for a medication. We used an 18-month period before the PsA diagnosis date and before the treatment index date to identify patients with new diagnoses and their first line of medication and to characterize the study population. We followed patients for a total of 12 months after the treatment index date and captured first-line and second-line medication use and any modifications of their therapies.

Medications of interest included OSMs methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, gold, cyclosporine, and azathioprine; TNFis adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab; and non-TNFi biologic medications abatacept, rituximab (approved for rheumatoid arthritis but not PsA), secukinumab, ustekinumab, ixekizumab, and brodalumab (approved for plaque psoriasis but not PsA). Newer oral therapies tofacitinib and apremilast (JAK inhibitor and PDE4 inhibitor, respectively) were analyzed separately from the other OSMs. When determining the index event, patients were required to have at least 1 refill for the index medication within 60 days of the index claim. Patients could receive monotherapy with any PsA medication or combination therapy with multiple PsA medications (≥ 2 medications initially prescribed within 15 days of index date and refilled ≥ 1 time within 60 days of run-out of original fill). Second-line treatments were defined as regimens among patients who switched or had first-line combination pharmacologic therapy and discontinued 1 of the 2 medications

TAKEAWAY POINTS

The initial treatment patterns across all medications in psoriatic arthritis (PsA) are not well known, especially the magnitude and type of initial medication use, either as monotherapy or in combination with other drugs. Our study fills this gap in the literature.

- ▶ Initial treatment for PsA is mostly methotrexate monotherapy, even without guideline recommendations for first-line use of methotrexate for treating PsA.
- ▶ Approximately 1 in 4 treatment-naïve patients initiated a tumor necrosis factor inhibitor monotherapy as the first treatment for PsA.
- ▶ Treatment with biologic monotherapy and combination therapy with oral small molecules, particularly methotrexate, were the most common second-line regimens.

during the follow-up period. In addition, second-line calculations excluded patients who persisted or restarted index medication therapy and patients who discontinued all pharmacologic therapies.

The data were previously collected and statistically deidentified and are compliant with the Health Insurance Portability and Accountability Act of 1996 Privacy Rule; therefore, institutional review board approval and patient informed consent were not required for this analysis of claims data.

Patient Identification

Eligible patients had at least 1 inpatient or 2 outpatient nondiagnostic medical claims at least 30 days apart carrying a diagnosis of PsA between January 1, 2010, and March 31, 2017 (**eAppendix Table 1** includes the list of billing codes used in this study [eAppendix available at ajmc.com]). Patients had to be 18 years or older at the index date and have at least 1 inpatient or 2 outpatient nondiagnostic medical claims for a PsA medication within 30 days before and up to 90 days after the PsA date; at least 18 months of continuous enrollment and pharmacy benefits preceding the initial PsA diagnosis and an absence of nondiagnostic medical claims for PsA before the date of PsA diagnosis; at least 18 months of continuous enrollment and pharmacy benefits before the index date; absence of any PsA medication use during the preindex period; absence of prescription fills for antituberculosis drugs, antivirals, anti-infectives, antimalarials, antifungals, antiglycosides, anthelmintics, sulfonamides, quinolones, amebicides, or antibiotics within 1 month before the index date; at least 12 months of continuous enrollment after the index date; and absence of any claim with a diagnosis code for rheumatoid arthritis, ankylosing spondylitis, Crohn disease, ulcerative colitis, juvenile idiopathic arthritis, tuberculosis, hepatitis B, hepatitis C, or HIV during the study period.

Study Outcomes

Study outcomes included index (first) therapy (ie, claims for PsA medication[s] on index date), the percentage of patients persistent on index therapy at 12 months post index, treatment patterns, and costs. Persistence was defined as no gap of at least 60 days for the index therapy and no switch to a different PsA medication. Treatment patterns included restarts (gap ≥ 60 days without switching), switches (claim for nonindex therapy with or without ≥ 60 -day gap), and the

TABLE 1. Demographic and Clinical Characteristics

	All patients (N = 3491)
Age in years, mean (SD)	49.5 (12.0)
Sex, female, n (%)	1802 (51.6)
Geographic region, n (%)	
Northeast	719 (20.6)
North Central	749 (21.5)
South	1475 (42.3)
West	527 (15.1)
Unknown	21 (0.6)
Payer, n (%)	
Commercial	3224 (92.4)
Medicare	267 (7.6)
Insurance plan type, n (%)	
Basic/comprehensive	195 (5.6)
EPO/PPO	2102 (60.2)
HMO	271 (7.8)
POS with/without capitation	452 (12.9)
CDHP/HDHP	373 (10.7)
Unknown	98 (2.8)
Physician specialty at PsA diagnosis, n (%)	
Rheumatologist	2026 (58.0)
Dermatologist	212 (6.1)
Primary care	843 (24.1)
Other physician specialist	229 (6.6)
Other physician	181 (5.2)
Deyo-Charlson Comorbidity Index score during preindex period, mean (SD)	0.4 (0.9)
Comorbid psoriasis, n (%)	1809 (51.8)

CDHP, consumer-directed health plan; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; PsA, psoriatic arthritis.

addition of a second medication. We defined combination therapy as a switch from monotherapy to combination therapy with a 30-day overlap in days' supply for both medications or a new single medication with an additional drug prescribed within 15 days of the second new drug (start of second line of therapy).

We calculated all-cause health care costs based on paid amounts of adjudicated claims, including insurer and health plan payments and patient cost sharing in the form of co-payment, deductible, and coinsurance. All costs were adjusted for inflation using the medical care component of the Consumer Price Index and expressed in 2018 US\$. We captured costs using 3 methods: as total costs summed over the 12-month follow-up period, as per-patient per-month (PPPM) costs over the unique period of time that a patient was on index therapy, and as PPPM costs over the second-line therapy for patients who received second-line therapy. Health care costs included inpatient, outpatient, emergency department, outpatient hospital, physician office visit, other outpatient services, outpatient

pharmacy, PsA medication costs, and total health care costs (the sum of all costs). Medication costs for drugs administered orally or subcutaneously were captured in outpatient pharmacy claims; medication costs for drugs administered intravenously were captured in medical/procedural claims.

Statistical Considerations

To account for the variable follow-up period, we calculated PPPM and total 12-month measures for costs. For example, PPPM costs were calculated by dividing the total costs incurred during follow-up by the number of days in follow-up while patients were persistent on index therapy and then multiplying the resultant per-day costs by 30 to normalize costs to a 30-day (monthly) unit. Total annual costs were estimated by summing costs and dividing by the months of follow-up (regardless of whether patients were still persistent on index therapy) and multiplying by 12.

Role of Sponsor

The study sponsor designed this retrospective study in collaboration with the nonsponsor authors, oversaw the data collection and analyses, and supported the development of this manuscript. Data interpretation and writing of this manuscript were performed by both the sponsor and nonsponsor authors.

RESULTS

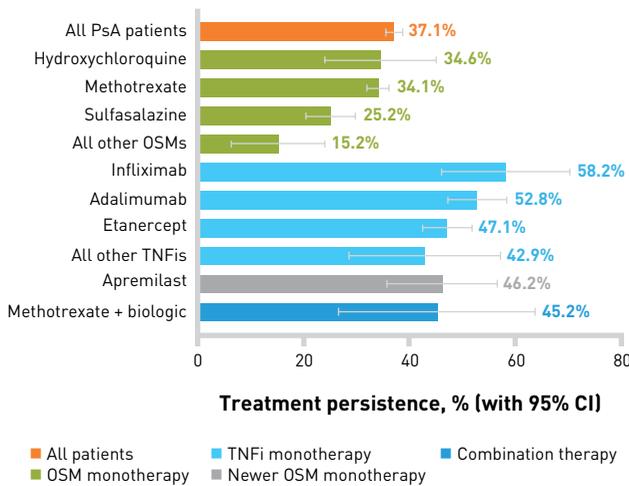
Study Population

A total of 3491 patients met the criteria to be included in this study (eAppendix Table 2). The distribution of index treatments was methotrexate (n = 2034; 58.3%), sulfasalazine (n = 342; 9.8%), hydroxychloroquine (n = 81; 2.3%), other OSMs (n = 66; 1.9%), adalimumab (n = 431; 12.3%), etanercept (n = 299; 8.6%), infliximab (n = 67; 1.9%), other TNFi (n = 49; 1.4%), and apremilast (n = 91; 2.6%). Thirty-one patients (0.9%) received combination therapy with methotrexate and a TNFi. Medication cohorts with fewer than 30 patients were included in the sample but were aggregated and reported in an "other" category (eg, "other OSMs" and "other TNFi"). The mean (SD) age at index date was 49.5 (12.0) years, approximately one-half of patients were women (51.6%), and most patients had commercial insurance (92.4%) (Table 1; eAppendix Table 3).

Treatment Patterns

The percentage of patients with newly diagnosed PsA who remained on index therapy at 12 months post index (ie, were persistent) with claims for OSM monotherapy ranged from 15.2% to 34.6%, whereas persistence for patients with claims for TNFi monotherapy ranged from 42.9% to 58.2% (Figure 1; Table 2). The percentages of patients with gaps in therapy (≥ 60 days without switching) ranged from 42.9% to 48.5% for OSMs and from 17.9% to 29.9% for TNFi monotherapy. The percentages of patients who added a medication to their index therapy ranged from 17.8% to 29.6% for OSMs, 6.1% to 11.9% for TNFi monotherapy, and 8.8% for apremilast.

FIGURE 1. Treatment Persistence During the 12-Month Postindex Period by Index Therapy Class^a



OSM, oral small molecule; PsA, psoriatic arthritis; TNFi, tumor necrosis factor inhibitor.

^aThe percentage of patients who had no treatment gaps or changes to index therapy during 1 year of follow-up is shown for all patients with PsA (orange bar) and for patients with claims for OSM monotherapy (green), TNFi monotherapy (light blue), newer OSM monotherapy (gray), and combination therapy with methotrexate and a biologic (medium blue).

For patients who switched from index therapy (n = 1349), the most common second-line therapy was combination therapy with methotrexate and a TNFi. Among those with a second-line regimen during the 12-month follow-up period, the percentage of patients receiving a TNFi as monotherapy was 29.3%, those receiving a TNFi in combination with an OSM was 41.5%, and those receiving an OSM

alone or in combination with a nonbiologic was 18.3%. The most common second-line OSM monotherapy was methotrexate (6.4%) and the most common second-line TNFi was adalimumab (12.8%), followed by etanercept (11%) (eAppendix Table 4).

Costs

The mean unadjusted total health care costs during the 12-month follow-up period for patients with newly diagnosed PsA ranged from \$19,173 to \$25,013 for patients on OSMs and \$45,635 to \$60,933 for those on TNFis and other biologics (Figure 2).

Patients with newly diagnosed PsA who were prescribed OSMs had mean (unadjusted) PPPM total health care costs ranging from \$1029 to \$1456, with outpatient prescription costs contributing the highest proportion of costs (range, \$299-\$547) (Figure 3). Patients with new PsA who were prescribed TNFis and other biologics had mean (unadjusted) PPPM total health care costs ranging from \$4203 to \$7063 (Figure 3). Similar to the OSM class, in the therapy class of TNFis and other biologics, outpatient prescriptions contributed the highest proportion of costs (range, \$225-\$4019).

For second-line therapies, mean PPPM all-cause health care costs were lowest for methotrexate and other OSMs (range, \$925-\$1342) and highest for TNFi and other biologic medications (range, \$4401-\$7095) (eAppendix Figure).

DISCUSSION

In this analysis of claims data from patients with newly diagnosed active PsA, the majority of patients (99.1%) started their treatment with medication monotherapy. Methotrexate monotherapy was the most common index therapy (58.3%), and approximately a quarter of patients (24.2%) started on TNFi monotherapy. Notably, patients with index claims for OSMs, including methotrexate, had

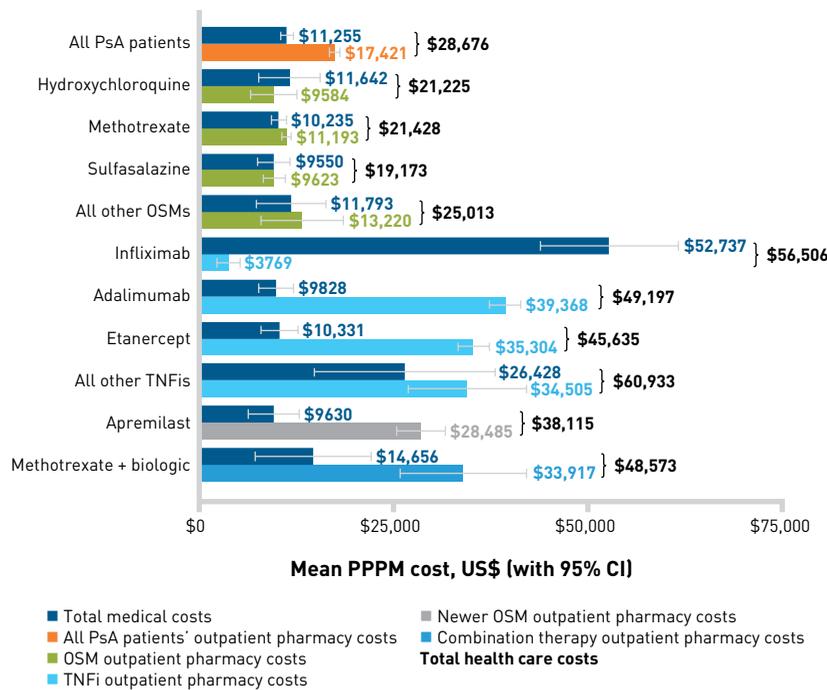
TABLE 2. Treatment Patterns by Index Therapy Class

Therapy class	n	Persistent n (%)	Gap ^a without switching n (%)	Switched		Added second medication n (%)
				With gap ^a n (%)	Without gap ^a n (%)	
OSM						
Methotrexate	2034	693 (34.1)	872 (42.9)	97 (4.8)	372 (18.3)	579 (28.5)
Sulfasalazine	342	86 (25.1)	160 (46.8)	13 (3.8)	83 (24.3)	61 (17.8)
Hydroxychloroquine	81	28 (34.6)	36 (44.4)	1 (1.2)	16 (19.8)	24 (29.6)
All other OSMs	66	10 (15.2)	32 (48.5)	3 (4.5)	21 (31.8)	19 (28.8)
TNFi						
Adalimumab	431	203 (47.1)	129 (29.9)	30 (7.0)	69 (16.0)	44 (10.2)
Etanercept	299	158 (52.8)	59 (19.7)	14 (4.7)	68 (22.7)	19 (6.4)
Infliximab	67	39 (58.2)	12 (17.9)	0	16 (23.9)	8 (11.9)
All other TNFis and biologics	49	21 (42.9)	10 (20.4)	12 (24.5)	6 (12.2)	3 (6.1)
Newer OSM						
Apremilast	91	42 (46.2)	22 (24.2)	8 (8.8)	19 (20.9)	8 (8.8)

OSM, oral small molecule; TNFi, tumor necrosis factor inhibitor.

^aGap was defined as ≥ 60 days without prescription refill.

FIGURE 2. Total Costs During the Postindex Period*



OSM, oral small molecule; PPPM, per-patient per-month; PsA, psoriatic arthritis; TNFi, tumor necrosis factor inhibitor.
 *Shown are the total medical costs (dark blue) and total outpatient prescription costs for all patients with PsA (orange) and patients with claims for OSMs (green), TNFi (light blue), newer OSM (gray), or combination therapy (medium blue) regimens. Costs are expressed in 2018 US\$. Medical and pharmacy costs may not add up to total costs due to rounding.

low rates of persistence with index therapy and high rates of gaps in their therapies, which likely affected the costs associated with these medications. Patients with index claims for OSMs also had low PPPM and mean total health care costs.

As noted in this analysis, biologic medications are more costly than other drugs, such as OSMs, used to treat PsA.¹⁰ However, the disease-modifying properties of TNFis and other biologics may translate into long-term savings and better outcomes for patients. Because medical and pharmacy claims data do not contain measures of disease severity, it is not possible to determine how the disease activity of each patient—or other patient and prescriber characteristics—influenced the treatment choice and cost outcomes for these patients. That is, although the medical costs were generally similar across OSMs, adalimumab, etanercept, and apremilast, there may be confounding by indication that we were unable to address in these analyses. There is evidence that direct medical costs of TNFi-treated patients decrease when examined longitudinally,¹¹ although additional studies are warranted. A recent systematic review of treatments for PsA suggested that TNFis are cost-effective compared with OSMs and that the costs of these drugs are offset by better efficacy in treating the signs and symptoms of the disease and improvements in quality of life.¹² Real-world evidence as provided in this study on medication use by patients may help

payers understand the total costs of PsA, not just those related to prescriptions.

Limitations

The study population was limited to individuals with commercial health coverage or private Medicare supplemental coverage and may not be generalizable to patients with PsA with other types of insurance or without health insurance coverage. The potential for misclassification of PsA or study outcomes exists, as patients were identified through administrative claims data, which are subject to data coding limitations and data entry errors. Our analysis was designed to evaluate treatment patterns and costs among the incident PsA population. In our sample, incident patients represented approximately 3% of the total PsA population and approximately 7% of patients with PsA receiving treatment. Therefore, the results of this study may not be generalizable to the entire patient population with PsA. Apremilast was not approved for the treatment of PsA during the entire study period, and relative utilization may therefore be underestimated. Costs of medications administered intravenously were included in medical claims and not outpatient pharmacy claims and therefore are not compared with costs of medications administered orally or

subcutaneously. Cost calculations using PPPM and total 12-month costs measure utilization differently, and thus the estimates for each medication may differ slightly. PPPM calculations take into account only costs incurred while patients were taking the index therapy. Confounding by indication and patient selection issues prevent us from drawing conclusions on the effect of medication regimen on outcomes, such as medication adherence, persistence, and health care costs. We believe that it would be interesting to map the treatment patterns seen in our study to the ACR treatment guidelines; however, to do so would require information on the severity of disease because the treatment guidelines are based on disease severity. Although an algorithm to estimate disease severity from insurance claims has been developed for patients with rheumatoid arthritis, a similar algorithm is, unfortunately, not available for patients with PsA. Because our study focuses on a snapshot of treatment patterns for patients during the years both before and after ACR guidelines were published, we believe that comparing our findings with the new ACR guidelines would be out of scope for this study.

CONCLUSIONS

We used administrative claims data to evaluate real-world treatment patterns and health care costs for patients with newly diagnosed

PsA. Our study fills the existing gap in research by identifying initial treatment patterns of treatment-naïve patients with PsA, providing a baseline for future studies to evaluate treatment trends and identify potential confounders. Most patients were initially prescribed monotherapy with the least expensive medications for PsA, despite evidence suggesting that TNFis may be more cost-effective than OSMs¹² and recommendations for using TNFis as first-line therapy by the most recent treatment guidelines. In addition, our study examined the costs of all medications, as well as the health care costs among the treatment-naïve patients with PsA. Real-world evidence on medication use by patients may help payers understand the true costs of therapy and health care, although variations in dosing, administration, and maintenance schedules across available treatments may complicate these efforts. Studies are warranted to further examine cost-effectiveness of therapies for PsA and their effect on overall health care costs. ■

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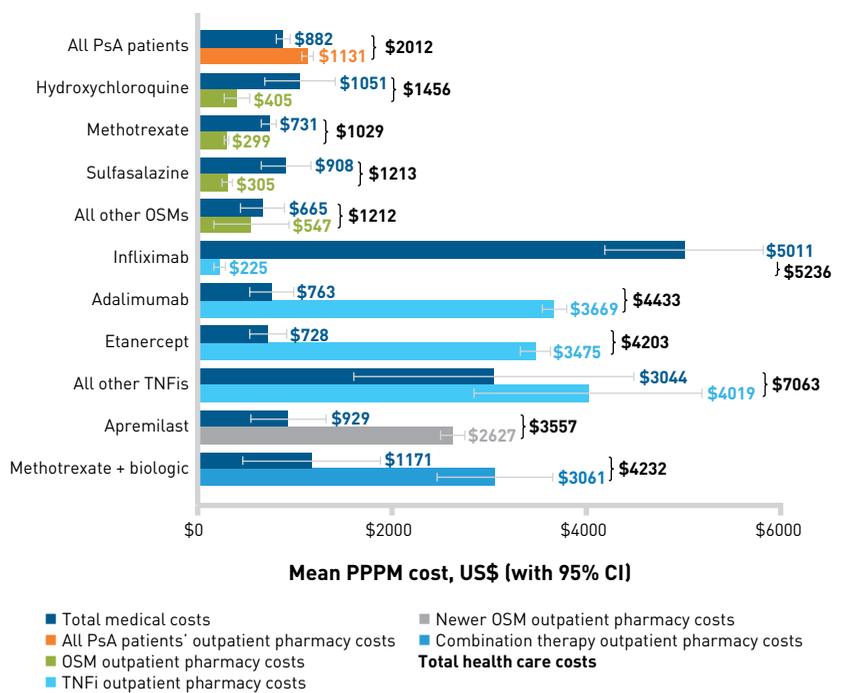
Authorship Information: Concept and design (EJMH, JT, LL-G, KH, AO, BSS); acquisition of data (LL-G); analysis and interpretation of data (EJMH, JT, LL-G, KH, AO, BSS); drafting of the manuscript (EJMH, JT, BSS); critical revision of the manuscript for important intellectual content (EJMH, JT, LL-G, AO, BSS); statistical analysis (EJMH, JT, LL-G); obtaining funding (EJMH, JT, BSS); administrative, technical, or logistic support (JT, LL-G, KH); and supervision (EJMH, LL-G).

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FIGURE 3. PPPM Costs During Index Treatment Regimen*



OSM, oral small molecule; PPPM, per-patient per-month; PsA, psoriatic arthritis; TNFi, tumor necrosis factor inhibitor.

*Shown are the total PPPM medical costs (dark blue) and total PPPM outpatient prescription costs for all patients with PsA (orange) and patients with claims for OSMs (green), TNFi (light blue), newer OSM (gray), or combination therapy (medium blue) regimens. Utilization and expenditures were captured from index date until the earliest date for index therapy discontinuation or switch or until 12 months post index for persistent patients. Costs are expressed in 2018 US\$. Medical and pharmacy costs may not add up to total costs due to rounding.

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Supplemental eAppendix

Psoriatic Arthritis Treatment Patterns and Costs Among Pharmacologic Treatment-Naïve Patients

eAppendix Table 1. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes used for included and excluded conditions

eAppendix Table 2. Patient identification

eAppendix Table 3. Demographic and clinical characteristics by index therapy

eAppendix Table 4. Secondary treatment incidence by index therapy

eAppendix Figure. Per-patient-per-month costs across second-line therapies

eAppendix Table 1. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes used for included and excluded conditions

Code Type	Code	Description	Condition
Inclusion criteria			
ICD-9-DX	696.0	Psoriatic arthropathy	Psoriatic arthritis
Exclusion criteria			
ICD-9 DX	7140	Rheumatoid arthritis	Rheumatoid arthritis
ICD-9 DX	7200	Ankylosing spondylitis	Ankylosing spondylitis
ICD-9 DX	5550	Regional enteritis of small intestine	Crohn's Disease
ICD-9 DX	5551	Regional enteritis of large intestine	Crohn's Disease
ICD-9 DX	5552	Regional enteritis of small intestine with large intestine	Crohn's Disease
ICD-9 DX	5559	Regional enteritis of unspecified site	Crohn's Disease
ICD-9 DX	71430	Polyarticular juvenile rheumatoid arthritis, chronic or unspecified	Juvenile idiopathic arthritis
ICD-9 DX	71431	Polyarticular juvenile rheumatoid arthritis, acute	Juvenile idiopathic arthritis
ICD-9 DX	71432	Pauciarticular juvenile rheumatoid arthritis	Juvenile idiopathic arthritis
ICD-9 DX	71433	Monoarticular juvenile rheumatoid arthritis	Juvenile idiopathic arthritis
ICD-9 DX	5560	Ulcerative (chronic) enterocolitis	Ulcerative colitis
ICD-9 DX	5561	Ulcerative (chronic) ileocolitis	Ulcerative colitis
ICD-9 DX	5562	Ulcerative (chronic) proctitis	Ulcerative colitis
ICD-9 DX	5563	Ulcerative (chronic) proctosigmoiditis	Ulcerative colitis
ICD-9 DX	5564	Pseudopolyposis of colon	Ulcerative colitis
ICD-9 DX	5565	Left-sided ulcerative (chronic) colitis	Ulcerative colitis
ICD-9 DX	5566	Universal ulcerative (chronic) colitis	Ulcerative colitis
ICD-9 DX	5568	Other ulcerative colitis	Ulcerative colitis
ICD-9 DX	5569	Ulcerative colitis, unspecified	Ulcerative colitis

ICD-9 DX	010 – 018	Tuberculosis	Tuberculosis
ICD-9 DX	0702 – 0703	Hepatitis B	Hepatitis B
ICD-9 DX	0704 – 0707	Hepatitis C	Hepatitis C
ICD-9 DX	795.71	Human immunodeficiency virus	Human immunodeficiency virus

eAppendix Table 2. Patient identification

Eligibility Criteria	Patients Remaining N
Patients with ≥ 1 inpatient or 2 outpatient nondiagnostic medical claims ≥ 30 days apart carrying a diagnosis of PsA between 1/1/2010 and 3/31/2017	110,144
Claim for conventional OSM, TNFI, or newer OSM within 30 days prior to or 90 days following PsA diagnosis (date of first claim = index date)	48,968
With ≥ 18 months of continuous enrollment and pharmacy benefits before PsA diagnosis date	23,259
No nondiagnostic medical claims for PsA prior to PsA diagnosis	14,163
With ≥ 18 months of continuous enrollment and pharmacy benefits during the pre-index period	13,802
No claim for OSM, TNFI, non-TNFI biologics, or newer OSM use during the 18-month pre-index period	7301
No prescription fill for antituberculosis, antivirals, anti-infectives, antimalarials, antifungals, antiglycosides, anthelmintics, sulfonamides, quinolones, amebicides, or antibiotics within 1 month before the index date	6176
Aged ≥ 18 years at index date	6083
With ≥ 12 months of continuous enrollment following the index date and no claims with an ICD-9-CM diagnosis code for rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, juvenile idiopathic arthritis, tuberculosis, hepatitis B and C, or human immunodeficiency virus during the study period	3509
Total analysis set (also excludes treatment cohorts with <30 patients)	3491

ICD-9-CM indicates International Classification of Diseases, Ninth Revision, Clinical Modification; OSM, oral small molecule drug;

PsA, psoriatic arthritis; TNFI, tumor necrosis factor inhibitor.

eAppendix Table 3. Demographic and clinical characteristics by index therapy

	OSMs			TNFI				Newer OSM		MTX + Biologic
	MTX n=2034	SSZ n=342	HCQ n=81	All Other OSMs n = 66	ADA n = 431	ETA n = 299	INF n = 67	All Other TNFI and Biologics n = 49	APR n = 91	
N=3491										
Age, mean (SD), years	50.1 (11.7)	50.2 (12.3)	51.0 (11.4)	52.2 (11.6)	45.9 (11.9)	47.8 (11.6)	53.4 (14.2)	49.7 (13.3)	52.6 (11.2)	45.7 (11.7)
Sex, female, n (%)	1092 (53.7)	180 (52.6)	57 (70.4)	31 (47.0)	203 (47.1)	123 (41.1)	24 (35.8)	22 (44.9)	53 (58.2)	17 (54.8)
Geographic region, n (%)										
Northeast	404 (19.9)	93 (27.2)	18 (22.2)	13 (19.7)	74 (17.2)	60 (20.1)	12 (17.9)	13 (26.5)	29 (31.9)	3 (9.7)
North central	463 (22.8)	80 (23.4)	16 (19.8)	14 (21.2)	76 (17.6)	47 (15.7)	14 (20.9)	8 (16.3)	22 (24.2)	9 (29.0)
South	837 (41.2)	116 (33.9)	35 (43.2)	33 (50.0)	219 (50.8)	136 (45.5)	31 (46.3)	22 (44.9)	33 (36.3)	13 (41.9)
West	319 (15.7)	51 (14.9)	12 (14.8)	6 (9.1)	57 (13.2)	55 (18.4)	10 (14.9)	6 (12.2)	6 (6.6)	5 (16.1)
Unknown	11 (0.5)	2 (0.6)	0	0	5 (1.2)	1 (0.3)	0	0	1 (1.1)	1 (3.2)
Payer, n (%)										
Commercial	1868 (91.8)	313 (91.5)	77 (95.1)	60 (90.9)	419 (97.2)	281 (94.0)	53 (79.1)	41 (83.7)	81 (89.0)	31 (100)
Medicare	166 (8.2)	29 (8.5)	4 (4.9)	6 (9.1)	12 (2.8)	18 (6.0)	14 (20.9)	8 (16.3)	10 (11.0)	0
Insurance plan, n (%)										
Basic/comprehensive	117 (5.8)	19 (5.6)	4 (4.9)	4 (6.1)	16 (3.7)	16 (5.4)	5 (7.5)	5 (10.2)	5 (5.5)	4 (12.9)
EPO/PPO	1205 (59.2)	206 (60.2)	51 (63.0)	41 (62.1)	285 (66.1)	169 (56.5)	41 (61.2)	27 (55.1)	61 (67.0)	16 (51.6)
HMO	168 (8.3)	21 (6.1)	8 (9.9)	6 (9.1)	28 (6.5)	21 (7.0)	6 (9.0)	1 (2.0)	7 (7.7)	5 (16.1)
POS ± capitation	253 (12.4)	58 (17.0)	8 (9.9)	6 (9.1)	55 (12.8)	46 (15.4)	12 (17.9)	6 (12.2)	5 (5.5)	3 (9.7)
CDHP/HDHP	225 (11.1)	27 (7.9)	6 (7.4)	9 (13.6)	39 (9.0)	40 (13.4)	3 (4.5)	9 (18.4)	13 (14.3)	2 (6.5)
Unknown	66 (3.2)	11 (3.2)	4 (4.9)	0	8 (1.9)	7 (2.3)	0	1 (2.0)	0	1 (3.2)

	OSMs			TNFI				Newer OSM		MTX + Biologic n = 31
	MTX n=2034	SSZ n=342	HCQ n=81	All Other OSMs n = 66	ADA n = 431	ETA n = 299	INF n = 67	All Other TNFI and Biologics n = 49	APR n = 91	
N=3491										
Physician specialty, n (%)										
Rheumatologist	1212 (59.6)	215 (62.9)	38 (46.9)	42 (63.6)	235 (54.5)	170 (56.9)	35 (52.2)	18 (36.7)	44 (48.4)	17 (54.8)
Dermatologist	70 (3.4)	4 (1.2)	0	1 (1.5)	65 (15.1)	31 (10.4)	4 (6.0)	12 (24.5)	22 (24.2)	3 (9.7)
Primary care	517 (25.4)	76 (22.2)	29 (35.8)	15 (22.7)	89 (20.6)	71 (23.7)	10 (14.9)	11 (22.4)	17 (18.7)	8 (25.8)
Other specialist	142 (7.0)	22 (6.4)	6 (7.4)	7 (10.6)	20 (4.6)	15 (5.0)	8 (11.9)	2 (4.1)	6 (6.6)	1 (3.2)
Other physician	93 (4.6)	25 (7.3)	8 (9.9)	1 (1.5)	22 (5.1)	12 (4.0)	10 (14.9)	6 (12.2)	2 (2.2)	2 (6.5)
Deyo-Charlson										
Comorbidity Index, mean										
(SD) score	0.4 (0.9)	0.4 (1.0)	0.5 (0.9)	0.8 (1.2)	0.3 (0.8)	0.3 (0.7)	0.4 (0.8)	0.7 (1.3)	0.8 (1.4)	0.5 (1.1)
Comorbid psoriasis, n (%)										
	982 (48.3)	119 (34.8)	17 (21.0)	31 (47.0)	296 (68.7)	191 (63.9)	54 (80.6)	39 (79.6)	61 (67.0)	19 (61.3)

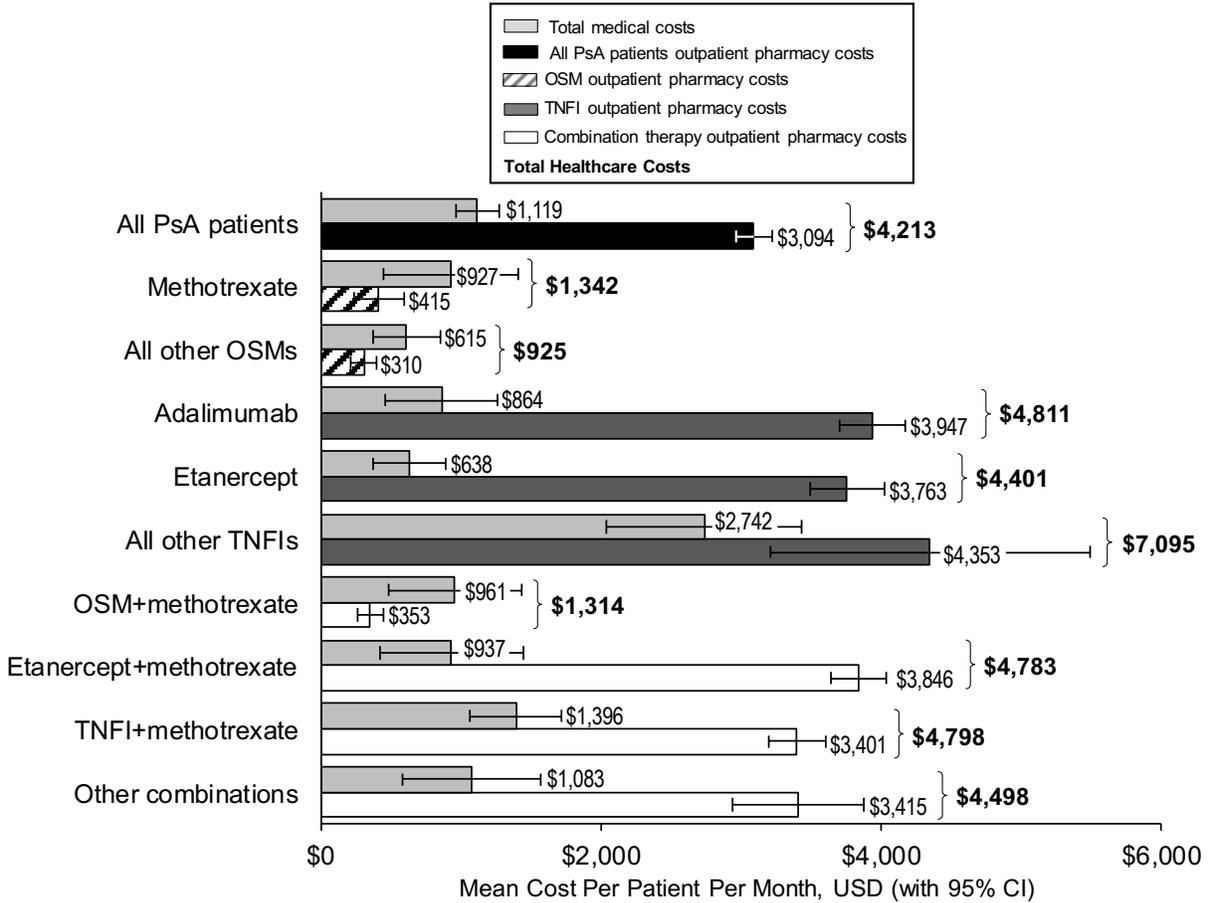
ADA indicates adalimumab; APR, apremilast; CDHP, consumer directed health plan; EPO, exclusive provider organization; ETA, etanercept; HCQ, hydroxychloroquine; HDHP, high deductible health plan; HMO, health maintenance organization; INF, infliximab; MTX, methotrexate; OSM, oral small molecule drug; POS, point of service; PPO, preferred provider organization; SD, standard deviation; SSZ, sulfasalazine; TNFI, tumor necrosis factor inhibitor.

eAppendix Table 4. Secondary treatment incidence by index therapy

Second-Line Therapy (N = 1349)	Patients Switching to Second-Line Therapy n (%)
OSMs	
Methotrexate	86 (6.4)
Sulfasalazine	18 (1.3)
Hydroxychloroquine	9 (0.7)
All other OSMs	39 (2.9)
TNFIs	
Adalimumab	172 (12.8)
Etanercept	149 (11.0)
Infliximab	29 (2.1)
All other TNFIs and biologics	45 (3.3)
Newer OSM	
Apremilast	30 (2.2)
Combination therapies	
Methotrexate + etanercept	204 (15.1)
Methotrexate + other TNFI and biologics	356 (26.4)
Methotrexate + other OSMs	95 (7.0)
All other combinations	117 (8.7)

OSM indicates oral small molecule drug; TNFI, tumor necrosis factor inhibitor.

eAppendix Figure. PPPM costs during second-line therapies.



The total PPPM medical costs (light gray) and total PPPM outpatient prescription costs for all patients with PsA (black) and patients with claims for OSMs (cross-hatched), TNFI (dark gray), or combination therapy (white) regimens are shown. CI indicates confidence interval; OSM, oral small molecule drug; PPPM, per-patient-per-month; PsA, psoriatic arthritis; TNFI, tumor necrosis factor inhibitor.