



REVIEW

Real-World Evidence for Ixekizumab in the Treatment of Psoriasis, Psoriatic Arthritis, and Axial Spondyloarthritis: Systematic Literature Review 2022–2023

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ABSTRACT

Objective: To describe the results of a systematic literature review of real-world outcomes with ixekizumab in psoriasis (PsO), psoriatic arthritis (PsA), or axial spondyloarthritis (axSpA).

Methods: Databases, conference proceedings, and additional sources were searched for

real-world studies in ≥ 25 patients treated with ixekizumab for PsO, PsA, or axSpA. Data on clinical effectiveness, patient-reported outcomes, treatment patterns, safety, and economic burden were extracted.

Results: A total of 118 publications were included, 96 in PsO, 16 in PsA, 5 in both PsO and PsA, and 1 in axSpA. Most focused on clinical effectiveness and treatment patterns. Ixekizumab was effective in real-world settings, and the anti-interleukin (IL)-17A biologics were more effective for skin clearance than comparator biologics. Anti-IL-17A biologics were effective for challenging body areas (nails, scalp, genitals, palmoplantar regions), and ixekizumab was associated with a higher chance of obtaining Dermatology Life Quality Index scores of 0/1 than secukinumab or other biologics. Ixekizumab was associated with generally high persistence/drug survival. No unexpected safety signals were identified.

Conclusion: Real-world ixekizumab use for PsO and PsA is effective and safe, with a positive impact on patient quality of life. More data are needed to draw conclusions for real-world ixekizumab use in axSpA.

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Key Summary Points

Ixekizumab is an interleukin-17A inhibitor that has demonstrated efficacy in the treatment of moderate-to-severe psoriasis, active psoriatic arthritis, and axial spondyloarthritis (axSpA).

In this systematic literature review, real-world data from over 100 relevant publications demonstrated high Psoriasis Area and Severity Index responses, with ixekizumab treatment and safety similar to that seen in the clinical trials.

In the real-world setting, ixekizumab was shown to have a positive impact on patient quality of life and generally high levels of persistence and drug survival.

This review updates a previous review and fills in some identified gaps, such as a need for patient-reported outcome data, but real-world data for ixekizumab in patients with axSpA are still needed.

INTRODUCTION

Ixekizumab, an interleukin (IL)-17A inhibitor, has been available for the treatment of moderate-to-severe plaque psoriasis (PsO) since 2016, for psoriatic arthritis (PsA) since 2017, and for axial spondyloarthritis (axSpA) since 2019 [1–3]. PsA and axSpA are both spondyloarthropathies—inflammatory rheumatic disorders of the peripheral joints and entheses, the axial skeleton, and sacroiliac joints [4, 5]—and PsO, a chronic inflammatory, immune-mediated skin disease, has a close epidemiologic, genetic, and pathogenetic association with PsA [6–9].

IL-17A, a member of the IL-17 family, is known to play an important role in skin, joint, and axial manifestations of the spondyloarthropathies [10], and targeting this cytokine is an effective strategy for treating PsO, PsA, and axSpA [11–15].

In patients with moderate-to-severe PsO, PsA, and axSpA, the burden of disease is high

and the impact on quality of life (QoL) substantial, affecting physical and social functioning and work productivity [16]. Therapeutic goals therefore include maximizing long-term health-related QoL (HRQoL) through control of symptoms and inflammation, preventing progressive structural damage, and preserving function and social participation [17, 18].

Clinical trials have shown the superiority of ixekizumab to tumor necrosis factor (TNF) inhibition and have highlighted its rapid onset of action relative to agents targeting IL-12 and IL-23, such as ustekinumab, or IL-23, such as guselkumab, in the treatment of PsO [19–21]. In PsA, there are several head-to-head trials, but only SPIRIT H2H has demonstrated the superiority of ixekizumab to adalimumab for the combined endpoint of joint and skin improvement after 24 and 52 weeks [22, 23]. While there is a lack of head-to-head trials in axSpA, the IL-17A inhibitors have been shown to inhibit radiographic disease progression [24], whereas there is no evidence supporting a role of the IL-23s [25], in those with this spondyloarthropathy.

Real-world evidence is increasingly important [26–28], as drugs are used in broader, less tightly defined patient populations than in clinical trials [28]. Since the marketing authorization of ixekizumab, a substantial volume of real-world evidence has been published, particularly in PsO [3]. A systematic literature review (SLR) covering real-world evidence for ixekizumab in the treatment of PsO and PsA from 2016 to 2021 identified 51 relevant publications and demonstrated that real-world use of ixekizumab was effective and safe, with generally high treatment persistence and adherence [3]. This review identified several gaps in the literature, including a lack of patient-reported outcome (PRO) data and data on the real-world use of ixekizumab in patients with PsA. The aim of the current publication is to describe the results of an updated SLR, covering the most recent literature [3], with the aim of presenting an up-to-date overview of real-world outcomes, including but not restricted to clinical effectiveness, PROs, treatment patterns, safety, and economic burden associated with the use of ixekizumab in PsO, PsA, and axSpA in the real-world setting.

PATIENTS AND METHODS

This SLR used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement-validated methodology [29].

Ethical Approval

This SLR is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Published Literature Search

A search of the published literature was conducted on July 19, 2023, covering June 8, 2022, to July 19, 2023, and was then repeated on November 15, 2023, covering July 20, 2023, to November 15, 2023, using the OvidSP® platform to search MEDLINE®, Embase, and EBM Reviews® databases using disease- and drug-related keywords relevant to PsO, PsA, and axSpA (Supplementary Table 1). MEDLINE® searches included publications online ahead of print, in-process publications, and other non-indexed citations and MEDLINE® Daily and Versions® 1946 to present. The EBM reviews database included the Cochrane Database of Systematic Reviews, Cochrane Clinical Answers, Cochrane Central Register of Controlled Trials, ACP Journal Club, and Cochrane Methodology Register. The search was restricted to English language publications and human studies.

Conference Proceedings and Grey Literature Search

The proceedings of selected international, national, and regional conferences held between June 2022 and November 2023 were searched (Supplementary Table 2). Targeted hand searches were conducted using tools such as Google and Google Scholar to capture any relevant outcomes reported separately from the literature of this review. Additionally, the reference lists of

relevant reviews were cross-checked to screen for potentially relevant studies. Additional studies were also sourced from publications or grey literature suggested for inclusion by the peer reviewers of Eli Lilly-sponsored publications and from iEnVision (Eli Lilly publications database).

Inclusion and Exclusion Criteria

The publication eligibility criteria were based on the Patients, Interventions, Comparators, Outcomes, Timeframe, and Setting (PICOTS) framework. The same criteria were applied to electronic databases, conference proceedings, targeted hand searches, and suggested literature. Full eligibility criteria are described in Supplementary Table 3. Briefly, included publications were those that involved patients with PsO, PsA, or axSpA, with ixekizumab as an intervention, without any restriction on comparators, investigating outcomes related to clinical effectiveness, QoL, and other PROs using validated tools, treatment patterns, safety, and economic outcomes. Eligible study designs were observational studies, pragmatic studies, and cost studies, with at least 25 patients treated with ixekizumab, whereas clinical trials, case reports, case series, protocols, commentaries and editorials, letters (unless reporting research results), and reviews were excluded. There were no restrictions on the country of the study.

Selection Process

The de-duplicated citations were screened using the automated literature review software, DistillerSR, based on the publication titles and/or abstracts. Abstracts unable to be excluded at the title/abstract screening phase were retained for full-text screening by a human reviewer. The full text of publications deemed potentially relevant in the title/abstract screening were retrieved for the next level of screening. At least 10% of publications at each selection level were referred to a second reviewer for quality checks. Any discrepancies were resolved by consensus.

Data Extraction

Data from eligible publications were extracted by one reviewer using a structured data extraction grid. The extracted data were quality-checked by a second reviewer against the source publication and any discrepancy resolved by consensus. Unresolved discrepancies in data extraction were referred to a senior reviewer for arbitration. Extracted data included publication information, identifying features of the study, methods, population characteristics, interventions, outcomes, and conclusions.

Assessment of Bias

The full text of all included publications was assessed for quality using the relevant UK National Institute for Health and Care Excellence checklists [30, 31].

RESULTS

Study Selection

The number of hits from databases on July 19, 2023, was 608, with 47 from conference proceedings, and 34 from the internal Eli Lilly database (iEnVision). An additional 223 hits were identified from databases on November 15, 2023, along with 20 from websites and 20 from conference proceedings (Fig. 1). Overall, a total of 121 publications met the inclusion criteria for review, 3 of which were subsequently excluded from this analysis as they were linked to other publications that provided results from the same study in greater detail.

Of the 118 included publications, 65 were full-text manuscripts and 53 were abstracts, with a main disease focus of PsO in 96 publications, PsA in 16 publications, both PsO and PsA in 5 publications, and axSpA in 1 publication.

Overall, the most frequently involved countries/regions of publication were North America ($n = 29$), followed by Italy ($n = 14$; including one study in Italy and Germany), China ($n = 12$), and Spain ($n = 7$). Three studies were conducted in

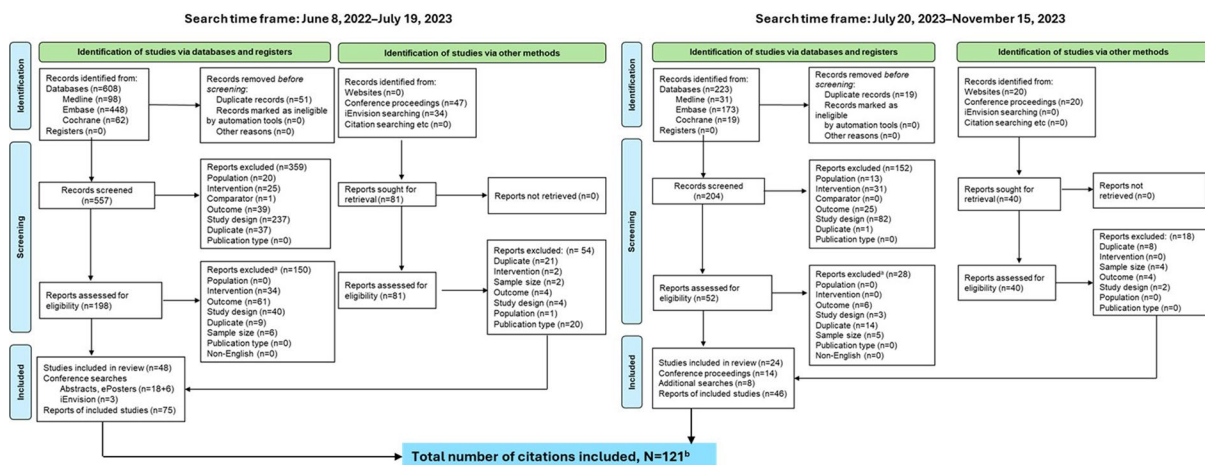


Fig. 1 PRISMA flow chart. No automation tools were used during study selection; all reasons for title and abstract screening exclusion (by humans) are shown. ^aSeveral studies were removed as they were identified as having been included in an earlier systematic literature review [3]. Additionally, four studies reporting patient

characteristics were excluded from the review but listed separately in the data extraction form. ^bOf 121 citations that are included in the data extraction, 14 are categorized under the linked category with primary citation, 3 of which were excluded from analyses as they did not report additional results

the UK/Ireland, and there were 13 publications with multinational cohorts; 2 studies did not report the country, and the remaining 38 studies were conducted in more than 15 different countries.

Study Characteristics and Treatments

There were 82 comparative publications (Supplementary Table 4) and 36 noncomparative publications (Supplementary Table 5), focusing on treatment patterns (including adherence, drug survival, persistence, treatment switching, dose escalation, treatment discontinuation, and prescription patterns), clinical-effectiveness outcomes, safety outcomes, QoL outcomes, and economic outcomes; most focused on more than one outcome (Fig. 2). Comparators investigated were most often other biologics, with most studies comparing ixekizumab with other anti-IL-17As, such as secukinumab and brodalumab, or anti-IL-12/23s, such as guselkumab, risankizumab, tildrakizumab, or ustekinumab.

Data Sources

Data for the 82 comparative publications most frequently came from multicenter cohorts ($n = 25$), whereas sources for the 36 noncomparative studies most frequently came from single-center cohorts ($n = 12$).

Patient Characteristics

Mean age ranged from 38 to 63 years, and, where reported, most studies ($\approx 70\%$) included more than 50% men (Supplementary Tables 4 and 5). In studies on patients with PsO, the percentage of patients with coexisting PsA, where reported, ranged between approximately 20% and 40% in most studies, and, where reported, most studies ($\approx 80\%$) included a mix of biologic-experienced and biologic-naïve patients (Supplementary Tables 4 and 5).

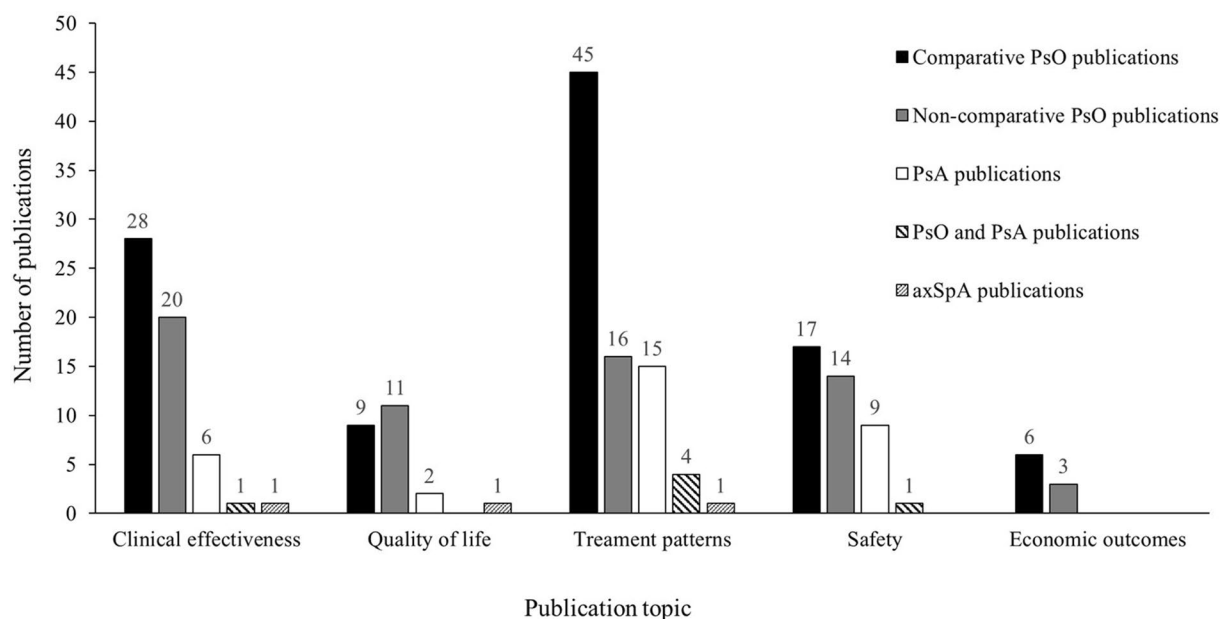


Fig. 2 Summary of included publications by topics covered. *axSpA* axial spondyloarthritis, *PsA* psoriatic arthritis, *PsO* psoriasis

Clinical Effectiveness

Comparative Studies

Of the comparative publications, 30 reported clinical-effectiveness outcomes. Of those, 28 were in patients with PsO, 1 included patients with PsO and patients with PsA, and 1 was in patients with axSpA.

In comparative studies in patients with PsO (Table 1), anti-IL-17A biologics were more effective in terms of skin clearance, measured by Psoriasis Area and Severity Index (PASI) score and PASI response rates of 75%, 90%, and 100% (PASI75/90/100), than comparator biologics in most studies [32–40]. Specifically, in a prospective multicenter cohort study, with an overall relapse rate (PASI > 10) of 14% [7.4 cases per 100 person-years (95% confidence interval 3.4–14.0)] among patients undergoing treatment optimization (dose reduction or increased dosing interval) with ixekizumab, ustekinumab, adalimumab, secukinumab, guselkumab, or etanercept, only patients receiving adalimumab and ustekinumab had experienced relapse at 8 months [40]. Additionally, in a prospective study ($n = 1981$) using the international non-interventional Psoriasis Study of Health Outcomes (PSoHO) cohort, anti-IL-17A biologics (ixekizumab and secukinumab) were associated with higher unadjusted response rates for PASI90 and/or static Physician's Global Assessment (sPGA) 0/1, and PASI90/100 at week 12 than other biologics (guselkumab, risankizumab, adalimumab, or ustekinumab) across all subgroups, except for Asian patients [32]. In the PSoHO cohort, higher response rates in moderate-to-severe plaque PsO were observed with anti-IL-17A agents than other biologics [37–39]. A retrospective cohort study ($n = 1057$) also demonstrated that anti-IL-17A biologics ($n = 648$) showed significantly better short-term effectiveness than anti-IL-23 biologics ($n = 409$), with faster achievement of PASI90 and PASI ≤ 3 (56% and 70% vs. 42% and 59% at week 16; $P < 0.001$) [36]. However, at week 52, a greater percentage of patients receiving anti-IL-23 biologics than patients receiving anti-IL-17A biologics had achieved a PASI ≤ 3 (89% vs. 83%; $P = 0.038$) [36]. Additionally, greater clinical

improvement was observed in patients receiving an anti-IL-17A ($n = 444$) than in those receiving other biologics ($n = 683$) in a prospective multicenter cohort study, with patients receiving ixekizumab ($n = 307$) showing high response rates (PASI90 and/or sPGA 0/1, or PASI100) at week 12 [41].

Studies consistently demonstrated the effectiveness of the anti-IL-17A agents ixekizumab, secukinumab, and brodalumab in patients with moderate-to-severe PsO in real-world settings [41–45]. In one large retrospective multicenter cohort study ($n = 949$), most patients receiving ixekizumab, secukinumab, or brodalumab experienced a PASI75 response after 3 months (88%, 84%, and 92%, respectively) and at 24 months (92%, 84%, and 96%, respectively) [42]. In a single-center cohort study conducted in Italy, ixekizumab and brodalumab were associated with significant PASI90/100 responses at week 24 ($P < 0.001$) [43]. Among patients treated with anti-IL-17A biologics in an observational cohort study, ixekizumab was associated with higher proportions of patients achieving PASI ≤ 2 and PASI = 0 (100% and 83%, respectively) than secukinumab (98% and 76%) or brodalumab (87% and 69%); P values were not reported [44]. Similarly, a higher likelihood of PASI100 or Patient's Global Assessment 0/1 with ixekizumab than with secukinumab and brodalumab for specific dosing regimens was observed in a retrospective single-center study [45]. In another retrospective single-center cohort study in Italy, compared with patients receiving secukinumab, those receiving brodalumab or ixekizumab experienced significantly higher effectiveness at weeks 12 and 24 (PASI90/100 and residual PASI < 3 at week 12; PASI90 and residual PASI < 3 at week 24; $P < 0.05$) [33]. Moreover, at week 48, although there were no differences in effectiveness for brodalumab versus secukinumab, the better effectiveness of ixekizumab versus secukinumab persisted ($P < 0.05$) [33]. Moreover, compared with secukinumab, ixekizumab was associated with statistically significantly higher PASI < 3 and PASI90/100 responses at weeks 12 and 48 in a retrospective cohort ($n = 638$); brodalumab was also associated with significantly better results at week 12 than secukinumab

Table 1 Comparative effectiveness in skin clearance in patients receiving ixekizumab for the treatment of psoriasis

Study author, year; country	Treatment	IXE vs. comparators: percentage of patients			
		Mean PASI score ($\pm$ SD)	PASI75	PASI90	PASI100
Kojanova et al. 2022 [42]; Czech Republic	IXE (275)		At 3 months:	At 3 months:	At 3 months:
	SEC (485)		IXE: 88.3	IXE: 71.3	IXE: 49.2
	BRO (296)		SEC: 84.0	SEC: 60.7	SEC: 38.6
			BRO: 91.7	BRO: 76.4	BRO: 58.7
			At 6 months:	At 6 months:	At 6 months:
			IXE: 91.8	IXE: 79.5	IXE: 54.9
			SEC: 87.7	SEC: 66.1	SEC: 45.7
			BRO: 94.6	BRO: 84.2	BRO: 64.6
			At 12 months:	At 12 months:	At 12 months:
			IXE: 91.3	IXE: 79.4	IXE: 51.3
			SEC: 86.9	SEC: 68.1	SEC: 45.0
			BRO: 95.7	BRO: 87.8	BRO: 71.3
			At 18 months:	At 18 months:	At 18 months:
			IXE: 90.5	IXE: 72.4	IXE: 46.1
			SEC: 88.5	SEC: 62.9	SEC: 45.7
			BRO: 97.9	BRO: 88.9	BRO: 75.7
			At 24 months:	At 24 months:	At 24 months:
			IXE: 92.2	IXE: 74.4	IXE: 46.7
			SEC: 84.3	SEC: 65.3	SEC: 41.6
			BRO: 96.0	BRO: 88.0	BRO: 66.0
Lynde et al. 2023 [32]; multinational	IXE (532)		NR	At week 12:	At week 12:
	SEC (241)			Unadjusted response rates for	Unadjusted response rates for
	GUS (303)			PASI90, % (95% CI) across patient	PASI100, % (95% CI)
	RIS (259)			subgroups	Anti-IL-17A: 35.8 (32.5–39.2)
	ADA (284)			Anti-IL-17A: 55.4 (51.9–58.9)	Other biologics: 21.9 (19.6–24.3)
	UST (127)			Other biologics: 39.3 (36.6–42.1)	IXE: 38.5 (34.4–42.7)
				IXE: 58.5 (54.3–62.6)	SEC: 29.9 (24.1–35.7)
				SEC: 48.5 (42.2–54.9)	GUS: 23.1 (18.4–27.8)
				GUS: 40.9 (35.4–46.5)	RIS: 29.3 (23.8–34.9)
				RIS: 50.6 (44.5–56.7)	ADA: 14.8 (10.7–18.9)
				ADA: 28.9 (23.6–34.1)	UST: 12.6 (6.8–18.4)
				UST: 26.0 (18.4–33.6)	
				Unadjusted PASI90 and/or sPGA	
				0/1, % (95% CI)	
				Anti-IL-17A: 71.4 (68.2–74.6)	
				Other biologics: 58.6 (55.8–61.4)	
				IXE: 74.2 (70.5–78.0)	
				SEC: 65.1 (59.1–71.2)	
				GUS: 57.1 (51.5–62.7)	
				RIS: 65.6 (59.9–71.4)	
				ADA: 55.3 (49.5–61.1)	
				UST: 52.8 (44.1–61.4)	
Megna et al. 2022 [43]; Italy	IXE (98)	Mean PASI:	NR	Week 4	Week 4
	BRO (41)	Baseline		IXE: 43.8	IXE: 20.4
		IXE: 18.4 ± 7.2 BRO: 16.2 ± 5.4		BRO: 39.0	BRO: 17.1
		Week 4		Week 12	Week 12
		IXE: 4.8 ± 3.7 ($P < 0.001$)		IXE: 74.5	IXE: 44.8
		BRO: 5.1 ± 3.6 ($P < 0.001$)		BRO: 68.2	BRO: 41.4
		Week 12		Week 24	Week 24
		IXE: 3.2 ± 0.9 ($P < 0.001$)		IXE: 83.6	IXE: 71.5
		BRO: 4.3 ± 0.8 ($P < 0.001$)		BRO: 75.6	BRO: 60.9
		Week 24			
		IXE: 0.9 ± 0.6 ($P < 0.001$)			
		BRO: 1.3 ± 0.4 ($P < 0.001$)			
		*No significant differences between BRO and IXE in percentage of pts achieving absolute PASI ≤ 1 , ≤ 3 , and ≤ 5			
Schots et al. 2023 [44]; Belgium	IXE, SEC, BRO (111)	Baseline PASI, median 9.5 (IQR 6.0–14.6)	NR	NR	NR
		PASI ≤ 2			
		SEC: 98.1			
		IXE: 100			
		BRO: 86.7 ($P = 0.047$)			
		PASI = 0			
		SEC: 76.0			
		IXE: 82.9			
		BRO: 68.8 ($P = 0.465$)			
Sermaksasithorn et al. 2023 [45]; Thailand	IXE (86)	NR	NR	NR	PASI100 or PGA0/1
	BRO (8)				SEC: 70.8
	SEC (48)				IXE: 83.7

Table 1 continued

Study author, year; country	Treatment	IXE vs. comparators: percentage of patients			
		Mean PASI score ($\pm$ SD)	PASI75	PASI90	PASI100
Tichy et al. 2022 [47]; Czech Republic	IXE (48) BRO (33) SEC (9)	Baseline	12 weeks	12 weeks	NR
		IXE: 14.4	IXE: 75	IXE: 44.4	
		BRO: 16.0	BRO: 73.3	BRO: 50	
		SEC: 11.1	SEC: 28.6	SEC: 0	
		12 weeks	24 weeks	24 weeks	
		IXE: 2.2	IXE: 81.3	IXE: 59.4	
		BRO: 2.3	BRO: 78.6	BRO: 57.1	
		SEC: 3.6	SEC: 66.7	SEC: 33.3	
		24 weeks	48 weeks	48 weeks	
		IXE: 2.0	IXE: 76	IXE: 52	
		BRO: 2.4	BRO: 75	BRO: 75	
		SEC: 3.5	SEC: 80	SEC: 40	
		48 weeks	72 weeks	72 weeks	
		IXE: 1.9	IXE: 76.5	IXE: 35.3	
		BRO: 1.0	BRO: 80	BRO: 70	
		SEC: 1.9	SEC: 0	SEC: 0	
		72 weeks			
		IXE: 2.9			
		BRO: 1.2			
		SEC: 5.3			
Khatti et al. 2023 [41]; multinational	IXE (500) SEC (219) RIS (230) BRO (60) TIL (83) GUS (272) ADA (225) UST (112)	Bio-naïve pts	NR	At week 12: PASI90 and/or sPGA (0,1) Bio-naïve pts	At week 12: Bio-naïve pts
		Baseline			IXE: 42.3
		IXE: 15.2		IXE: 79.5	SEC: 32.1
		SEC: 16.6		SEC: 70.1	RIS: 33.1
		RIS: 16.6		RIS: 66.9	BRO: 50.0
		BRO: 15.7		BRO: 71.1	TIL: 21.1
		TIL: 15.8		TIL: 63.2	GUS: 31.8
		GUS: 16.8		GUS: 70.1	ADA: 16.9
		ADA: 13.6		ADA: 56.5	UST: 13.6
		UST: 15.2		UST: 50.6	Bio-experienced pts
		Bio-experienced pts		Bio-experienced pts	IXE: 33.7
		Baseline		IXE: 67.9	SEC: 29.3
		IXE: 13.2		SEC: 58.5	RIS: 24.7
		SEC: 12.4		RIS: 63.9	BRO: 22.7
		RIS: 14.6		BRO: 63.6	TIL: 23.1
		BRO: 17.1		TIL: 50.0	GUS: 18.2
		TIL: 10.6		GUS: 50.3	ADA: 16.7
		GUS: 13.8		ADA: 61.1	UST: 9.7
		ADA: 12.6		UST: 58.1	
		UST: 12.9			
Costanzo et al. 2022 [46]; multinational	IXE (272) SEC (120) Other biologics (518)	NR	NR	PASI90 and/or sPGA 0/1	Week 12
				Week 12	IXE: 46.7
				IXE: 81.3	BRO: 41.4
				BRO: 79.3	SEC: 31.7
				SEC: 70.8	GUS: 23.2
				GUS: 58.1	RIS: 32.6
				RIS: 66.3	TIL: 22.2
				TIL: 61.1	ADA: 15.3
				ADA: 59.5	UST: 17.3
				UST: 59.6	Week 26
				Week 26	IXE: 50.0
				IXE: 79.0	BRO: 48.3
				BRO: 72.4	SEC: 50.8
				SEC: 79.1	GUS: 32.9
				GUS: 67.0	RIS: 40.7
				RIS: 73.2	TIL: 24.1
				TIL: 70.3	ADA: 32.4
				ADA: 73.0	UST: 36.5
				UST: 71.15	Week 52
				Week 52	IXE: 54.0
				IXE: 81.9	BRO: 48.3
				BRO: 75.8	SEC: 52.5
				SEC: 85.0	GUS: 43.9
				GUS: 75.4	RIS: 53.5
				RIS: 87.2	TIL: 38.9
				TIL: 81.5	ADA: 45.0
				ADA: 82.0	UST: 36.5
				UST: 69.2 ($P < 0.001$)	

Table 1 continued

Study author, year; country	Treatment	IXE vs. comparators: percentage of patients			
		Mean PASI score ($\pm$ SD)	PASI75	PASI90	PASI100
Akbulut et al. 2022 [48]; NR	SEC to IXE switch (109) IXE to SEC switch (15)	Baseline: PASI Mean 10.8	Baseline (at the time of switching) SEC to IXE: 91.5 IXE to SEC: 81.3 Week 52 SEC to IXE: 83 IXE to SEC: 81.3	Baseline (at time of switch) SEC to IXE: 84.9 IXE to SEC: 62.5 Week 52 SEC to IXE: 79.2 IXE to SEC: 68.8	Baseline (at time of switch) SEC to IXE: 57.5 IXE to SEC: 37.5 Week 52 SEC to IXE: 65.1 IXE to SEC: 37.5
Mastorino et al. 2023 [33]; Italy	BRO, SEC, IXE (638)	NR	NR	Weeks 12 and 24 IXE and BRO higher efficacy than SEC in achieving PASI90 ($P < 0.05$) Week 48 IXE superiority vs. SEC in all relative PASI scores ($P < 0.05$) No significant difference between SEC and BRO	Weeks 12 and 24 IXE and BRO higher efficacy than SEC in achieving PASI100 ($P < 0.05$) Week 48 IXE superiority vs. SEC in all relative PASI scores ($P < 0.05$) No significant difference between SEC and BRO
Burzi et al. 2023 [49]; Italy	Anti-IL-17A or anti-IL-23 agents (1053)	NR	NR	NR	Week 52 IXE: 80 BRO: 88 SEC: 87 TIL: 95
Ting et al. 2023 [34, 35]; Australia	Total (312)	NR	IXE: 94.9 GUS: 93.8 ETA: 73.1	NR	IXE: 71.2 GUS: 46.9 ETA: 19.2
Mastorino et al. 2023 [36]; Italy	IXE (189) SEC (256) BRO (203) GUS (74) RIS (236) TIL (99)	At baseline: SEC: 15.82 ± 5.64 IXE: 17.79 ± 7 BRO: 13.63 ± 6.12 GUS: 11.04 ± 6.38 RIS: 14.78 ± 7.17 TIL: 9.78 ± 3.43 ($P < 0.001$) At week 16: SEC: 2.76 ± 3.72 IXE: 2.88 ± 6.04 BRO: 1.92 ± 4.2 GUS: 2.47 ± 3.14 RIS: 2.69 ± 3.82 TIL: 2.59 ± 2.17 ($P = 0.306$) At week 28: SEC: 2.05 ± 3.42 IXE: 1.8 ± 4.17 BRO: 0.87 ± 1.82 GUS: 1.22 ± 1.82 RIS: 1.23 ± 3.03 TIL: 1.77 ± 1.82 ($P = 0.004$) At week 52: SEC: 1.69 ± 3.36 IXE: 0.98 ± 2.17 BRO: 1.36 ± 3.37 GUS: 0.79 ± 1.63 RIS: 0.68 ± 1.66 TIL: 1.26 ± 1.79 ($P = 0.01$)	NR	At week 16: SEC: 47 IXE: 61 BRO: 66 GUS: 44 RIS: 49 TIL: 24 ($P < 0.001$) At week 28: SEC: 60 IXE: 68 BRO: 77 GUS: 62 RIS: 75 TIL: 37 ($P < 0.001$) At week 52: SEC: 68 IXE: 79 BRO: 78 GUS: 73 RIS: 82 TIL: 59 ($P = 0.012$)	NR
Travaglini et al. 2023 [37]; multinational	Anti-IL-17A (23): IXE (19) SEC (4) Other biologics (36): GUS (18) ADA (7) BRO (3) ETA (4) INF (1) RIS (2) UTE (1)	NR	NR	At week 12: PASI90 and/or sPGA 0/1 Anti-IL-17A: 65.2 Other biologics: 47.2 IXE: 73.7 GUS: 55.6 PASI90 Anti-IL-17A: 56.5 Other biologics: 27.8 IXE: 68.4 GUS: 22.2	At week 12: Anti-IL-17A: 34.8 Other biologics: 13.9 IXE: 42.1 GUS: 0

Table 1 continued

Study author, year; country	Treatment	IXE vs. comparators: percentage of patients			
		Mean PASI score ($\pm$ SD)	PASI75	PASI90	PASI100
Mastorino et al. 2023 [50]; Italy	Scalp PsO: anti-IL-17A (212)	Scalp: PSSI (0–72) mean	Scalp: PSSI 75:	Scalp: PSSI 90:	Scalp: PSSI 100:
	Anti-IL-23 (96)	At baseline:	At 16 weeks:	At 16 weeks:	At 16 weeks:
SEC (55)	Anti-IL-17A: 17.6 $\pm$ 10.5	Anti-IL-17A: 17.6 $\pm$ 10.5	Anti-IL-17A: 69.7	Anti-IL-17A: 64.1	Anti-IL-17A: 59
IXE (49)	Anti-IL-23: 18.9 $\pm$ 11 ($P = 0.394$)	Anti-IL-23: 18.9 $\pm$ 11 ($P = 0.394$)	Anti-IL-23: 56.8 ($P = 0.034$)	Anti-IL-23: 39.8 ($P < 0.001$)	Anti-IL-23: 39.8 ($P = 0.003$)
BRO (108)	SEC: 17.1 $\pm$ 9	SEC: 17.1 $\pm$ 9	SEC: 42.6	SEC: 42.6	SEC: 35.2
GUS (28)	IXE: 16.7 $\pm$ 8.9	IXE: 16.7 $\pm$ 8.9	IXE: 63	IXE: 50	IXE: 44
RIS (38)	BRO: 18.6 $\pm$ 11.4	BRO: 18.6 $\pm$ 11.4	BRO: 85.3	BRO: 79.6	BRO: 75
TIL (30)	GUS: 17.4 $\pm$ 10.7	GUS: 17.4 $\pm$ 10.7	GUS: 75	GUS: 39.3	GUS: 39.3
Genital PsO: anti-IL-17A (109)	RIS: 25 $\pm$ 10.6	RIS: 25 $\pm$ 10.6	RIS: 53	RIS: 42.1	RIS: 42.1
anti-IL-23 (27)	TIL: 10 $\pm$ 3 ($P < 0.001$)	TIL: 10 $\pm$ 3 ($P < 0.001$)	TIL: 40.9 ($P < 0.001$)	TIL: 36.4 ($P < 0.001$)	TIL: 36.4 ($P < 0.001$)
SEC (32)	At 16 weeks:	At 16 weeks:	At 28 weeks:	At 28 weeks:	At 28 weeks:
IXE (30)	Anti-IL-17A: 3 $\pm$ 5.5	Anti-IL-17A: 3 $\pm$ 5.5	Anti-IL-17A: 89.7	Anti-IL-17A: 80.9	Anti-IL-17A: 76.8
BRO (47)	Anti-IL-23: 5 $\pm$ 6.4 ($P = 0.004$)	Anti-IL-23: 5 $\pm$ 6.4 ($P = 0.004$)	Anti-IL-23: 78.2 ($P = 0.01$)	Anti-IL-23: 62.1 ($P = 0.001$)	Anti-IL-23: 60.9 ($P = 0.006$)
GUS (13)	SEC: 4.7 $\pm$ 5.3	SEC: 4.7 $\pm$ 5.3	SEC: 90.7	SEC: 74.1	SEC: 72.2
RIS (9)	IXE: 4.5 $\pm$ 6.5	IXE: 4.5 $\pm$ 6.5	IXE: 80.6	IXE: 65	IXE: 55
TIL (5)	BRO: 1.9 $\pm$ 4.6	BRO: 1.9 $\pm$ 4.6	BRO: 91.7	BRO: 85.3	BRO: 85.3
Palmoplantar PsO: Anti-IL-17A (71)	GUS: 4.1 $\pm$ 5.6	GUS: 4.1 $\pm$ 5.6	GUS: 82.1	GUS: 64.3	GUS: 64.3
Anti-IL-23 (23)	RIS: 6.7 $\pm$ 7.9	RIS: 6.7 $\pm$ 7.9	RIS: 67.6	RIS: 45.9	RIS: 43.2
SEC (32)	TIL: 3 $\pm$ 3.1 ($P < 0.001$)	TIL: 3 $\pm$ 3.1 ($P < 0.001$)	TIL: 90.9 ($P = 0.007$)	TIL: 86.4 ($P < 0.001$)	TIL: 86.4 ($P < 0.001$)
IXE (13)	At 28 weeks:	At 28 weeks:	At 52 weeks:	At 52 weeks:	At 52 weeks:
BRO (26)	Anti-IL-17A: 1.2 $\pm$ 3.7	Anti-IL-17A: 1.2 $\pm$ 3.7	Anti-IL-17A: 91.7	Anti-IL-17A: 91.7	Anti-IL-17A: 86.5
GUS (5)	Anti-IL-23: 2.6 $\pm$ 4.5 ($P = 0.013$)	Anti-IL-23: 2.6 $\pm$ 4.5 ($P = 0.013$)	Anti-IL-23: 72.6 ($P < 0.001$)	Anti-IL-23: 72.6 ($P < 0.001$)	Anti-IL-23: 71.4 ($P = 0.003$)
RIS (8)	SEC: 1.1 $\pm$ 2.7	SEC: 1.1 $\pm$ 2.7	SEC: 90.7	SEC: 90.7	SEC: 87
TIL (10)	IXE: 2 $\pm$ 2.1	IXE: 2 $\pm$ 2.1	IXE: 97	IXE: 97	IXE: 80
	BRO: 1.3 $\pm$ 4.4	BRO: 1.3 $\pm$ 4.4	BRO: 89	BRO: 89	BRO: 88
	GUS: 1.9 $\pm$ 3.6	GUS: 1.9 $\pm$ 3.6	GUS: 92.6	GUS: 71.4	GUS: 67.9
	RIS: 4.5 $\pm$ 5.5	RIS: 4.5 $\pm$ 5.5	IXE: 100	RIS: 62.2	RIS: 62.2
	TIL: 0 $\pm$ 1 ($P < 0.001$)	TIL: 0 $\pm$ 1 ($P < 0.001$)	BRO: 93.5	TIL: 94.7 ($P < 0.001$)	TIL: 94.7 ($P = 0.002$)
	At 52 weeks:	At 52 weeks:	GUS: 89.3	Palmoplantar: ppPASI 90:	Palmoplantar: ppPASI 100:
	Anti-IL-17A: 0.8 $\pm$ 3.2	Anti-IL-17A: 0.8 $\pm$ 3.2	RIS: 73	At 16 weeks:	At 16 weeks:
	Anti-IL-23: 2 $\pm$ 4 ($P = 0.037$)	Anti-IL-23: 2 $\pm$ 4 ($P = 0.037$)	TIL: 94.7 ($P = 0.003$)	Anti-IL-17A: 50.7	Anti-IL-17A: 49.3
	SEC: 0.7 $\pm$ 2.5	SEC: 0.7 $\pm$ 2.5	Palmoplantar: ppPASI 75:	Anti-IL-23: 43.5 ($P = 0.627$)	Anti-IL-23: 43.5 ($P = 0.547$)
	IXE: 1.2 $\pm$ 1.6	IXE: 1.2 $\pm$ 1.6	At 16 weeks:	SEC: 46.9	SEC: 46.9
	BRO: 1.1 $\pm$ 3.9	BRO: 1.1 $\pm$ 3.9	Anti-IL-17A: 54.9	IXE: 0	IXE: 0
	GUS: 1.3 $\pm$ 2.5	GUS: 1.3 $\pm$ 2.5	Anti-IL-23: 47.8 ($P = 0.553$)	BRO: 76.9	BRO: 76.9
	RIS: 3.4 $\pm$ 5.4	RIS: 3.4 $\pm$ 5.4	SEC: 56.3	GUS: 40	GUS: 40
	TIL: 0 $\pm$ 0.7 ($P < 0.001$)	TIL: 0 $\pm$ 0.7 ($P < 0.001$)	IXE: 8.3	RIS: 62.7	RIS: 62.7
	Palmoplantar: ppPASI (0–72)	Palmoplantar: ppPASI (0–72)	BRO: 76.9	TIL: 30 ($P = 0.001$)	TIL: 30 ($P < 0.0001$)
	At baseline:	At baseline:	GUS: 40	At 28 weeks:	At 28 weeks:
	Anti-IL-17A: 24.2 $\pm$ 9.6	Anti-IL-17A: 24.2 $\pm$ 9.6	RIS: 75	Anti-IL-17A: 64.3	Anti-IL-17A: 62.9
	Anti-IL-23: 19.8 $\pm$ 7.7 ($P = 0.029$)	Anti-IL-23: 19.8 $\pm$ 7.7 ($P = 0.029$)	TIL: 30 ($P = 0.002$)	Anti-IL-23: 47.6 ($P = 0.212$)	Anti-IL-23: 47.6 ($P = 0.171$)
	SEC: 27.6 $\pm$ 7.8	SEC: 27.6 $\pm$ 7.8		SEC: 59.4	SEC: 59.4
	IXE: 24 $\pm$ 5.4	IXE: 24 $\pm$ 5.4		IXE: 27.3	IXE: 27.3
	BRO: 21.2 $\pm$ 11.4	BRO: 21.2 $\pm$ 11.4		BRO: 84.6	BRO: 84.6
	GUS: 18 $\pm$ 7.8	GUS: 18 $\pm$ 7.8		GUS: 75	GUS: 75
	RIS: 24 $\pm$ 9.6	RIS: 24 $\pm$ 9.6		RIS: 57	RIS: 57
	TIL: 18.3 $\pm$ 4.2 ($P = 0.007$)	TIL: 18.3 $\pm$ 4.2 ($P = 0.007$)		TIL: 30 ($P = 0.006$)	TIL: 30 ($P = 0.006$)
	At 16 weeks:	At 16 weeks:	At 28 weeks:	GUS: 75	At 52 weeks:
	Anti-IL-17A: 7.6 $\pm$ 9.5	Anti-IL-17A: 7.6 $\pm$ 9.5	Anti-IL-17A: 71.4	RIS: 57	Anti-IL-17A: 66.7
	Anti-IL-23: 6.5 $\pm$ 7.6 ($P = 0.979$)	Anti-IL-23: 6.5 $\pm$ 7.6 ($P = 0.979$)	Anti-IL-23: 57.1 ($P = 0.931$)	TIL: 30 ($P = 0.015$)	Anti-IL-23: 47.4 ($P = 0.096$)
	SEC: 9 $\pm$ 10.8	SEC: 9 $\pm$ 10.8	SEC: 75	At 52 weeks:	SEC: 59.4
	IXE: 18 $\pm$ 5.4	IXE: 18 $\pm$ 5.4	IXE: 36.4	Anti-IL-17A: 68.1	IXE: 50
	BRO: 2.3 $\pm$ 4.8	BRO: 2.3 $\pm$ 4.8	BRO: 84.6	Anti-IL-23: 47.4 ($P = 0.124$)	BRO: 84.6
	GUS: 6 $\pm$ 4.8	GUS: 6 $\pm$ 4.8	GUS: 75	SEC: 59.4	GUS: 75
	RIS: 6.4 $\pm$ 8.4	RIS: 6.4 $\pm$ 8.4	RIS: 57	IXE: 50	RIS: 57
	TIL: 8.4 $\pm$ 7.8 ($P < 0.001$)	TIL: 8.4 $\pm$ 7.8 ($P < 0.001$)	TIL: 50 ($P = 0.075$)	BRO: 84.6	TIL: 25 ($P = 0.035$)
	At 28 weeks:	At 28 weeks:	At 52 weeks:	GUS: 75	
	Anti-IL-17A: 4.6 $\pm$ 7.8	Anti-IL-17A: 4.6 $\pm$ 7.8	Anti-IL-17A: 73.9	RIS: 57	
	Anti-IL-23: 5.7 $\pm$ 7 ($P = 0.303$)	Anti-IL-23: 5.7 $\pm$ 7 ($P = 0.303$)	Anti-IL-23: 57.9 ($P = 0.175$)	TIL: 25 ($P = 0.072$)	
	SEC: 6 $\pm$ 9.6	SEC: 6 $\pm$ 9.6	SEC: 75		
	IXE: 6 $\pm$ 6	IXE: 6 $\pm$ 6	IXE: 50		
	BRO: 1.4 $\pm$ 3.5	BRO: 1.4 $\pm$ 3.5	BRO: 84.6		
	GUS: 6 $\pm$ 3	GUS: 6 $\pm$ 3	GUS: 75		
	RIS: 6.1 $\pm$ 8.4	RIS: 6.1 $\pm$ 8.4	RIS: 57		
	TIL: 7.2 $\pm$ 6.6 ($P = 0.045$)	TIL: 7.2 $\pm$ 6.6 ($P = 0.045$)	TIL: 50 ($P = 0.292$)		
	At 52 weeks:	At 52 weeks:			
	Anti-IL-17A: 3.8 $\pm$ 6.9	Anti-IL-17A: 3.8 $\pm$ 6.9			
	Anti-IL-23: 6 $\pm$ 7.2 ($P = 0.177$)	Anti-IL-23: 6 $\pm$ 7.2 ($P = 0.177$)			
	SEC: 5.4 $\pm$ 8.4	SEC: 5.4 $\pm$ 8.4			
	IXE: 6 $\pm$ 6	IXE: 6 $\pm$ 6			
	BRO: 1.4 $\pm$ 3.5	BRO: 1.4 $\pm$ 3.5			
	GUS: 5.8 $\pm$ 3	GUS: 5.8 $\pm$ 3			
	RIS: 5.6 $\pm$ 9.6	RIS: 5.6 $\pm$ 9.6			
	TIL: 6.6 $\pm$ 0.6 ($P = 0.094$)	TIL: 6.6 $\pm$ 0.6 ($P = 0.094$)			

Table 1 continued

Study author, year; country	Treatment	IXE vs. comparators: percentage of patients			
		Mean PASI score ($\pm$ SD)	PASI75	PASI90	PASI100
Egeberg et al. 2023 [51]; multinational	Pts with nail PsO at baseline (263) Anti-IL-17A (123) IXE (94) SEC (29) Other biologics (140)	At baseline Pts with nail PsO: 16.4 ± 8.9 Pts without nail PsO: 14.2 ± 9.3 ($P = 0.013$)	NR	NR	NR
Mastorino et al. 2023 [33]; Italy	SEC (255) IXE (189) BRO (194)	At baseline: SEC: 15.82 ± 5.6 IXE: 17.79 ± 7 BRO: 13.78 ± 6.2 At week 12 SEC: 2.76 ± 3.7 IXE: 2.88 ± 6 BRO: 1.91 ± 4.2 At week 24: SEC: 2.05 ± 3.4 IXE: 1.8 ± 4.2 BRO: 0.85 ± 1.8 At week 48: SEC: 1.69 ± 3.4 IXE: 0.98 ± 2.2 BRO: 1.29 ± 3.3	NR	At week 12: SEC: 48.3 IXE: 63.8 BRO: 68.3 At week 24: SEC: 61.2 IXE: 71.9 BRO: 77.2 At week 48: SEC: 69.2 IXE: 80.0 BRO: 74.4	At week 12 SEC: 42 IXE: 54.1 BRO: 53.2 At week 24: SEC: 52.7 IXE: 61.2 BRO: 64.8 At week 48: SEC: 59.5 IXE: 72.5 BRO: 64.7
Xiao et al. 2023 [53]; China	IXE (55) ADA (79) SEC (278) UST (52)	NR	At week 28 Head and neck regions IXE: 96.29 SEC: 88.76 At week 52: Lower extremities ADA: 53.06 IXE: 89.66 Upper extremities ADA: 57.44 IXE: 92.00	At week 28: Head and neck regions IXE: 96.29 SEC: 76.33	NR
Pinter et al. 2023 [132]; multinational	Anti-IL-17A (773) Other biologics (1208) Pts with < 2 years' disease duration IXE (38) SEC (22) GUS (19) RIS (18) ADA (16) UST (9) Pts with ≥ 2 years' disease duration: IXE (494) SEC (219) GUS (284) RIS (241) ADA (268) UST (118)	Pts with < 2 years' disease duration: Anti-IL-17A biologics (IXE or SEC): 17.6 ± 10.2 Other biologics: 15.1 ± 8.4 Pts with ≥ 2 years' disease duration: Anti-IL-17A biologics (IXE or SEC): 14.4 ± 8.3 Other biologics: 14.4 ± 8.6	NR	NR	At week 12: Pts with < 2 years' disease duration: Anti-IL-17A biologics (IXE or SEC): 36.7 Other biologics: 21.8 IXE: 42.1 SEC: 27.3 GUS: 31.6 RIS: 33.3 ADA: 6.3 UST: 11.1 Pts with ≥ 2 years' disease duration: Anti-IL-17A biologics (IXE or SEC): 35.8 Other biologics: 21.9 IXE: 38.3 SEC: 30.1 GUS: 22.5 RIS: 29.0 ADA: 15.3 UST: 12.7
Smith et al. 2023 [38]; Australia	IXE (30) SEC (6) TIL (42) RIS (14) GUS (9) UST (6) ADA (3)	At baseline: 14.7 ± 9.1 At week 12 (change from baseline): Anti-IL-17A: -14.0 ± 7.9 Other biologics: -11.1 ± 10.6	NR	At week 12 PASI90 and/or sPGA 0/1 Anti-IL-17A: 80.6 Other biologics: 62.2 PASI90 Anti-IL-17A: 61.1 Other biologics: 39.2	Anti-IL-17A: 47.2 Other biologics: 17.6

Table 1 continued

Study author, year; country	Treatment	IXE vs. comparators: percentage of patients			
		Mean PASI score ($\pm$ SD)	PASI75	PASI90	PASI100
Pinter et al. 2023 [39]; multinational	IXE (532) SEC (241) BRO (64) TIL (95) GUS (303) RIS (259) ADA (284) UST (127)	NR	NR	At 6 months PASI90 and/or sPGA 0/1 Anti-IL-17A: 73.4 Other biologics: 65.2 IXE: 74.6 SEC: 70.5 BRO: 60.9 TIL: 67.4 GUS: 66.0 RIS: 73.0 ADA: 59.2 UST: 62.2 PASI90 Anti-IL-17A: 61.6 Other biologics: 50.2 IXE: 64.3 SEC: 55.6 BRO: 54.7 TIL: 51.6 GUS: 51.5 RIS: 60.2 ADA: 40.5 UST: 44.1 At 12 months: Anti-IL-17A: 53.9 Other biologics: 51.7 IXE: 55.6 SEC: 50.2 BRO: 50.0 TIL: 51.6 GUS: 52.5 RIS: 61.4 ADA: 46.1 UST: 41.7	At 6 months: Anti-IL-17A biologics: 43.3 Other biologics: 31.5 IXE: 44.9 SEC: 39.8 BRO: 37.5 TIL: 24.2 GUS: 32.3 RIS: 40.2 ADA: 27.1 UST: 25.2 At 12 months: Anti-IL-17A: 40.5 Other biologics: 37.1 IXE: 41.5 SEC: 38.2 BRO: 35.9 TIL: 32.6 GUS: 37.0 RIS: 48.3 ADA: 32.0 UST: 27.6
Piaserico et al. 2023 [52, 133]; multinational	IXE (532) SEC (241) Other biologics (1208)	NR	NR	At week 12: Anxiety: Anti-IL-17A: 67.6 Other biologics: 59.8 No anxiety: Anti-IL-17A: 75.1 Other biologics: 58.6 Depression: Anti-IL-17A: 65.7 Other biologics: 56.8 No depression: Anti-IL-17A: 74.7 Other biologics: 60.4 Dyslipidemia: Anti-IL-17A: 72.4 Other biologics: 56.0 No dyslipidemia: Anti-IL-17A: 71.3 Other biologics: 59.1 Diabetes: Anti-IL-17A: 72.0 Other biologics: 54.0 No diabetes: Anti-IL-17A: 71.4 Other biologics: 59.1 Hypertension: Anti-IL-17A: 71.6 Other biologics: 51.1 No hypertension: Anti-IL-17A: 71.5 Other biologics: 60.8 Smoking: Anti-IL-17A: 69.3 Other biologics: 60.3 No smoking: Anti-IL-17A: 71.9 Other biologics: 58.3	At week 12: Anxiety: Anti-IL-17A: 34.3 Other biologics: 23.1 No anxiety: Anti-IL-17A: 37.5 Other biologics: 21.0 Depression: Anti-IL-17A: 33.1 Other biologics: 20.4 No depression: Anti-IL-17A: 37.6 Other biologics: 22.8 Dyslipidemia: Anti-IL-17A: 35.9 Other biologics: 17.0 No dyslipidemia: Anti-IL-17A: 36.1 Other biologics: 22.9 Diabetes: Anti-IL-17A: 30.1 Other biologics: 22.6 No diabetes: Anti-IL-17A: 36.9 Other biologics: 21.8 Hypertension: Anti-IL-17A: 34.3 Other biologics: 15.4 No hypertension: Anti-IL-17A: 36.7 Other biologics: 23.8 Smoking: Anti-IL-17A: 36.2 Other biologics: 25.0 No smoking: Anti-IL-17A: 35.4 Other biologics: 20.2

Table 1 continued

ADA adalimumab, *BRO* brodalumab, *CI* confidence interval, *ETA* etanercept, *GUS* guselkumab, *IL* interleukin, *INF* infliximab, *IQR* interquartile range, *IXE* ixekizumab, *NR* not reported, *PASI* Psoriasis Area and Severity Index, *PGA* Physician's Global Assessment, *ppPASI* Palmoplantar Pustulosis Area and Severity Index, *PsO* psoriasis, *PSSI* Psoriasis Scalp Severity Index, *pts* patients, *RIS* risankizumab, *SEC* secukinumab, *SD* standard deviation, *sPGA* static Physician's Global Assessment, *TIL* tildrakizumab, *UST* ustekinumab

for PASI100, $PASI < 3$, and PASI90, with no significant differences between brodalumab and ixekizumab [33]. At week 48, ixekizumab was superior to brodalumab and secukinumab for $PASI < 3$.

Compared with those receiving other biologics, patients receiving anti-IL-17A agents have been shown to be more likely to maintain response at 12 months [46], and ixekizumab has been associated with significantly higher odds of maintaining PASI90/100 from week 12 through months 6 and 12 than secukinumab, tildrakizumab, guselkumab, adalimumab, and ustekinumab, with no significant differences between ixekizumab and brodalumab or risankizumab [39].

Evidence also suggests that biologic-naïve patients may respond more quickly to anti-IL-17A treatment than those who are biologic-experienced [44] and exhibit higher overall response rates (PASI90 and/or sPGA 0/1 or PASI100 at week 12) [41].

In patients with severe chronic plaque PsO and treatment failure with secukinumab, switching to ixekizumab can lead to remission, with a study reporting PASI75/90 responses at weeks 12 and 24 of 74.2%/41.9% and 79.3%/55.2%, respectively [47]. Similarly, in patients with moderate-to-severe plaque PsO, switching between secukinumab and ixekizumab following the failure of either appears to be effective: week 52 PASI75/90/100 response rates for a switch from secukinumab to ixekizumab were 83%, 79%, and 65%, respectively, and those for a switch from ixekizumab to secukinumab were 81%, 69%, and 38%, respectively. The PASI100 response rates were significantly better for those switching from secukinumab to ixekizumab ($P = 0.035$) [48].

Both anti-IL-23 and anti-IL-17A biologics have demonstrated effectiveness in challenging

body areas, including the nails, scalp, genitals, and palmoplantar regions [49–52]. In one retrospective cohort study in patients with scalp ($n = 308$), genital ($n = 136$), and palmoplantar ($n = 94$) area involvement, anti-IL-17A agents were associated with statistically significantly better control of scalp PsO than anti-IL-23 agents: Psoriasis Scalp Severity Index 100 at week 16 was achieved by 59% of patients receiving anti-IL-17A agents compared with 40% of patients receiving anti-IL-23 biologics, and these differences persisted through to week 52 (87% vs. 71%; $P < 0.003$) [50]. Additionally, in Chinese patients with PsO, ixekizumab demonstrated higher PASI75/90 response rates in challenging body areas and the head and neck area than did adalimumab, secukinumab, and ustekinumab [53]. In the PSoHO study, patients with scalp PsO had a 10–20% higher response rate and higher odds of achieving clearance with ixekizumab than with other biologics [52]. Ixekizumab was also associated with significantly higher odds of nail PsO clearance at week 12 than guselkumab and adalimumab [52]. In a subset of patients from the PSoHO cohort with nail PsO ($n = 263$), a numerically higher proportion of patients treated with anti-IL-17A biologics reported nail improvements compared with other biologics out to month 12, and this difference reached statistical significance at months 3 and 6 [51].

In the only study in patients with axSpA ($n = 83$) or peripheral spondyloarthropathies ($n = 189$), there were no significant differences between patients initiating ixekizumab ($n = 46$) or secukinumab ($n = 226$) on physician or patient global assessment, Bath Ankylosing Spondylitis Disease Activity Index, or Bath Ankylosing Spondylitis Functional Index out to 1 year [54].

Non-comparative Studies

Of the non-comparative publications, 24 reported effectiveness outcomes. Of these, 20 focused on PsO and four focused on PsA (Table 2 and Supplementary Table 5). Overall, ixekizumab was an effective biologic treatment in moderate-to-severe plaque PsO, as measured by high PASI75/90/100 responses maintained from 4 weeks to 3 years [55–58]. Three retrospective cohort studies demonstrated that biologic-experienced patients had lower PASI responses than biologic-naïve patients [55, 59, 60]. Other factors associated with a lower likelihood of response included the involvement of challenging body areas ($P = 0.047$) [55]. Of note, response to ixekizumab was significantly slower in patients with obesity than in patients without obesity, with fewer patients with obesity achieving PASI90 at week 4 (33% vs. 70%; $P = 0.042$), but this difference was no longer significant at week 16 (82% vs. 90%; $P = 0.405$) [55]. Studies have also demonstrated ixekizumab effectiveness in patients with and without concomitant PsA [59–61]. Additionally, the US Ixekizumab Customer Support Program data demonstrated improvements in body surface area (BSA) and Patient Global Assessment after 24 weeks of treatment in patients with PsO and comorbid PsA [62]. In another study based on data from the same program, patients receiving ixekizumab met treatment-to-target goals set by the US National Psoriasis Foundation [63]. The real-world studies identified in this SLR also demonstrated that ixekizumab also appears to be effective in patients of various geographic ancestries; in addition to the study in Chinese patients with PsO in challenging body areas described in the previous section, four other studies included in this review showed favorable effectiveness in the treatment of PsO in Chinese patients [64–67].

The four non-comparative studies that focused on patients with PsA demonstrated the clinical effectiveness of ixekizumab, with improvements in joint disease activity and global assessment at 6 months and maintenance of response out to 12 months [68], statistically significant decreases in Disease Activity in Psoriatic Arthritis (DAPSA) score [69, 70], and reduced disease severity as measured by

both patient- and physician-reported symptoms ($P < 0.0001$; see Table 2 for more details) [71].

Patient-Reported Outcomes

In total, 22 publications that focused on PsO, 2 that focused on PsA, and 1 that focused on axSpA reported on PROs.

Comparative Studies

Ixekizumab was associated with a higher chance of obtaining Dermatology Life Quality Index (DLQI) scores of 0/1 than secukinumab (odds ratio 3.753; $P = 0.037$) on multivariate regression analysis in a retrospective single-center cohort study ($n = 335$) in patients with moderate-to-severe PsO [72]. This finding was supported by the results of a retrospective 48-week study ($n = 638$) where ixekizumab was associated with a significantly greater reduction from baseline in DLQI scores than secukinumab ($P = 0.04$) [33]. Additionally, data from the PSoHO cohort demonstrated that the anti-IL-17A biologics were associated with significantly higher adjusted odds of achieving DLQI scores of 0/1 at 6 months than were other biologics (38.3% vs. 33.2%); in this study, the DLQI response rate with ixekizumab was numerically higher than with most other biologics between months 6 and 12 [39].

Data from the PSoHO cohort ($n = 1981$) also highlighted the rapid and sustained (to week 12) improvement in patient-reported PsO symptoms (itch, burning, skin tightness, stinging, and pain) and signs (scaling, dryness, redness, cracking, shedding/flaking, and bleeding) in patients receiving anti-IL-17A biologics, particularly those receiving ixekizumab, with significant differences on Psoriasis Symptoms and Signs Diary score measures favoring ixekizumab over secukinumab, guselkumab, risankizumab, adalimumab, and ustekinumab [73]. Another retrospective single-center cohort study in patients with moderate-to-severe PsO found that patients receiving ixekizumab had a significantly higher DLQI 0/1 response (65%) than those receiving secukinumab (57%), whereas the DLQI 0/1 response rate with brodalumab (76%) was

significantly higher than with ixekizumab or secukinumab [33].

In patients with severe chronic plaque PsO, QoL improved after switching ixekizumab, secukinumab, and brodalumab from one to another, with a reduction in psoriatic inflammation symptoms and relief from aesthetic impacts and itchy lesions [43]. Switching from treatment with other biologics to ixekizumab also improved skin clearance outcomes and QoL [74].

Non-comparative Studies

Ixekizumab improved HRQoL measures in patients with PsO and PsA, including the DLQI, Patient Satisfaction Questionnaire, Health Assessment Questionnaire–Disability Index, patient pain, itch, and fatigue [71, 75, 76]. More specifically, ixekizumab has been associated with significant and rapid improvements in DLQI score [42, 57, 60, 62, 65, 77–79] that were sustained up to 24 months in one retrospective cohort study ($n = 198$) [56]. Improvements were also reported in patients receiving ixekizumab for itch numerical rating scale, skin pain numerical rating scale, and Patient-Reported Outcomes Measurement Information System sleep-related impairment scores, with improvement regardless of prior biologic use, PsA status, and PsO nail involvement [76].

Significant improvements in PROs, including DLQI scores, have been reported for ixekizumab across patient subgroups, including PASI score at baseline, weight at baseline, and presence of concomitant PsA [61]. Importantly, prior biologic exposure does not appear to affect the DLQI 0/1 response in patients with PsO receiving ixekizumab or secukinumab [80]. Evidence suggests that complete skin clearance after 12 weeks of ixekizumab is more likely to be associated with a DLQI score of 0 than almost clear skin in patients receiving ixekizumab, highlighting the importance of skin clearance for patient QoL [67]. Patients initiating treatment with ixekizumab also experienced improvements in most Work Productivity and Activity Impairment domains after 6 months, and the magnitude of the change was higher among patients

with PASI > 12 than those with PASI < 12 at baseline [61].

In a large retrospective cohort study ($n = 1812$), ixekizumab was also associated with improvements in PROs in patients with PsA (82.2% of whom also had PsO), such as the Routine Assessment of Patient Index Data 3, fatigue and pain visual analog scales, and the Multidimensional Health Assessment Questionnaire Functional Index after 6 months, with responses maintained up to 12 months [68].

Treatment Patterns

A total of 81 publications reported treatment patterns, of which 61 focused on patients with PsO, 15 on patients with PsA, 4 on both patients with PsO and patients with PsA, and 1 on patients with axSpA.

Treatment Adherence

In patients with PsO, adherence to ixekizumab is higher than adherence to other biologics, with results from four studies demonstrating higher adherence to ixekizumab (as measured by proportion of days covered) than to adalimumab or secukinumab [81–84], and a fifth study showing high adherence to ixekizumab as measured by a medication possession ratio $\geq 80\%$ [85, 86].

Drug Survival and Persistence

Both the anti-IL-17A and anti-IL-23 biologics have high drug survival rates. Five studies in patients with PsO identified in this review found that guselkumab had higher drug survival than most other biologics, although most differences were not statistically significant [34, 87–90]. Additionally, in one retrospective cohort study in patients with moderate-to-severe PsO ($n = 1057$), the anti-IL-23 agents were associated with higher drug survival than the anti-IL-17A agents, at 88% versus 75% ($P < 0.001$) at 24 weeks, with discontinuation rates of 10% for anti-IL-23 agents and 25% for IL-17A biologics; rates for individual drugs were 33% for secukinumab, 25% for ixekizumab, 14% for brodalumab, 12% for guselkumab, 11% for

Table 2 Real-world effectiveness of ixekizumab in patients with psoriatic arthritis

Study author, year	Study design (country)	Pts	Main findings
Rohekar et al. 2023 [71]	Retrospective database (USA)	Pts aged ≥ 18 years with active PsA receiving ixekizumab enrolled in the US database in 2022	<ul style="list-style-type: none">• Ixekizumab was associated with significant decreases in mean number of symptoms after a mean treatment duration of 12.5 months (from 5.61 to 3.12 symptoms), with decreases in the presence of (physician-reported) tender joints, swollen joints, enthesitis, dactylitis, inflammatory back pain, persistent lower back pain, stiffness in the morning and fatigue/exhaustion• Asymptomatic pts increased from 0/88 at baseline to 22/88 at time of data extraction; $P < 0.0001$• There were significant decreases in physician-recorded pt pain and fatigue (0–10 VAS) from mean $\pm$ SD values at baseline of 5.60 ± 1.46 and 4.74 ± 2.38, respectively, to 1.94 ± 1.83 and 1.92 ± 1.87, respectively (both $P < 0.0001$)• Values for pt-reported pain VAS were 6.15 ± 1.97 at baseline, decreasing to 2.11 ± 2.06 at time of data extraction ($P < 0.0001$)• Both physician- and pt-reported disease severity demonstrated significant improvements from baseline

Table 2 continued

Study author, year	Study design (country)	Pts	Main findings
Tillert et al. 2023 [68]	Retrospective cohort/claims dataset + EMR (USA)	Pts aged ≥ 18 years initiating ixekizumab from Dec 1, 2017 through Jan 2021, who did not have a diagnosis code for ankylosing spondylitis in the baseline period	<ul style="list-style-type: none">• Ixekizumab treatment was associated with improvements in total CDAL, TJC/SJC, and PGA from baseline to 6 and 12 months, with improvements seen at 6 months to be maintained or further improved from 6 to 12 months• After adjustment for age, sex, and baseline values, there were statistically significant reductions in disease activity with ixekizumab treatment, as measured by PatGA, PGA, TJC, and SJC at both 6 and 12 months• Mean DAPSA scores decreased significantly for ixekizumab-treated pts from a mean ± SD of 23.7 ± 9.8 at baseline to 14.8 ± 10.3 at 12 weeks, and 14.3 ± 7.4 at 24 weeks ($P = 0.005$)
Joven et al. 2022 [70]	Retrospective cohort/multicenter cohort	Pts who started ixekizumab between January 1, 2019, and December 31, 2020, with a minimum follow-up of 24 weeks until treatment interruption/end of follow-up	
Joven et al. 2023 [69]	(Spain)		

CDAL Clinical Disease Activity Index, DAPSA Disease Activity Index for Psoriatic Arthritis, EMR electronic medical records, PGA Physician Global Assessment, PsA psoriatic arthritis, $pt(s)$ patient(s), PatGA Patient Global Assessment, SD standard deviation, SJC swollen joint count, TJC tender joint count, VAS visual analog scale

tildrakizumab, and 9% for risankizumab [36]. One study showed that patients with PsO who started treatment with an anti-IL agent were more persistent in their treatment after 1 year than were patients starting treatment with an anti-TNF [91]. Moreover, patients with PsO with or without previous biologic experience had a higher probability of persistence with guselkumab than with ixekizumab and secukinumab at 12 and 18 months ($P < 0.001$) [92, 93].

In a single-center study in patients with PsO ($n = 111$), overall anti-IL-17A drug survival was 69 months, with no significant differences between agents, although ixekizumab showed numerically higher survival, and drug survival was significantly higher in patients naïve to biologics than in biologic-experienced patients [44]. Another retrospective cohort study in PsO ($n = 176$) reported cumulative survival rates for anti-IL-23 and anti-IL-17A biologics at 18 months of 73.5% and 72.8%, respectively (not statistically significant) [94]. For individual agents, drug survival for risankizumab and ixekizumab was significantly higher than that for secukinumab. Of note, after 2 and 4 years, patients with severe PsO treated with ixekizumab were more persistent with and adherent to treatment than were patients treated with secukinumab (88% vs. 75% and 80% vs. 67%, respectively) [84]. In addition, in another study, Kaplan–Meier analysis showed that drug persistence in patients with moderate-to-severe PsO switching from secukinumab to ixekizumab was 83.9% at year 1, compared with 58.9% at year 1 in the group that switched from ixekizumab to secukinumab (log rank $P = 0.022$) [48].

There do not appear to be any significant differences in drug survival rates between disease groups (PsO, PsA) for secukinumab, guselkumab, or ixekizumab [95]. However, some evidence suggests that the presence of PsA or nail involvement may affect the survival of biologic drugs, but this differs by agent, with lower survival for such patients receiving ustekinumab than for those without PsA or nail involvement (hazard ratio 1.18; 95% confidence interval 1.03–1.35) but not for those receiving adalimumab, guselkumab, ixekizumab, or secukinumab [88]. In addition, discontinuation rates for anti-IL-17A biologics were higher than those

for anti-IL-23 agents in patients receiving treatment for PsO with involvement at special sites; secukinumab had the highest drop-out rate, and the palmoplantar site was the most affected by treatment discontinuation [50].

Reasons for Treatment Discontinuation

In patients with PsO and PsA treated with ixekizumab, the primary reason for discontinuation was lack or loss of effectiveness [56, 69, 96]. Similar rates of discontinuation at 1 year for all reasons have been reported for ixekizumab (12.2%), secukinumab (11.2%), guselkumab (12.5%), and risankizumab (6.6%) in the PSoHO cohort study [96].

Treatment Switching

Treatment switching in a real-world context appears to be lower in patients treated with ixekizumab than in those treated with secukinumab [48, 84]. Importantly, failure of a first-line anti-IL-17A should not preclude treatment with a second-line anti-IL-17A biologic [97]. One retrospective cohort study ($n = 534$) showed similar adherence to therapy and that treatment failure was more common with first-line than with second-line switching [97]. Notably, in another study, among patients initiating a new biologic ($n = 7997$), the anti-IL-23 agents were associated with the lowest switch rates at 12 and 24 months compared with the anti-IL-17A, anti-IL-12/23, and anti-TNF agents, with the highest switch rates reported in anti-TNFs [98].

Dose Escalation

In a Japanese database study in patients with moderate-to-severe PsO, significant differences were reported between biologics in rates of dose escalation (defined as an increase of $\geq 20\%$ in average daily dose) at 6 and 12 months (ixekizumab 31% and 39%, ustekinumab 31% and 42%, brodalumab 8% and 11%, secukinumab 6% and 17%, guselkumab 1% and 2%, and risankizumab 0% and 0%), with the exception of guselkumab when compared with risankizumab [99]. A second publication highlighted lower

odds of dose escalation for risankizumab than with other anti-IL-23, anti-IL-12/23, anti-TNF, and anti-IL-17A agents (all $P < 0.0001$) [100].

Prescription Patterns

A study that utilized data from a French PsO cohort to investigate switching between biologics in patients with moderate-to-severe PsO reported that patients transitioning from adalimumab to ustekinumab—the most common first- and second-line treatments—typically then received anti-IL-17A agents (secukinumab or ixekizumab) or guselkumab as a third-line biologic [101]. Similarly, data from the Danish DERMBIO prospective registry demonstrated that, in Denmark, ixekizumab and guselkumab were primarily given to patients with PsO as third-line or later treatment [102]. In a database study looking at trends in use of biologic treatment in the USA, the use of biologics in patients with PsA increased steadily from 20.9% in 2014 to 51.8% in 2021, with increases seen for ixekizumab, certolizumab, guselkumab, and secukinumab [103]. A second study using the same dataset found similar results for patients with PsO, with an increase in exposure to any biologic therapy from 7% in 2014 to 22% in 2021 [104].

Safety

In total, 31 publications focusing on PsO, 8 focusing on PsA, 1 focusing on both PsO and PsA, and 1 focusing on axSpA reported safety outcomes with ixekizumab. Overall, the biologics available for the treatment of PsO, PsA, and axSpA were generally associated with good tolerability profiles, with no unexpected safety signals associated with ixekizumab use in real-world settings. Most reported adverse events with ixekizumab were mild, including injection-site reactions [66, 105], and did not lead to treatment discontinuation [58, 64, 66, 106–108]. More patients discontinued biologic treatment (including ixekizumab) because of a loss or lack of effectiveness of therapy than because of adverse events [42–44, 55, 57, 59, 70, 74, 87, 89, 90, 96, 109–113]. Importantly, ixekizumab had a good long-term safety profile

in patients with moderate-to-severe PsO for up to 3 years in retrospective multicenter studies [59, 114].

Economic Burden

Nine publications reporting economic outcomes were identified, all of which focused on PsO. The US Institute for Clinical and Economic Review (ICER)-adjusted all-cause and PsO-related costs were comparable between ixekizumab- and secukinumab-treated patients with PsO [82] and remained comparable after adjusting for ICER discounts and treatment adherence [82]. In a retrospective US claims database study, index drug costs were comparable for ixekizumab and adalimumab users over 2 years after adjusting for ICER and adherence rates (index drug costs were comparable) [81]. Treatment discontinuation and switching are important factors when assessing the cost effectiveness of biologic therapies [115]. It was demonstrated in two China-based real-world publications that costs associated with ixekizumab were able to be reduced by switching from a 2- to a 4-week dosing interval for the induction period without loss of benefit, although it should be noted that this is an off-label approach [60, 116]. In one US-based retrospective database analysis of patients with PsO who switched biologics, ixekizumab was associated with the highest median total pharmacy costs among anti-IL-17A agents [117]. Another US-based study demonstrated that, while costs of biologic medications for PsO varied greatly in 2013, by 2017 these costs appeared to have converged towards similar prices [118].

DISCUSSION

This SLR identified a total of 118 publications describing the real-world use of ixekizumab in PsO, PsA, and axSpA, more than half of which were full publications, with 82 comparative publications and 36 focusing on ixekizumab alone, covering clinical effectiveness, PROs, treatment patterns, safety, and economic burden.

The effectiveness of ixekizumab in the treatment of PsO as observed in routine clinical practice was consistent across multiple real-world studies and supported the findings from randomized controlled trials. More specifically, anti-IL-17A agents, including ixekizumab, were more effective than anti-IL-23 biologics in terms of early skin clearance [36, 119]. Evidence also indicates that ixekizumab is associated with greater skin clearance than secukinumab [33, 44, 45, 53], a finding consistent with network meta-analyses conducted to indirectly compare biologic treatments in PsO [120–123]. The anti-IL-17As were also more likely to be associated with a sustained response than were other biologics [39, 46].

Importantly, the anti-IL-17As have demonstrated effectiveness for PsO of the nails, scalp, genitals, and palmoplantar regions, which are considered to be challenging body areas [49–52, 76]. PsO of the nails is of particular concern, as it is linked with an increased risk of PsA development in patients with PsO [124, 125]. The findings of our review of real-world use of these agents align with those from clinical trials of ixekizumab, which consistently demonstrated that a high proportion of patients with PsO or PsA achieve complete resolution of PsO of the nails with ixekizumab treatment [126]. This finding is also consistent with the results of three network meta-analyses, all of which demonstrated that ixekizumab is one of the most efficacious biologics for treating nail PsO [127–129]; this was again confirmed in a 2023 update to one of these meta-analyses, which demonstrated that, of included biologics, ixekizumab had the highest absolute probability of achieving complete resolution of nail PsO [130]. Moreover, the results of an interim analysis of the ongoing Prospective Observational Study of Patients with Psoriasis in Special Areas study demonstrated improvements in both nail and scalp PsO by week 4 of ixekizumab treatment [131].

A total of 12 publications identified in this SLR reported on patients enrolled in the Eli Lilly and Company-sponsored PSoHO study [32, 37–39, 41, 46, 51, 52, 73, 96, 132, 133]. Collectively, these publications highlight the real-world effectiveness of ixekizumab, relative to

other biologics, in the treatment of moderate-to-severe PsO. In an additional study published after the searches for this SLR were conducted, data from the PSoHO patient cohort were used to identify predictors of PASI100 response in patients with PsO receiving biologics [134]. This analysis found that patients without nail involvement appeared to be more likely to achieve skin clearance with biologic treatment than were patients with nail PsO, a finding that highlights the importance of considering the performance of different biologics in specifically addressing nail PsO. In another PSoHO analysis published after the SLR searches, the effectiveness of anti-IL-17A agents for the treatment of nail PsO was demonstrated regardless of baseline severity of nail PsO, with significantly faster and greater reductions from baseline in modified Nail Psoriasis Severity Index scores in the IL-17A cohort than in the other biologics cohort after up to 6 months of treatment [135]. In these real-world studies in patients with moderate-to-severe plaque PsO, ixekizumab was an effective biologic treatment option across a variety of patient subgroups, including both biologic-experienced and biologic-naïve patients [55, 59, 60], patients with PsO in challenging body areas [61], and patients with concomitant PsA [59–61].

Real-world evidence focusing specifically on PsA is more limited, with only 21 publications identified in this review focusing on patients with PsA, including 5 studies evaluating patients with PsO and patients with PsA. Many of the studies focusing on PsO included a high proportion of patients with concomitant PsA, and there was no indication of differences in effectiveness in these disease groups. Of note, since the searches for this review were conducted, findings from the PRO-SPIRIT trial, which includes 1192 adult patients with PsA across six countries who initiated or switched to a new biologic disease-modifying anti-rheumatic drug (bDMARD) or targeted synthetic DMARD, have been published [136]. The results of this large real-world trial demonstrated that ixekizumab was as effective as anti-TNF biologics and Janus kinase (JAK) inhibitors at improving joint disease activity in patients with PsA, despite the ixekizumab population in this trial having greater bDMARD/targeted

synthetic DMARD experience and longer disease duration than those receiving an anti-TNF, as well as fewer patients on concomitant conventional synthetic DMARDs than those on anti-TNFs and JAK inhibitors [136]. More specifically, ixekizumab was as effective as anti-TNF agents and JAK inhibitors in terms of improvement of clinical DAPSA scores and tender joint counts and swollen joint counts; at 3 months, ixekizumab outperformed anti-IL-12/23 and anti-IL-23 treatments [136]. In addition, ixekizumab was associated with significantly greater improvement in BSA than were anti-TNF agents [137].

Only one study focused on axSpA, for which ixekizumab was approved in 2019, compared with 2016 for PsO [54], limiting the conclusions that can be drawn [1, 2].

Improvements have also been reported with the real-world use of ixekizumab regarding PROs, with studies highlighting improvements in DLQI scores in patients with PsO [33, 60, 61, 72, 74]. Furthermore, complete skin clearance with ixekizumab treatment increased the likelihood of achieving a DLQI score of 0, highlighting the link between skin clearance and patient QoL [67].

Most publications in this review included data on treatment patterns such as adherence, drug survival/persistence, treatment switching, and treatment discontinuation. In patients with PsO, adherence to ixekizumab treatment was high compared with that for other biologics [81–84, 106]. Both the anti-IL-17As and anti-IL-23 s have high drug survival rates; although some studies reported differences between agents, these were not consistent. One study showed that patients with PsO who started treatment with an anti-IL agent (ixekizumab, secukinumab, ustekinumab, or guselkumab) were more persistent in their treatment after 1 year than patients starting treatment with an anti-TNF agent [91], and there was also some evidence that patients receiving ixekizumab were more persistent and adherent after 2 and 4 years than those receiving secukinumab [84].

Treatment switching in a real-world context appears to occur at a lower rate in biologic-experienced than in biologic-naïve patients with PsO [92, 93], and in patients with PsO treated with

ixekizumab than in those treated with secukinumab [84].

Ixekizumab has also been reported to have good long-term safety in patients with moderate-to-severe PsO, with results for up to 3 years [114]. Importantly, the safety profile highlighted in these real-world studies in patients with PsO is consistent with that reported in clinical trials, and no new or unexpected safety signals were identified [138]. Of note, although there is a risk of serious infections with the biologics, including the anti-IL-17As, discontinuation due to infection occurs infrequently [90], with injection-site reactions with ixekizumab generally mild, easy to manage, and infrequently leading to discontinuation [66, 105]. Importantly, these injection-site reactions with ixekizumab are likely to become less frequent with the development of a bioequivalent citrate-free formulation, which started to replace the original formulation in select countries after 2022 [137, 139, 140]. The most frequent reason for treatment discontinuation of ixekizumab reported in these real-world studies was lack or loss of effectiveness.

It should be noted that several limitations are associated with some of the study types included in this review, such as retrospective studies, cohort/registry studies, and claims databases, where there is the potential for missing or poor-quality data. Limitations inherent to observational studies also include the potential for unmeasured confounders and selection bias. Moreover, comparative analyses are limited by methods used to adjust for any variables that may influence findings. Several studies also had small sample sizes. The findings of this review are also limited by the date limits on the literature searches. Given the much higher number of publications identified in the time frame of this review compared with a previous review covering a longer time period [3], it is likely that further real-world evidence in this area will be generated, including in patients with PsA and axSpA, for whom data are currently relatively limited. A high number of conference abstracts was also included among the identified studies, many of which contained limited data, and data may be inconsistent. Comparison between studies is limited by differences in study design, approaches to data collection,

and patient population. Many of the studies also lacked adjustment for potential confounders, such as prior biologic use and coexisting PsA. The real-world study results presented here should be considered within the context of these limitations.

Overall, the findings of this SLR confirm the findings of our earlier SLR of ixekizumab in the treatment of PsO and PsA. Importantly, the need for additional data on PROs that was identified in this earlier review has been met, at least in part, by the additional real-world studies identified here, which serve to highlight the substantial improvements in DLQI scores in patients with PsO.

CONCLUSION

Real-world data on the use of ixekizumab in the treatment of PsO and PsA support the effectiveness and safety seen in clinical trials. Importantly, these real-world trials highlight the positive impact of ixekizumab on patient QoL. Overall, ixekizumab is associated with high levels of adherence, less switching than with other biologics, and generally high persistence and drug survival. The lack of real-world data for ixekizumab in patients with axSpA highlights a need for further research in this important topic.

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Declarations

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Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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