



Review

Therapeutic challenges in managing pediatric psoriasis

Yamila Goenaga-Vázquez MD^{a,*}, Kyle C. Lauck BA^a, Adelaide A. Hebert MD^{a,b}^a Department of Dermatology, UTHealth McGovern Medical School, Houston, TX, United States^b Department of Pediatrics, UTHealth McGovern Medical School, Houston, TX, United States

ARTICLE INFO

Article history:

Received 19 May 2020

Received in revised form 24 September 2020

Accepted 30 September 2020

Keywords:

Psoriasis

Systemic therapy

Topical therapy

Inflammatory disorders

Nutritional/metabolic diseases

ABSTRACT

Background: Each year, 20,000 patients aged <10 years are diagnosed with psoriasis. Pediatric-onset psoriasis has many similarities to adult-onset disease, and previous studies suggest that the incidence might be increasing in both populations.

Objective: The challenges that arise when treating patients with psoriasis, especially those age <12 years, are summarized, as well as the limited available treatment options for treating pediatric patients with psoriasis and the evidence supporting each of them.

Methods: Recently published guidelines by the American Academy of Dermatology and the National Psoriasis Foundations, as well as guidelines published by the German Society of Dermatology, provide considerable insight in managing patients who have this condition. The latest studies on pediatric psoriasis treatment were reviewed, including recent and current clinical trials with U.S. Food and Drug Administration approved and nonapproved medications, case reports, case series, and reviews. The authors also reviewed American and European guidelines, as well as recommendations from expert panels.

Results: Currently, only six medications are approved by the U.S. Food and Drug Administration for the treatment of pediatric psoriasis: three biologics and three topical. Many off-label topical treatments have been used in pediatric psoriasis, with variable effectiveness and safety profiles. Data from adult clinical trials, as well as case reports and series from pediatric patients, suggest that other biologic medications are effective for pediatric psoriasis.

Conclusion: Many questions remain unanswered, leaving clinicians facing multiple challenges when encountering pediatric patients with psoriasis. This summation will help provide an overview of current on- and off-label medications for pediatric psoriasis. Pediatric clinical trials should be implemented to obtain data that can result in expanding the therapeutic spectrum for this population, parallel to their adult counterparts.

© 2020 Published by Elsevier Inc. on behalf of Women's Dermatologic Society. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Contents

Introduction	315
U.S. Food and Drug Administration-approved products for pediatric psoriasis	315
Off-label therapies for pediatric psoriasis	316
Conclusion	317
Conflicts of Interest	317
Funding	317
Study Approval	317
References	317

* Corresponding author.

E-mail address: Yamila.goenagavazquez@uth.tmc.edu (Y. Goenaga-Vázquez).

Introduction

Each year, 20,000 children age <10 years are diagnosed with psoriasis (Menter et al., 2019). Pediatric-onset psoriasis has many similarities to adult-onset disease, and previous studies suggest that the incidence might be increasing in both populations (Icen et al., 2009; Tollefson et al., 2010). The cardiovascular and metabolic comorbidities identified in the adult population with psoriasis have increasingly been associated with pediatric psoriasis as well (Menter et al., 2019; Osier et al., 2017). The risks associated with these comorbidities potentially pose a greater burden to both the physical and mental health of affected children due to the longer duration of exposure and cumulative risk of systemic inflammation. Early identification of risk factors, routine screening for associated comorbidities, and prompt intervention are critical to reduce long-term adverse health consequences (Kimball et al., 2012; Paller et al., 2013).

When compared with the expanding treatment options for adults, the relatively limited number of medications approved by the U.S. Food and Drug Administration with an indication for pediatric patients with psoriasis promotes off-label use of older and less effective medications. Children with psoriasis may require treatment into adulthood, resulting in a longer duration of therapy and increasing the cumulative risks. Thus, there remains an unmet need for effective therapies that minimize serious risks. Other challenges when treating pediatric patients with psoriasis include aversion to injections, provider hesitancy to change from one biologic drug to another or to combine drugs that are routinely combined in adults, patient discomfort with the feeling of topical medications on their skin, and the taste of oral medications (one of the major reasons children refuse medications overall). Similarly, when choosing an appropriate biologic therapy for a patient, the decision is usually made based on the presence of comorbidities. This decision becomes more difficult in the pediatric population, given the limited number of FDA-approved drugs. These challenges (Table 1) limit the adherence to available therapeutic options and may lead to frequent flare-ups and worsening of psychologic, cardiovascular, and metabolic comorbidities, which ultimately increase costs for families and the health care system (Eisert et al., 2019; Menter et al., 2019; Osier et al., 2017).

The purpose of this manuscript is to help clinicians address challenges when managing pediatric patients with psoriasis by providing a comprehensive review of the limited available treatment options and the evidence supporting each of them.

U.S. Food and Drug Administration-approved products for pediatric psoriasis

Currently, only six medications are FDA-approved for the treatment of pediatric psoriasis: three biologics and three topicals (Table 2). Traditionally, for mild-to-moderate disease, topical therapy, including topical steroids alone or in combination with vitamin D analogs, are considered first-line therapy. Products for topical use in pediatric patients include calcipotriol 0.005%/betamethasone 0.064% foam and suspension approved for children aged ≥12 years for use on the body and scalp, respectively.

Table 1
Challenges to treating pediatric psoriasis.

1. Limited number of medications, biologics and non-biologics, approved by the U.S. Food and Drug Administration
2. Emphasis on the need to minimize treatment adverse effects due to longer duration of treatment often required when psoriasis begins in childhood
3. Hesitancy of pediatric providers to change between biologic regimens or combine regimens involving biologics
4. Pediatric aversion to injections
5. Discomfort due to application of topical medications
6. Taste of oral medications

Table 2
U.S. Food and Drug Administration-approved drugs for pediatric psoriasis.

	Drug	Patient age, years
Topical	Calcipotriene foam 0.005%	≥4
	Calcipotriene 0.005% and betamethasone 0.064% foam	≥12
	Calcipotriene 0.005% and betamethasone 0.064% suspension	≥12
Systemic	Etanercept	≥4
	Ustekinumab	≥12
	Ixekizumab	≥6
	Adalimumab ^a	≥4

^a Only approved by the European Medicines Agency.

Recently, calcipotriol foam 0.005% was approved by the FDA for patients aged ≥4 years for use on the scalp and body. Biologic products that are FDA-approved for pediatric psoriasis include etanercept (a tumor necrosis factor [TNF] alpha antagonist approved in 2016 for children aged ≥4 years), ustekinumab (IL12/23 inhibitor approved in 2017 for children aged ≥12 years), and ixekizumab (approved in March 2020 for children aged ≥6 years with moderate-to-severe psoriasis; Table 2). This renders a far more limited therapeutic spectrum for the pediatric population compared with available and approved adult therapies.

Etanercept has often been considered a first choice for moderate-to-severe pediatric psoriasis in biologic therapy due to the multiplicity of data available on its safety and efficacy, including randomized clinical trials (Nguyen et al., 2020; Paller et al., 2008, 2010). Challenges include the weekly injections and annual monitoring for tuberculosis. A recent retrospective chart review has reported both a greater reduction in severity scores and higher drug survival rates when etanercept was compared with methotrexate in a real-world setting (Bronckers et al., 2020).

The safety, efficacy, and pharmacokinetics of ustekinumab have recently been studied in patients aged ≥6 years with moderate-to-severe psoriasis, with promising results (Philipp et al., 2020). This open-label study enrolled 44 patients aged ≥6 to ≤12 years. The subcutaneous administration of ustekinumab was weight-based and injected at weeks 0 and 4 and then every 12 weeks until week 40. In the study endpoints at week 12, 77% of patients achieved a Physician's Global Assessment score of cleared or minimal, 84% achieved a Psoriasis Area and Severity Index (PASI) response of 75, and 64% achieved a PASI response of 90.

A phase 3 randomized, double-blind, placebo-controlled study was conducted to evaluate the efficacy, tolerability, and safety of ixekinumab, an IL 17 inhibitor, in the treatment of pediatric patients with moderate-to-severe psoriasis. The recent FDA approval of ixekinumab in March 2020 for the treatment of psoriasis in patients aged ≥6 years adds this medication to the therapeutic spectrum available for pediatric psoriasis (Petronelli, 2020).

Studies have also been conducted with adalimumab, a recombinant monoclonal TNF alpha antibody, approved in Europe for patients aged ≥4 years with moderate-to-severe psoriasis. A double-blind, phase 3, long-term extension study enrolled 114 patients aged ≥4 and <18 years with severe plaque psoriasis

Table 3
Summary of on- and off-label systemic agents for pediatric psoriasis.

Drug	Mode of administration/ frequency of maintenance dose	Mechanism of action	Warnings/precautions	Monitoring Parameters
Etanercept	Subcutaneous/ once weekly	Recombinant DNA-derived protein composed of TNF alpha receptor linked to the Fc portion of human IgG1 that binds to TNF and blocks its interaction with cell surface receptors	Serious infections (TB, HBV reactivation, invasive fungal infections), malignancies (lymphoma) ^a , injection site reactions, autoimmune disorder, demyelinating disease, heart failure, hematologic toxicity	TB and HBV screening, CBC with differential
Adalimumab	Subcutaneous/ every other week	Recombinant monoclonal antibody that binds to TNF alpha, thereby interfering with binding to TNF receptor sites and subsequent cytokine-driven inflammatory processes	Serious infections (TB, HBV reactivation, invasive fungal infections), malignancies (lymphoma) ^a , injection site reactions, autoimmune disorder, demyelinating disease, heart failure, hematologic toxicity	TB and HBV screening, CBC with differential
Infliximab	Intravenous/ every 8 weeks	Chimeric monoclonal antibody that targets TNF alpha	Serious infections (TB, HBV reactivation, invasive fungal infections), autoimmune disorders, malignancies (lymphoma) ^a , cardiovascular reactions during and after infusion, hematologic toxicity (pancytopenia)	TB and HBV screening, CBC with differential, LFTs
Ustekinumab	Subcutaneous/ every 12 weeks	Human monoclonal antibody that targets the p40 subunit of the proinflammatory cytokines, IL-12 and IL-23	Antibody formation, hypersensitivity reactions, infections (fungal most common), malignancies (multiple aggressive cutaneous SCCs) ^a , interstitial pneumonia	TB screening, ustekinumab-antibody formation, CBC
Guselkumab	Subcutaneous/ every 8 weeks	Human IgG1 monoclonal antibody selectively binds with IL-23, thereby reducing serum levels of proinflammatory cytokines IL-17A, IL-17F, and IL-22	Infections (herpes simplex, tinea, TB), hypersensitivity reactions	TB screening
Secukinumab	Subcutaneous/ every 4 weeks	Human IgG1 monoclonal antibody that selectively binds to the IL-17A cytokine	Infections (mucocutaneous candidiasis, TB), hypersensitivity reactions, drug-drug interactions	TB screening
Ixekizumab	Subcutaneous/ every 4 weeks	Humanized IgG4 monoclonal antibody that selectively binds with the IL-17A cytokine	Infections (TB, upper respiratory tract, oral candidiasis, conjunctivitis, tinea), injection site reactions	TB screening
Tofacitinib	Oral/twice daily	Nonselective Janus kinases 1 and 3 inhibitor	Serious infections (TB, invasive fungal, viral), malignancies (lymphoma, cutaneous SCCs) ^a , thrombosis (pulmonary embolism, deep vein thrombosis), hematologic toxicity (pancytopenia)	CBC with differential, lipid profile, LFTs, hepatitis B and C viral screening
Apremilast	Oral/twice daily	Inhibits phosphodiesterase 4, which results in increased intracellular cAMP levels and regulation of numerous inflammatory mediators including TNF alpha and IL-23	Gastrointestinal effects (diarrhea, nausea, vomiting), neuropsychiatric effects (depression, suicidal ideation), weight loss	If patient has renal impairment, monitor renal function
Methotrexate	Oral or subcutaneous/ weekly	Inhibits dihydrofolate reductase, reducing nucleic acid synthesis	Gastrointestinal distress, hepatotoxicity, bone marrow suppression, pulmonary toxicity	CBC, LFTs, renal function
Cyclosporine	Oral/ twice daily	Binds to cyclophilin on lymphocytes and the subsequent cyclosporine-cyclophilin complex inhibits calcineurin and transcription of IL-2	Renal toxicity, hypertension, immunosuppression, nonmelanoma skin cancers	CBC, serum electrolytes, renal function, lipid profile, regular blood pressure monitoring

CBC, complete blood count; HBV, hepatitis B virus; IgG, immunoglobulin G; IL, interleukin; LFT, liver function test; SSC, squamous cell carcinoma; TB, tuberculosis; TNF, tumor necrosis factor.

^a No malignancies have been reported in pediatric patients with psoriasis treated with anti-TNF alpha agents.

(Thaçi et al., 2019). Patients were randomized to adalimumab or methotrexate. At 16 weeks, of the 93 patients who received adalimumab, all achieved a 75% improvement from baseline in PASI response. This efficacy was maintained or improved at the end of the long-term extension (52 weeks). The biologic was well tolerated, and no new safety risks were identified (Di Lernia et al., 2019; Thaçi et al., 2019; Zangrilli et al., 2020).

Off-label therapies for pediatric psoriasis

Many off-label topical treatments have been used in pediatric psoriasis, including topical calcineurin inhibitors, tar-based therapies, and tazarotene, with variable effectiveness and safety profiles (Frantz et al., 2019). Topical steroids have been used off-label for multiple inflammatory skin disorders, including psoriasis, for

patients of all ages in the absence of safety data across much of the pediatric spectrum.

Several off-label nonbiologic systemic therapies are widely used to treat refractory, moderate, and severe pediatric psoriasis. Various forms of ultraviolet (UV) light therapy may be used in the treatment of refractory pediatric psoriasis, including narrowband UV B phototherapy (preferred) and various forms of psoralen in conjunction with UV A therapy in patients aged ≥10 years. However, robust data supporting the efficacy of phototherapies in children with plaque and pustular psoriasis are insufficient at this time (Menter et al., 2019). One uncontrolled study that supports the efficacy of narrowband UV B phototherapy for psoriasis in children is a retrospective study that included 88 children. Of the 79 children available for final analysis, 73 (92%) achieved at least 75% clinical improvement, including 40 children (51%) who achieved

complete clearance of skin lesions. The mean duration of treatment was approximately 3 months, and the median duration of remission was approximately 20 months (Pavlovsky et al., 2011). Side effects of phototherapy may include erythema, pruritus, blistering, hyperpigmentation, and an increased risk for cutaneous neoplasms with chronic use of psoralen in conjunction with UV A therapy (Menter et al., 2019).

Methotrexate and cyclosporine are the most commonly used oral medications for pediatric psoriasis (Dadlani and Orlow, 2005; Frantz et al., 2019; Napolitano et al., 2016). Advantages of methotrexate include a long history of use for children with psoriasis, availability of both oral and injectable formulations, and low cost compared with other psoriasis therapies (Dadlani and Orlow, 2005). However, methotrexate has a relatively slow onset of action and may lead to hepatotoxicity. In addition, methotrexate appears to be less effective than some biologic agents (Bronckers et al., 2020; Dadlani and Orlow, 2005; Thaçi et al., 2019).

Acitretin has also been used in a more limited number of patients, with good outcome (Di Lernia et al., 2016). The advantages of oral retinoids include oral administration and lack of immunosuppression. Teratogenicity of oral retinoids is a concern for female adolescent and teenage patients. Isotretinoin, which has a shorter half-life than acitretin, might help address this challenge, but its effectiveness in pediatric psoriasis has not been established. Apremilast, an oral PDE4 inhibitor approved for adult psoriasis, was demonstrated to be safe and efficacious in a recent phase 2, open-label study that enrolled 42 patients 6 to 17 years old (Paller et al., 2020). In this study, patients aged 6 to 11 years had a 79% improvement from baseline in PASI score, and adolescents aged 12 to 17 years achieved an improvement of 68% overall. Thus, apremilast represents an attractive option: This medication is not an antineoplastic, has limited side effects, has no recommended laboratory monitoring, and is administered orally.

Data from adult clinical trials, as well as case reports and series from pediatric patients, suggest that other biologic medications are effective for pediatric psoriasis. These medications include guselkumab (a selective IL-23 monoclonal antibody), tofacitinib (a Jak 1/3 inhibitor), and infliximab (a TNF alpha inhibitor; AlMutairi and Nour, 2020; Kim et al., 2019; Tegtmeyer et al., 2019). Currently, two phase 3 clinical trials are being conducted to evaluate the efficacy and safety of secukinumab (a selective IL-17A monoclonal antibody) in children aged ≥ 6 years with moderate-to-severe psoriasis (Wells et al., 2019; Wu et al., 2020). One disadvantage of secukinumab is that it requires more injections than other biologics, which may pose challenges for acceptance by the pediatric population given their reticence to endure injections. However, secukinumab may have decreased risk of injection site reactions compared with other biologics (Henderson Berg and Carrasco, 2017). Although secukinumab is in ongoing development for the treatment of children aged >6 years with psoriasis, available evidence of the safety and efficacy of this medication in children is currently limited. Recommendations for use of these biologic agents is based on expert opinion and case studies rather than on evidence from randomized clinical trials (AlMutairi and Nour, 2020; Henderson Berg and Carrasco, 2017; Kim et al., 2019; Lansang et al., 2020; Tegtmeyer et al., 2019; Wells et al., 2019; Wu et al., 2020). Table 3 provides a summary of all systemic agents that are currently used on- or off-label for pediatric psoriasis.

Conclusion

Psoriasis is a chronic inflammatory disease that can be extremely debilitating and can significantly affect the quality of life of patients. The impact on mental and physical health is probably more prominent in the pediatric population because of the

chronology of onset. Patients with psoriasis should be approached from a global perspective, taking into consideration the disease's potential to affect the cardiovascular system and metabolic pathways, as well as the potential for joint disease with sequelae. Recently published guidelines by the American Academy of Dermatology and the National Psoriasis Foundation (Menter et al., 2019), as well as guidelines published by the German Society of Dermatology (Eisert et al., 2019), provide considerable insight for the management of patients with psoriasis. Many clinicians believe they are facing multiple challenges when encountering pediatric patients with psoriasis. This summation will help provide an overview of current on- and off-label medications for pediatric psoriasis.

In the future, pediatric clinical trials should be undertaken to expand the therapeutic spectrum for this population, parallel to the adult armamentarium. Approved systemic therapeutic options are particularly limited, and the ideal dosages and adverse effect profiles for many agents still need to be determined for the pediatric population. Considering the chronicity of psoriasis, studies on the long-term safety of potential therapeutic alternatives are needed. Clinicians should educate patients on effective strategies to help them manage their condition in a confident manner while maximizing adherence to available treatments. Such measures can potentially have a profound impact on the long-term morbidity and mortality of pediatric patients with psoriasis.

Conflicts of Interest

Dr. Hebert reports research funds paid to UTHealth McGovern Medical School: Amgen, Ortho Dermatologics, Leo, GSK, Arcutis, Sienna, Promius, Mayne, Pfizer, and Galderma, as well as honoraria from Ortho Dermatologics, Amgen, Galderma, Mayne, Promius, and Leo.

Funding

None.

Study Approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

References

- AlMutairi N, Nour T. Tofacitinib in pediatric psoriasis: an open-label trial to study its safety and efficacy in children. *Dermatology* 2020;236(3):191–8.
- Bronckers IMGJ, Paller AS, West DP, Lara-Corrales I, Tollefson MM, Tom WL, et al. A comparison of psoriasis severity in pediatric patients treated with methotrexate vs biologic agents. *JAMA Dermatol* 2020;156(4):384–92.
- Dadlani C, Orlow SJ. Treatment of children and adolescents with methotrexate, cyclosporine, and etanercept: Review of the dermatologic and rheumatologic literature. *J Am Acad Dermatol* 2005;52(2):316–40.
- Di Lernia V, Bonamonte D, Lasagni C, Belloni Fortina A, Cambiaghi S, Corazza M, et al. Effectiveness and safety of acitretin in children with plaque psoriasis: a multicenter retrospective analysis. *Pediatr Dermatol* 2016;33(5):530–5.
- Di Lernia V, Bianchi L, Guerriero C, Stingeni L, Gisondi P, Filoni A, et al. Adalimumab in severe plaque psoriasis of childhood: A multi-center, retrospective real-life study up to 52 weeks observation. *Dermatol Ther* 2019;32(6):e13091.
- Eisert L, Augustin M, Bach S, Dittmann M, Eiler R, Fölster-Holst R, et al. S2k guidelines for the treatment of psoriasis in children and adolescents-Short version part 2. *J Dtsch Dermatol Ge* 2019;17(9):959–73.
- Frantz T, Wright EG, Balogh EA, Cline A, Adler-Neal AL, Feldman SR. Topical and oral therapies for childhood atopic dermatitis and plaque psoriasis. *Children (Basel)* 2019;6(11):125.
- Henderson Berg MH, Carrasco D. Injection site reactions to biologic agents used in psoriasis and psoriatic arthritis. *J Drugs Dermatol* 2017;16(7):695–8.
- Icen M, Crowson CS, McEvoy MT, Dann FJ, Gabriel SE, Maradit Kremers H. Trends in incidence of adult-onset psoriasis over three decades: A population-based study. *J Am Acad Dermatol* 2009;60(3):394–401.

- Kim SR, Kibbi N, Craiglow BG. Guselkumab for the treatment of severe refractory psoriasis in a pediatric patient. *JAAD Case Rep* 2019;5(6):552–4.
- Kimball AB, Wu EQ, Guérin A, Yu AP, Tsaneva M, Gupta SR, et al. Risks of developing psychiatric disorders in pediatric patients with psoriasis. *J Am Acad Dermatol* 2012;67(4):651–7.
- Lansang P, Bergman JN, Fiorillo L, Joseph M, Lara-Corrales I, Marcoux D, et al. Management of pediatric plaque psoriasis using biologics. *J Am Acad Dermatol* 2020;82(1):213–21.
- Menter A, Cordoro KM, Davis DMR, Kroshinsky D, Paller AS, Armstrong AW, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients. *J Am Acad Dermatol* 2019;81(3):775–804.
- Napolitano M, Megna M, Balato A, Ayala F, Lembo S, Villani A, et al. Systemic treatment of pediatric psoriasis: a review. *Dermatol Ther (Heidelb)* 2016;6(2):125–42.
- Nguyen Q-B, Starling CT, Hebert AA. The use of TNF α inhibitors in treating pediatric skin disorders. *Pediatr Drugs* 2020;22(3):311–9.
- Osier E, Wang AS, Tollefson MM, Cordoro KM, Daniels SR, Eichenfield A, et al. Pediatric psoriasis comorbidity screening guidelines. *JAMA Dermatol* 2017;153(7):698–704.
- Paller AS, Siegfried EC, Langley RG, Gottlieb AB, Pariser D, Landells I, et al. Etanercept treatment for children and adolescents with plaque psoriasis. *N Engl J Med* 2008;358(3):241–51.
- Paller AS, Siegfried EC, Eichenfield LF, Pariser D, Langley RG, Creamer K, et al. Long-term etanercept in pediatric patients with plaque psoriasis. *J Am Acad Dermatol* 2010;63(5):762–8.
- Paller AS, Mercy K, Kwasny MJ, Choon SE, Cordoro KM, Girolomoni G, et al. Association of pediatric psoriasis severity with excess and central adiposity: an international cross-sectional study. *JAMA Dermatol* 2013;149(2):166–76.
- Paller AS, Hong Y, Becker EM, de Lucas R, Paris M, Zhang W, et al. Pharmacokinetics and safety of apremilast in pediatric patients with moderate to severe plaque psoriasis: Results from a phase 2 open-label study. *J Am Acad Dermatol* 2020;82(2):389–97.
- Petronelli M. Ixekizumab approved for pediatric plaque psoriasis [Internet]. 2020 [cited xxx]. Available at: <https://www.dermatologytimes.com/view/ixekizumab-approved-pediatric-plaque-psoriasis>.
- Philipp S, Menter A, Nikkels AF, Barber K, Landells I, Eichenfield LF, et al. Ustekinumab for the treatment of moderate-to-severe plaque psoriasis in paediatric patients (≥ 6 to < 12 years of age): Efficacy, safety, pharmacokinetic and biomarker results from the open-label CADMUS Jr study. *Br J Dermatol* 2020;183(4):664–72.
- Pavlovsky M, Baum S, Shpiro D, Pavlovsky L, Pavlitsky F. Narrow band UVB: Is it effective and safe for paediatric psoriasis and atopic dermatitis? *J Eur Acad Dermatol Venereol* 2011;25:727–9.
- Tegtmeier K, Zhao J, Maloney NJ, Atassi G, Beestrup M, Lio PA. Off-label studies on tofacitinib in dermatology: A review. *J Dermatolog Treat* 2019:1–11.
- Thaçi D, Papp K, Marcoux D, Weibel L, Pinter A, Ghislain PD, et al. Sustained long-term efficacy and safety of adalimumab in paediatric patients with severe chronic plaque psoriasis from a randomized, double-blind, phase III study. *Br J Dermatol* 2019;181(6):1177–89.
- Tollefson MM, Crowson CS, McEvoy MT, Maradit KH. Incidence of psoriasis in children: A population-based study. *J Am Acad Dermatol* 2010;62(6):979–87.
- Wells LE, Evans T, Hilton R, Wine Lee L, Ruth N. Use of secukinumab in a pediatric patient leads to significant improvement in nail psoriasis and psoriatic arthritis. *Pediatr Dermatol* 2019;36(3):384–5.
- Wu JJ, Merola JF, Feldman SR, Menter A, Lebwohl M. Treatment of psoriasis with secukinumab in challenging patient scenarios: A review of the available evidence. *Dermatol Ther (Heidelb)* 2020;10(3):351–64.
- Zangrilli A, Bavetta M, Bianchi L. Adalimumab in children and adolescents with severe plaque psoriasis: A safety evaluation. *Expert Opin Drug Saf* 2020;19(4):433–8.