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ADIS DRUG EVALUATION

Secukinumab: A Review in Moderate to Severe Pediatric Plaque Psoriasis

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Abstract

Subcutaneous secukinumab (Cosentyx®) is a recombinant, fully human, immunoglobulin (Ig) G1κ monoclonal antibody targeted against interleukin (IL)-17A, a proinflammatory cytokine involved in the pathogenesis of psoriasis. Secukinumab is approved in the EU and the USA for the treatment of moderate to severe plaque psoriasis in pediatric patients aged ≥ 6 years. In pivotal phase III trials in pediatric patients aged 6 to < 18 years, both low (75–150 mg) and high (75–300 mg) doses of secukinumab were significantly better than placebo and numerically better than etanercept at week 12 in terms of the proportion of patients achieving ≥ 75% improvement from baseline in Psoriasis Area and Severity Index and significantly better than placebo and etanercept in terms of the proportion of patients achieving an Investigator's Global Assessment score of 0 or 1. The clinical efficacy of secukinumab observed during the first 12 weeks of treatment was maintained over the longer term. Treatment with secukinumab improved health-related quality of life and was generally well tolerated. In conclusion, secukinumab represents a valuable new addition to the limited treatment options available for children and adolescents with moderate to severe plaque psoriasis.

Plain Language Summary

Plaque psoriasis is a chronic, inflammatory skin condition that can have a negative impact on the quality of life of affected children and their families. Compared with the expanding treatment options for adults with plaque psoriasis, the number of approved medications for pediatric plaque psoriasis is relatively low. Subcutaneous secukinumab (Cosentyx®) is one of several targeted biologic agents that have recently been approved for treating plaque psoriasis in pediatric patients. Secukinumab binds to IL-17A and inhibits the release of proinflammatory cytokines and chemokines. Treatment with secukinumab provided fast and durable skin clearance and continuous improvements in health-related quality of life in children and adolescents aged 6 to < 18 years with moderate to severe plaque psoriasis. The benefits of secukinumab were maintained over the longer term and the drug was generally well tolerated. With a convenient 4-weekly maintenance dosing regimen and the option of caregiver administration, secukinumab is a valuable option for the treatment of moderate to severe pediatric plaque psoriasis.

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1 Introduction

Plaque psoriasis is a chronic, immune-mediated, inflammatory disease [1, 2] affecting approximately 1% of children [3–5]. It is often associated with metabolic, cardiovascular, gastrointestinal, and psychological comorbidities [1, 4], and can have a significant negative impact on quality of life (QOL) [3–5]. In pediatric patients, the impact of psoriasis on QOL is estimated to be greater than that of diabetes or epilepsy and comparable to that of asthma or arthritis [6].

Although many effective and well-tolerated therapies are available for the treatment of plaque psoriasis in adults [1], treatment options for children and adolescents with plaque

Secukinumab: clinical considerations in moderate to severe pediatric plaque psoriasis
Fully human IgG1κ monoclonal antibody that selectively targets IL-17A
Provides fast and durable skin clearance in children and adolescents aged 6 to < 18 years
Beneficial effects maintained over the longer term
Improves health-related quality of life
Generally well tolerated

psoriasis are much more limited [1, 2, 4, 5]. This is due, at least in part, to the unpredictability of adult-approved treatments in the pediatric population [1]. Recently, several targeted biologic agents have been approved for the treatment of pediatric plaque psoriasis, including the tumor necrosis factor-α inhibitors etanercept and adalimumab (EU only), the interleukin (IL)-12/23 inhibitor ustekinumab, and the IL-17 inhibitors ixekizumab and secukinumab [1].

IL-17 is a key proinflammatory cytokine implicated in the pathogenesis of psoriasis [7]. IL-17A (a member of the IL-17 family) is upregulated in psoriatic lesional and non-lesional skin [7]. Secukinumab (Cosentyx®), an IL-17A antagonist, is approved in the EU [8] and the USA [9] for the treatment of moderate to severe plaque psoriasis in children and adolescents aged ≥ 6 years. The pharmacological properties of secukinumab have been reviewed in detail previously and are summarized in Table 1. This review focuses on the clinical use of secukinumab in pediatric plaque psoriasis. Discussion of the use of secukinumab in other approved indications (i.e. adult plaque psoriasis [10], psoriatic arthritis [11, 12], ankylosing spondylitis [13, 14], and non-radiographic axial spondyloarthritis) is outside the scope of this article.

2 Therapeutic Efficacy of Secukinumab

The efficacy of secukinumab for the treatment of pediatric plaque psoriasis was evaluated in two phase III trials: a randomized, double-blind, multicentre, placebo- and active comparator-controlled trial in patients with severe plaque psoriasis [15] and an open-label, multicentre trial in patients with moderate to severe plaque psoriasis [16].

2.1 Severe Plaque Psoriasis

The first trial enrolled pediatric patients aged 6 to < 18 years with severe chronic plaque psoriasis for ≥ 3 months who were candidates for systemic therapy [15]. All patients had a Psoriasis Area Severity Index (PASI) score of ≥ 20, an Investigator's Global Assessment modified 2011 (IGA) score of 4, and body surface area (BSA) involvement of ≥ 10%. The mean age of patients at baseline was 13.5 years and most (77.2%) patients were aged ≥ 12 years. The mean total BSA affected by plaque psoriasis was 40% and the mean duration of plaque psoriasis was 5.22 years. Overall, 8.6% of patients had a diagnosis of psoriatic arthritis at baseline [15].

Patients were randomized to receive low-dose secukinumab (75 mg in patients weighing < 50 kg and 150 mg in patients weighing ≥ 50 kg), high-dose secukinumab (75 mg in patients weighing < 25 kg, 150 mg in patients weighing 25 to < 50 kg, and 300 mg in patients weighing ≥ 50 kg), subcutaneous etanercept 0.8 mg/kg (up to a maximum of 50 mg), or placebo [15]. Secukinumab and placebo were administered at weeks 0, 1, 2, 3, and 4, then every 4 weeks, while etanercept was administered once weekly. The trial included a 12-week placebo- and active comparator-controlled induction period, followed by an active comparator-controlled maintenance period (week 12 to week 52), an extension treatment period (week 52 until week 236), and a 16-week treatment-free follow-up period. At week 12, patients in the placebo group who were classified as non-responders were switched to either low- or high-dose secukinumab; placebo responders were discontinued from the trial. At week 52, patients in the etanercept group discontinued treatment and entered the treatment-free follow-up period, while all secukinumab recipients entered the extension treatment period, which is ongoing [15].

The co-primary endpoints were the proportion of patients achieving ≥ 75% improvement in the PASI score (PASI 75) and the proportion of patients achieving an IGA score of 0 or 1 (IGA 0/1) at week 12 for secukinumab compared with placebo [15]. The key secondary endpoint was superiority of secukinumab versus placebo for the proportion of patients achieving PASI 90 at week 12. The efficacy of secukinumab versus etanercept for the proportions of patients achieving PASI 75/90/100 or IGA 0/1 was evaluated as an exploratory objective [15].

2.1.1 Clinical Response

Secukinumab was efficacious for the treatment of severe plaque psoriasis in pediatric patients [15]. The clinical efficacy of secukinumab was seen as early as week 4. At week 12, PASI 75, IGA 0/1, and PASI 90 response rates were significantly higher with both low- and high-dose secukinumab than with placebo (Table 2). Low- and high-dose secukinumab were associated with significantly higher IGA 0/1 and PASI 90 response rates, and numerically higher PASI 75 and PASI 100 response rates, than etanercept at week 12 (Table 2). Among patients weighing

Table 1 Overview of key pharmacologic properties of secukinumab [8, 9]

Mechanism of action	Recombinant, fully human IgG1κ monoclonal antibody
	Binds selectively to and neutralizes IL-17A, thereby inhibiting its interaction with the IL-17 receptor; inhibits the release of proinflammatory cytokines and chemokines
	Reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases
Pharmacodynamics	Initial ↑ in serum levels of total IL-17A (free + SEC-bound IL-17A), followed by slow ↓ due to reduced clearance of SEC-bound IL-17A
	Clinically relevant levels of SEC reach the skin, resulting in ↓ local inflammatory markers and ↓ erythema, induration, and desquamation in PP lesions
	↓ Epidermal neutrophils and neutrophil-associated markers in lesional skin of PP pts after 1–2 wks of treatment
	↓ Levels of C-reactive protein (marker of inflammation) within 1–2 wks of treatment
Pharmacokinetics[a]	
Dose-proportional pharmacokinetics over dose range of 25–300 mg; C_{max} reached ≈ 6 days following single dose (150 or 300 mg); steady-state concentrations reached after 20–24 wks of monthly administration; bioavailability 60–77%	
Mean trough concentrations at wks 4 and 12 were ↑ 23–30% after administration via Sensoready® pen than after administration of lyophilized powder and ↑ 23–26% than after administration via prefilled syringe	
Steady-state mean trough concentrations at wk 24 were 32.6 µg/mL in pediatric pts weighing < 25 kg receiving SEC 75 mg, 19.8 µg/mL in pts weighing 25–49 kg receiving SEC 75 mg, and 27.3 µg/mL in pts weighing ≥ 50 kg receiving SEC 150 mg	
Vd during terminal phase 7.10–8.60 L (following single IV dose); SEC concentrations in interstitial fluid in lesional and non-lesional skin were 27–40% of those in serum following single 300 mg dose	
Most elimination of IgG occurs via intracellular catabolism (following endocytosis); systemic clearance ≈ 0.19 L/day; mean half-life 22–31 days	
Special populations[b]	↑ SEC clearance and Vd with ↑ bodyweight
	Hepatic impairment and abnormal kidney function are not expected to influence SEC clearance (lack of data)
Drug interactions[b]	Formation of CYP enzymes can be altered by ↑ levels of certain cytokines during chronic inflammation
	No interaction when SEC is coadministered with methotrexate ± corticosteroids or with midazolam (CYP3A4 substrate)
	Consider monitoring and dosage adjustment when initiating or discontinuing SEC in pts receiving concomitant CYP450 substrates (particularly those with narrow therapeutic index)

↓ decrease(d), ↑ increase(d), C_{max} maximum plasma concentration, *Ig* immunoglobulin, *IL* interleukin, *IV* intravenous, *PP* plaque psoriasis, *pts* patients, *SEC* secukinumab, *Vd* volume of distribution, *wk(s)* week(s)

[a]All pharmacokinetic parameters are for subcutaneous SEC in pts with PP unless otherwise stated

[b]Consult local prescribing information for detailed recommendations

≥ 25 to < 50 kg, PASI 75/90/100 and IGA 0/1 response rates at week 12 were numerically higher with high-dose secukinumab ($n = 15$) than with low-dose secukinumab ($n = 17$) [15]. At week 12, mean PASI scores decreased (improved) from baseline by 82.9% in the low-dose secukinumab group and 79.9% in the high-dose secukinumab group, compared with 29.3% in the placebo group and 74.2% in the etanercept group [15].

The clinical responses reported with secukinumab at week 12 were maintained over the longer term [15, 17]. PASI response rates reached a peak between weeks 20 and 28 and were sustained through week 52 [15] and week 104 [17] in both secukinumab groups. Similarly, IGA 0/1 response rates peaked at week 24 and were sustained through week 52 [15] and week 104 [17] in both secukinumab groups. At week 52, PASI 75 response rates in the low- and high-dose secukinumab groups were numerically higher than those in the etanercept group (87.5 and 87.5 vs 68.3%, respectively) [15]. Similar results were seen with regard to IGA 0/1 (72.5 and 75.0 vs 56.1%), PASI 90 (75.0 and 80.0 vs 51.2%), and PASI 100 (40.0 and 47.5 vs 22.0%) response rates. Among patients weighing ≥ 50 kg, PASI 75/90/100 and IGA 0/1 response rates at week 52 were numerically higher with high-dose secukinumab ($n = 21$) than with low-dose secukinumab ($n = 22$). However, in the ≥ 25 to < 50 kg subgroup, PASI and IGA response rates at week 52 were numerically higher with low- ($n = 17$) versus high-dose ($n = 15$) secukinumab [15].

Among patients initially randomized to placebo who switched to secukinumab at week 12, PASI 75/90/100 and IGA 0/1 response rates at week 52 were similar to those in patients initially randomized to secukinumab [15].

Table 2 Efficacy of secukinumab at week 12 in pediatric patients aged 6 to < 18 years with moderate to severe plaque psoriasis in pivotal phase III trials

Trial	Treatment (no. of pts)	PASI response (% of pts)			IGA 0/1 (% of pts)[a]	CDLQI 0/1 (% of pts)
		PASI 75[a]	PASI 90[b]	PASI 100		
Severe psoriasis [15]	SEC LD (40)	80.0**	72.5**†	30.0	70.0**†	44.7*
	SEC HD (40)	77.5**	67.5**†	27.5	60.0**†	50.0*
	ETA (41)	63.4	29.3	17.1	34.1	36.6
	PL (41)	14.6	2.4	0.0	4.9	15.0
Moderate to severe psoriasis [16, 18]	SEC LD (42)	92.9	69.0	59.5	78.6	50.0
	SEC HD (42)	92.9	76.2	54.8	83.3	61.9

Efficacy analyses were conducted in the full analysis set

CDLQI Children's Dermatology Life Quality Index, *ETA* etanercept, *HD* high dose, *IGA* Investigator's Global Assessment modified 2011, *LD* low dose, *PASI* Psoriasis Area and Severity Index, *PASI x* improvement of ≥ x% from baseline in PASI score, *PL* placebo, *pts* patients, *SEC* secukinumab

*$p < 0.01$, **$p < 0.0001$ vs PL; †$p < 0.05$ vs ETA

[a]Co-primary endpoint for SEC vs PL (historical [16])

[b]Key secondary endpoint for SEC vs PL (historical [16])

2.1.2 Health-Related Quality of Life

Secukinumab improved health-related QOL (HR-QOL) in pediatric patients with severe plaque psoriasis [15]. At week 12, the proportion of patients achieving a Children's Dermatology Life Quality Index (CDLQI) score of 0 or 1 (i.e. no impact on QOL) was significantly higher with low- and high-dose secukinumab versus placebo and numerically higher versus etanercept (Table 2). The proportion of patients with a CDLQI score of 0 or 1 at week 52 was 60.6% in the low-dose secukinumab group, 66.7% in the high-dose secukinumab group and 44.4% in the etanercept group [15]. At week 104, the proportion of patients with a CDLQI score of 0 or 1 was 61.1% with any low dose of secukinumab and 65.0% with any high dose of secukinumab [17].

At week 12, the mean change from baseline in CDLQI total score (scores range from 0 to 30 [18]) was − 9.05 with low-dose secukinumab, − 7.71 with high-dose secukinumab, − 3.79 with placebo, and − 6.49 with etanercept [15]. The mean change from baseline in CDLQI total score at week 52 was − 9.2 with low-dose secukinumab, − 8.3 with high-dose secukinumab, and − 5.7 with etanercept. At weeks 12 and 52, improvements from baseline in CDLQI individual domain scores (symptoms and feelings, personal relationships, leisure, school or holidays, sleep, and treatment) were numerically higher in both secukinumab groups than in the etanercept group, with the exception of the personal relationship score which was numerically higher with etanercept than secukinumab at week 12 [15].

2.2 Moderate to Severe Plaque Psoriasis

The second trial enrolled patients aged 6 to < 18 years with moderate to severe plaque psoriasis for ≥ 3 months who were eligible for systemic therapy [16]. They had a PASI score of > 12, an IGA score of > 3, and BSA involvement of > 10%. At baseline, 72.6% of patients had moderate disease and 27.4% had severe disease. The mean age of patients was 12.6 years and 60.7% of patients were 12 to < 18 years of age. The mean total BSA involvement was 30%. Patients were randomized (with stratification by bodyweight and disease severity) to receive low-dose secukinumab (75 mg in patients weighing < 50 kg and 150 mg in patients weighing ≥ 50 kg) or high-dose secukinumab (75 mg in patients weighing < 25 kg, 150 mg in patients weighing 25 to < 50 kg, and 300 mg in patients weighing ≥ 50 kg). Secukinumab was administered at weeks 0, 1, 2, 3, and 4, then every 4 weeks. Historical placebo data from placebo-controlled trials in adult and pediatric patients with plaque psoriasis were used for the primary and key secondary endpoint analyses. The co-primary endpoints were the proportions of patients achieving PASI 75 and IGA 0/1 responses at week 12 for secukinumab compared with historical placebo [16].

2.2.1 Clinical Response

Secukinumab demonstrated efficacy in pediatric patients with moderate to severe plaque psoriasis [16]. At week 12, both low- and high-dose secukinumab were superior to historical placebo in terms of PASI 75, IGA 0/1, and PASI 90 response rates (*p*-values not stated; Table 2); the estimated probability of a positive treatment effect over historical placebo was 1 (100%) [16]. PASI 75 and IGA 0/1 response rates increased until week 24 (low-dose: 95.2 and 88.1%; high-dose: 95.2 and 92.9%) [16] and were sustained up to week 52 (low-dose: 88.1 and 85.7%; high-dose: 90.5 and 83.3%) [19].

PASI 90/100 response rates at week 52 were 76.2/52.4% in the low-dose secukinumab group and 83.3/69.0% in the high-dose secukinumab group [19]. PASI 90 response rates were numerically higher with high- versus low-dose secukinumab at weeks 32, 48 and 52 (but not at week 40). Similarly, PASI 100 response rates were numerically higher with high- versus low-dose secukinumab from week 32 until week 52 [19]. The efficacy of secukinumab was consistent across bodyweight (< 25 kg, 25 to < 50 kg, and ≥ 50 kg) and age (6 to < 12 years and 12 to < 18 years) subgroups [20].

2.2.2 Health-Related Quality of Life

Secukinumab improved HR-QOL in pediatric patients with moderate to severe plaque psoriasis [18]. At week 12, ≥ 50% of patients treated with secukinumab achieved a CDLQI 0/1 response at week 12 (Table 2). These response rates further increased up to week 24 in the low-dose secukinumab group (70.7%) and from week 24 to week 52 in the high-dose secukinumab group (70.3%). Consistently, the mean CDLQI total score decreased (improved) through week 24 in the low-dose group and through week 52 in the high-dose group. The mean absolute change from baseline in CDLQI total score at week 52 was − 8.7 with low-dose secukinumab and − 11.9 with high-dose secukinumab. Similarly, improvements in all individual domain scores (except personal relationships and treatment) were numerically higher with high- versus low-dose secukinumab at week 52 [18].

3 Tolerability of Secukinumab

Secukinumab was generally well tolerated in pediatric patients with plaque psoriasis, with no new safety signals identified [15, 16, 21]. The safety profile in this population was consistent with that reported in adults with plaque psoriasis [8, 9].

In a pooled analysis of the phase III trials discussed in Sect. 2 ($n = 198$), the overall incidence of adverse events (AEs) up to week 52 was 74.5% with any low dose of secukinumab, 74.0% with any high dose of secukinumab, and 82.9% with etanercept [21]. Corresponding rates of serious AEs were 7.1, 6.0, and 12.2%, respectively. The most common (incidence ≥ 10%) AEs reported up to week 52 were nasopharyngitis (23.5% with any low dose of secukinumab and 26.0% with any high dose of secukinumab vs 26.8% with etanercept) and headache (10.2 and 10.0 vs 9.8%) [21].

In the severe plaque psoriasis trial, 3% of secukinumab recipients and 2% of etanercept recipients discontinued treatment due to AEs [15]. No deaths were reported and there were no new safety concerns with long-term secukinumab exposure (up to week 104) [17]. In the moderate to severe plaque psoriasis trial, AEs leading to treatment discontinuation occurred in 2% of patients [16].

3.1 Adverse Events of Special Interest

Treatment with secukinumab may increase [9], or has the potential to increase [8], the risk of infection. In the pooled analysis, infections and infestations occurred in 58% of secukinumab recipients and 66% of etanercept recipients up to week 52 [21]. The incidence of infections and infestations did not differ based on age (< 12 and ≥ 12 years) or bodyweight (< 25, ≥ 25 to < 50, and ≥ 50 kg). Up to week 52, neutropenia occurred in 3% of secukinumab recipients and 2% of etanercept recipients, while *Candida* infections occurred in 2% of secukinumab recipients and 0% of etanercept recipients [21]. Caution is advised when considering the use of secukinumab in patients with chronic infections or a history of recurrent infection [8, 9]. Before starting secukinumab, patients should be evaluated for tuberculosis infection [9], as secukinumab should not be given to patients with active tuberculosis [8, 9]. Secukinumab should be discontinued in patients who develop a serious infection; close monitoring of these patients is also recommended [8, 9].

Cases of new or exacerbations of inflammatory bowel disease (IBD) have occurred in adult patients receiving secukinumab [8, 9]. There were no reports of IBD in the severe plaque psoriasis trial [15]. One potential case of IBD in the moderate to severe plaque psoriasis trial was ruled out as mild, non-serious hemorrhagic diarrhea [16]. The use of secukinumab in patients with IBD is not recommended in the EU [8]. In the USA, caution is advised when prescribing secukinumab to patients with IBD [9].

In the pooled analysis, 4% of secukinumab injections (vs 10% of etanercept injections) were associated with injection-site reactions (ISRs) up to week 52 [21]. All ISRs were mild in severity and most required no treatment [15].

There have been reports of hypersensitivity reactions (including anaphylaxis and urticaria) in patients receiving secukinumab [8, 9]. In the pooled analysis, hypersensitivity reactions occurred in 10% of secukinumab recipients and 12% of etanercept recipients up to week 52 [21]. Secukinumab is contraindicated in patients with a previous hypersensitivity reaction to secukinumab [8, 9]. Anaphylactic or other serious allergic reactions to secukinumab should be treated with appropriate therapy, and the drug should be discontinued [8, 9].

As with all therapeutic proteins, secukinumab has the potential for immunogenicity [9]. However, among pediatric patients treated with secukinumab in the severe plaque psoriasis trial, no anti-drug antibodies were detected [22].

4 Dosage and Administration of Secukinumab

Subcutaneous secukinumab is approved in the EU [8] and the USA [9] for the treatment of moderate to severe plaque psoriasis in pediatric patients aged ≥ 6 years who are candidates for systemic therapy (or phototherapy [9]). It is available as a lyophilized powder in a vial for reconstitution or as a solution for injection in a prefilled syringe or Sensoready® pen [8, 9]. The powder formulation should be administered by healthcare providers only, while the prefilled syringe or pen may be administered by an adult caregiver after proper training in subcutaneous injection technique [8, 9].

Secukinumab is administered at weeks 0, 1, 2, 3, and 4, followed by maintenance dosing every 4 weeks [8, 9]. Each injection should be administered at a newer anatomic location (e.g. thigh, abdomen, upper arm) than the previous injection, avoiding areas where the skin is tender, bruised, erythematous, indurated, or scaly. The recommended dose of secukinumab is 75 mg in patients weighing < 50 kg and 150 mg in patients weighing ≥ 50 kg [8, 9]. In the EU, the dose of secukinumab may be increased to 300 mg in patients weighing ≥ 50 kg [8]. Discontinuation of secukinumab should be considered if patients do not respond after 16 weeks of treatment; patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks [8].

The concomitant administration of live vaccines with secukinumab is not recommended [8, 9]. Patients should receive all age-appropriate immunizations prior to starting secukinumab. The efficacy and tolerability of secukinumab in pediatric patients aged < 6 years has not been established [8, 9]. Consult local prescribing information for details regarding contraindications, warnings and precautions, drug interactions, and use in special patient populations.

5 Place of Secukinumab in the Management of Moderate to Severe Pediatric Plaque Psoriasis

Secukinumab is a targeted biologic recently approved for use in children aged ≥ 6 years and over with moderate to severe plaque psoriasis (Sect. 4). Joint American Academy of Dermatology and National Psoriasis Foundation guidelines for pediatric psoriasis published prior to the approval of secukinumab strongly recommend biologics as effective therapies for patients aged ≥ 4 years (e.g. etanercept, adalimumab) and ≥ 12 years (e.g. ustekinumab) with moderate to severe psoriasis [3]. Likewise, prior to the approval of secukinumab, European consensus-based guidelines for the treatment of psoriasis in children and adolescents recommend adalimumab as the only approved first-line treatment [23]. Etanercept, ustekinumab, ixekizumab, and secukinumab are among the second-line systemic agents that may be recommended or considered for the treatment of moderate to severe psoriasis in children and adolescents who have not sufficiently responded to at least one other systemic treatment or phototherapy, or who do not tolerate these treatments [23]. The National Institute for Health and Care Excellence recommends secukinumab as a treatment option for children and adolescents aged 6–17 years with severe plaque psoriasis who have not responded to other systemic treatments, or where these options are contraindicated or not tolerated [24].

Approval of secukinumab was based on the findings of two pivotal phase III trials, in which secukinumab provided fast and durable skin clearance in pediatric patients aged 6 to < 18 years with moderate to severe plaque psoriasis (Sects. 2.1.1 and 2.2.1). The co-primary endpoints were met, with both low (75–150 mg) and high (75–300 mg) doses of secukinumab demonstrating significantly higher PASI 75 and IGA 0/1 response rates than placebo (Sects. 2.1.1 and 2.2.1). In the severe plaque psoriasis trial, secukinumab was associated with greater clinical improvement than etanercept (Sect. 2.1.1). Moreover, higher response rates were observed with high- versus low-dose secukinumab in patients weighing ≥ 50 kg (Sect. 2.1.1), confirming that patients in this subgroup who do not respond sufficiently to the lower dose may derive additional benefit from the higher dose [8, 15]. Indeed, in the EU, the dose of secukinumab can be increased from 150 to 300 mg in patients weighing ≥ 50 kg (Sect. 4).

The clinical efficacy of secukinumab observed during the first 12 weeks of treatment was sustained over the longer term, up to 52 weeks (Sect. 2.2) and 104 weeks (Sect. 2.1). Both trials are ongoing, with efficacy and tolerability data being collected up to 224 and 236 weeks, including 16 weeks of treatment-free follow-up [15, 19]. Final results of these trials will provide additional data and are awaited with interest.

Plaque psoriasis is a chronic, multisystem disease which can have a significant negative impact on QOL in terms of physical, emotional, social, and psychological function [3]. Treatment of pediatric psoriasis must take into account the unique psychosocial burden of the disease on patients and their families [6]. Alleviation of symptoms is an important goal in the management of psoriasis, which can be assessed not only in terms of improvement in skin lesions, but also in terms of improvement in HR-QOL [4]. In both phase III trials, secukinumab was associated with continuous improvement in HR-QOL (Sects. 2.1.2 and 2.2.2). Of note, up to two-thirds of secukinumab recipients reported that psoriasis had no impact on QOL at the end of maintenance treatment;

this was maintained over the longer term, up to 104 weeks (Sect. 2.1.2).

The tolerability profile of secukinumab in pediatric patients with plaque psoriasis was consistent with that observed in adults with plaque psoriasis (Sect. 3). Secukinumab was generally well tolerated, with nasopharyngitis being the most commonly reported AE (Sect. 3). The rates of AEs of special interest with secukinumab were generally low (Sect. 3.1). It should be noted that secukinumab was associated with fewer ISRs than etanercept (Sect. 3.1). No new safety signals were identified through 52 and 104 weeks of treatment; longer-term follow-up is ongoing.

Targeted biologic agents offer several advantages over conventional systemic therapies, including less frequent dosing, enhanced efficacy, and reduced laboratory monitoring [6]. As with all of the biologic agents currently approved for pediatric plaque psoriasis, secukinumab is administered via subcutaneous injection (Sect. 4). After proper training, secukinumab may be administered by an adult caregiver using a pre-filled syringe or pen (Sect. 4). Unlike etanercept, which is administered once weekly, and adalimumab, which is administered every 2 weeks, maintenance doses of secukinumab (and ustekinumab and ixekizumab) are administered once every 4 weeks (Sect. 4). The convenience of less frequent dosing and the option of caregiver administration may result in better treatment adherence.

In conclusion, although longer-term data will more definitively place secukinumab in relation to other biologic agents in the management of pediatric plaque psoriasis, it is an effective and generally well-tolerated treatment for children and adolescents with moderate to severe plaque psoriasis, and represents a valuable new addition to the limited treatment options available for this population.

Data Selection Secukinumab: 84 records identified	
Duplicates removed	10
Excluded during initial screening (e.g. press releases; news reports; not relevant drug/indication; preclinical study; reviews; case reports; not randomized trial)	42
Excluded during writing (e.g. reviews; duplicate data; small patient number; non-randomized/phase I/II trials)	8
Cited efficacy/tolerability articles	10
Cited articles not efficacy/tolerability	14
Search Strategy: EMBASE, MEDLINE and PubMed from 1946 to present. Clinical trial registries/databases and websites were also searched for relevant data. Key words were secukinumab, Cosentyx, pediatric, plaque psoriasis. Records were limited to those in English language. Searches last updated 27 September 2021	

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40272-021-00476-w.

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