PEDIATRIC PSORIASIS UPDATE

ADELAIDE A HEBERT, MD

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- RESEARCH GRANTS PAID TO MEDICAL SCHOOL: LEO, DERMAVANT, ARCUTIS, ORTHO DERMATOLOGICS
- HONORARIA: PFIZER, DERMAVANT, ARCUTIS, LEO, ORTHO DERMATOLOGICS, MAYNE
- DSMB: SANOFI REGENERON, ORTHO DERMATOLOGICS, GSK



PEDIATRIC PSORIASIS

• MOST COMMON ANATOMIC SITES: SCALP, FACE, FLEXURES

Pediatric Health, Medicine and Therapeutics

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REVIEW

Management Strategies for Pediatric Moderate-to-Severe Plaque Psoriasis: Spotlight on Biologics

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Pharmacokinetics and safety of **apremilast** in **pediatric** patients with moderate to severe plaque **psoriasis**: Results from a phase 2 open-label study.

Paller AS, Hong Y, Becker EM, de Lucas R, Paris M, Zhang W, Zhang Z, Barcellona C, Maes P, Fiorillo L.

J Am Acad Dermatol. 2020 Feb;82(2):389-397. doi: 10.1016/j.jaad.2019.08.019. Epub 2019 Aug 10.

PMID: 31408686 Free article. Clinical Trial.

EFFICACY AND SAFETY OF **APREMILAST** IN **PEDIATRIC** PATIENTS WITH MODERATE-TO-SEVERE PLAQUE **PSORIASIS**: 16-WEEK RESULTS FROM SPROUT, A RANDOMIZED CONTROLLED TRIAL.

Fiorillo L, Becker E, de Lucas R, Belloni-Fortina A, Armesto S, Elewski B, Maes P, Oberoi RK, Paris M, Zhang W, Zhang Z, Arkin L.

J Am Acad Dermatol. 2024 Jan 22:S0190-9622(24)00108-7. doi: 10.1016/j.jaad.2023.11.068. Online ahead of print.

PMID: 38266683

Only **7 FDA medications approved** for pediatric patients **Biologics**:

- Etanercept: ≥ 6 years
- Ustekinumab : ≥ 6 years approved for psoriatic arthritis in children
- Ixekizumab: ≥ 6 years
- Secukinumab: ≥ 6 years (May 2021)

- UP TO 20 % OF ALL CHILDHOOD ARTHRITIS IS PSORIATIC ARTHRITIS
- IF A CHILD HAS PSORIATIC ARTHRITIS, ASSESS FOR UVEITIS
- ADALIBUMAB:
 - NOT APPROVED IN USA FOR PEDI PSORIASIS
 - IS APPROVED DOWN TO 2 YEARS OF AGE FOR UVEITIS

Only **7 FDA medications approved** for pediatric patients

Topicals: Roflumilast: PDE 4 inhibitor: ≥6 years

- used systemically in COPD in adults
 - Calcipotriene Foam 0.005%: ≥ 4 years scalp and body
 - Calcipotriene 0.005% and betamethasone 0.064% **foam** or **ointment**
 - ≥12 years: mild to severe plaque psoriasis
 - Calcipotriene 0.005% and betamethasone 0.064%
 - **suspension**: scalp and body: ≥ 12 years

Topical roflumilast

INVESTIGATOR GLOBAL ASSESSMENT AT 8 WEEKS

Patients aged ≥ 2 years with 2 to 20% BSA psoriasis

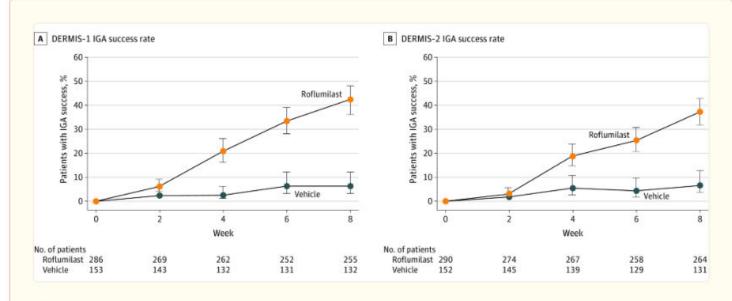


Figure 2.

Percentage of Patients Achieving IGA Success Over Time in DERMIS-1 and DERMIS-2



JAMA. 2022 Sep 20; 328(11): 1073-1084.

Published online 2022 Sep 20. doi: <u>10.1001/jama.2022.15632</u>

PMCID: PMC9490499 PMID: <u>36125472</u>

Effect of Roflumilast Cream vs Vehicle Cream on Chronic Plaque Psoriasis

Methotrexate for inflammatory skin disease in pediatric patients: Consensus treatment guidelines.

Siegfried EC, Arkin LM, Chiu YE, Hebert AA, Callen JP, Castelo-Soccio L, Co DO, Cordoro KM, Curran ML, Dalrymple AM, Flohr C, Gordon KB, Hanna D, Irvine AD, Kim S, Kirkorian AY, Lara-Corrales I, Lindstrom J, Paller AS, Reyes M, Begolka WS, Tom WL, Van Voorhees AS, Vleugels RA, Lee LW, Davies OMT, Brandling-Bennett HA.

Pediatr Dermatol. 2023 Sep-Oct;40(5):789-808. doi: 10.1111/pde.15327. Epub 2023 Jun 14.

PMID: 37316462

Tapinarof

PHYSICIAN GLOBAL ASSESSMENT AT 12 WEEKS

Approved for psoriasis in patients ≥ 18 years of age

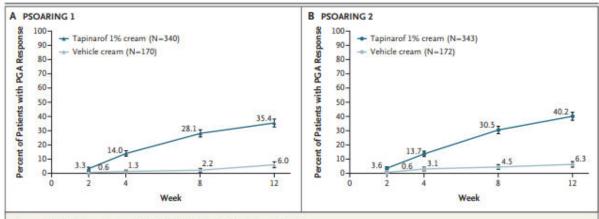


Figure 1. PGA Response at Each Visit (Intention-to-Treat Population).

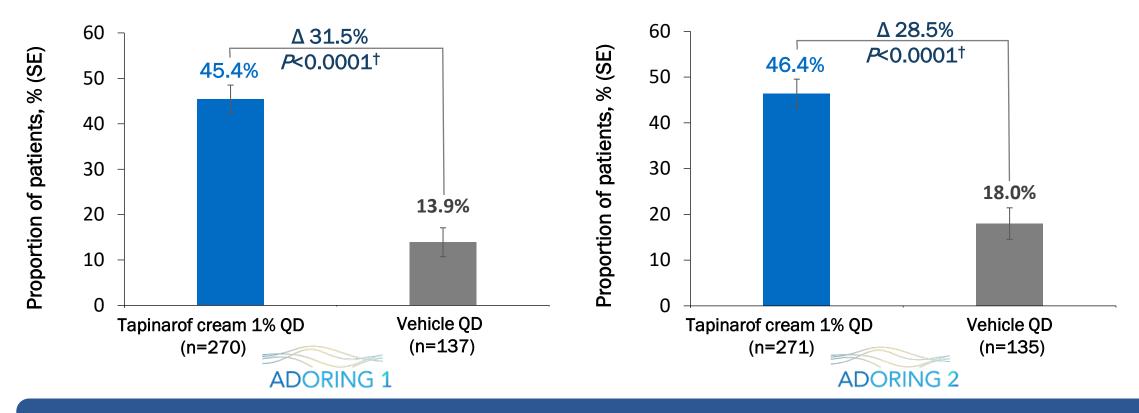
A Physician's Global Assessment (PGA) response was defined as a PGA score of 0 (clear) or 1 (almost clear) and a decrease from baseline of at least 2 points at week 12 (range, 0 to 4, with higher scores indicating more severe psoriasis). Data represent the mean percentage of patients with a PGA response on the basis of 100 imputed data sets. 1 bars indicate the standard error. The multiple-imputation standard error reflects variation both within and across imputations. At weeks 2, 4, 8, and 12, respectively, the percentages of patients who had data imputed for the PGA response were 4.1%, 6.8%, 13.5%, and 19.1% in the tapinarof group and 5.9%, 11.2%, 15.3%, and 22.4% in the vehicle group in the PSOARING 1 trial (Panel A) and 2.9%, 6.4%, 11.7%, and 15.7% in the tapinarof group and 2.3%, 4.1%, 12.2%, and 16.3% in the vehicle group in the PSOARING 2 trial (Panel B).



Phase 3 Trials of Tapinarof Cream for Plaque Psoriasis

Mark G. Lebwohl, M.D., Linda Stein Gold, M.D., Bruce Strober, M.D., Ph.D, Kim A. Papp, M.D., Ph.D.,
April W. Armstrong, M.D., Jerry Bagel, M.D., Leon Kircik, M.D., Benjamin Ehst, M.D., Ph.D., H. Chih-ho Hong, M.D.,
Jennifer Soung, M.D., Jeff Fromowitz, M.D., Scott Guenthner, M.D., Stephen C. Piscitelli, Pharm.D.,
David S. Rubenstein, M.D., Ph.D., Philip M. Brown, M.D., J.D., Anna M. Tallman, Pharm.D., and Robert Bissonnette, M.D.

Tapinarof Cream 1% QD: Primary Endpoint ofATOPIC DERMATITIS VIGA-ADTM Response* at Week 8 was Achieved in Both Trials

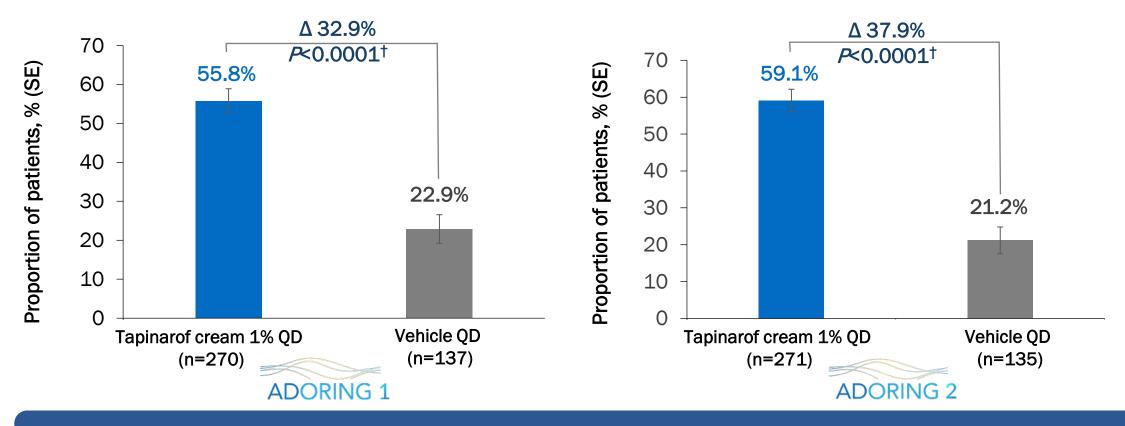


vIGA-ADTM response* was highly statistically significant with tapinarof cream 1% QD versus vehicle in both ADORING 1 & 2: 45.4% vs 13.9% and 46.4% vs 18.0% (both P < 0.0001), respectively

Copyright ©2017 Eli Lilly and Company – Used with the permission of Eli Lilly and Company under a Creative Commons Attribution-NoDerivatives 4.0 International License. $*vIGA-AD^{TM}$ score of 0 or 1 and \geq 2-grade improvement from baseline. $^{\dagger}P$ value based upon Cochran-Mantel-Haenszel analysis stratified by baseline $vIGA-AD^{TM}$ score and age group. Intention-to-treat, multiple imputation.

QD, once daily; SE, standard error; vIGA-ADTM, Validated Investigator Global Assessment for Atopic DermatitisTM.

Tapinarof Cream 1% QD: Secondary Endpoint of Atopic DERMATITIS EASI75 Response* at Week 8 was Achieved in Both Trials

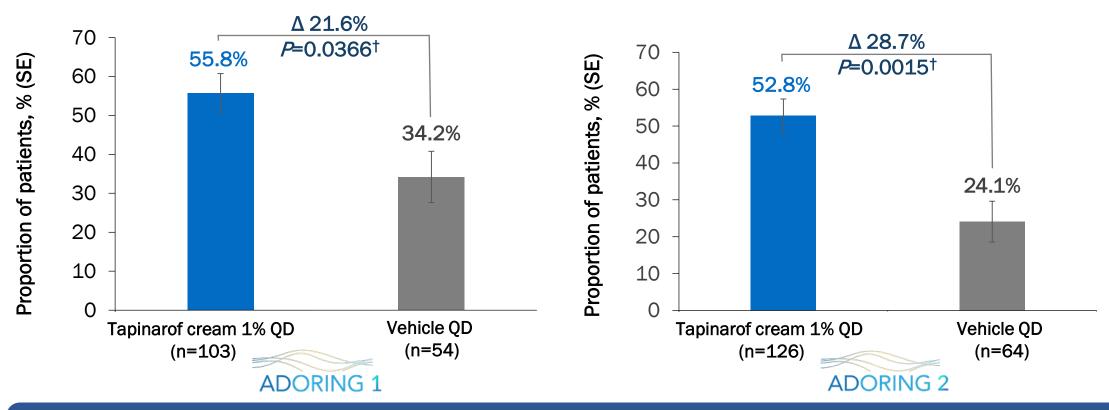


EASI75 response* at Week 8 was highly statistically significant in the tapinar of cream 1% QD group versus vehicle in both ADORING 1 and 2: 55.8% vs 22.9% and 59.1% vs 21.2% (both P<0.0001), respectively

EASI75, \geq 75% improvement in Eczema Area and Severity Index score; QD, once daily; SE, standard error; vIGA-ADTM, Validated Investigator Global Assessment for Atopic DermatitisTM.

^{*≥75%} improvement in Eczema Area and Severity Index score from baseline. †P value based upon Cochran-Mantel-Haenszel analysis stratified by baseline vIGA-AD™ score and age group. Intention-to-treat, multiple imputation.

Tapinarof Cream 1% QD: PP-NRS Response* (Patients Aged ≥12 Years) at Week 8 was Achieved in Both Trials



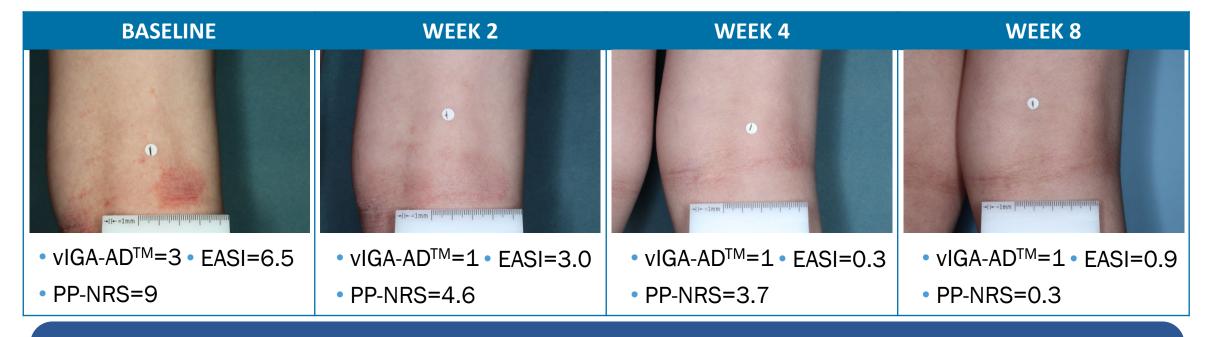
PP-NRS response* (patients aged \geq 12 years) at Week 8 was statistically significant in the tapinarof cream 1% QD group versus vehicle in both ADORING 1 and 2: 55.8% vs 34.2% (P=0.0366) and 52.8% vs 24.1% (P=0.0015), respectively

^{*≥4-}point reduction in the average weekly PP-NRS total score from baseline. †P value based upon Cochran-Mantel-Haenszel analysis stratified by baseline vIGA-AD™ score and age group. Intention-to-treat, multiple imputation.

PP-NRS, Peak Pruritus Numerical Rating Scale; QD, once daily; SE, standard error; vIGA-AD™, Validated Investigator Global Assessment for Atopic Dermatitis™.

8-Year-Old Patient with Moderate AD Treated with Tapinarof Cream 1% QD Who Achieved the Primary Endpoint as Early as Week 2 and Complete Resolution of Itch at Week 8

ATOPIC DERMATITIS



- Patient (aged 8 years) with moderate disease (vIGA-ADTM=3) at baseline who achieved almost clear skin (vIGA-ADTM=1) by Week 2
- Patient also had severe itch (PP-NRS=9) at baseline, achieving a clinically meaningful ≥4-point reduction in PP-NRS by Week 2, with improvement to an itch-free state by Week 8 (PP-NRS=0.3)

AAD PEDIATRIC PSORIASIS GUIDELINES



Joint American Academy of Dermatology—National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients

Alan Menter, MD (Co-Chair), Kelly M. Cordoro, MD, Dawn M. R. Davis, MD, Daniela Kroshinsky, MD, MPH, Amy S. Paller, MD, April W. Armstrong, MD, MPH, Cody Connor, MD, Boni E. Elewski, MD, Joel M. Gelfand, MD, MSCE, Kenneth B. Gordon, MD, Alice B. Gottlieb, MD, PhD, Daniel H. Kaplan, MD, PhD, Arthur Kavanaugh, MD, Matthew Kiselica, BA/BS, Dario Kivelevitch, MD, Neil J. Korman, MD, PhD, Mark Lebwohl, MD, Craig L. Leonardi, MD, Jason Lichten, MD, Henry W. Lim, MD, Nehal N. Mehta, MD, MSCE, Sylvia L. Parra, MD, Arun L. Pathy, MD, Elizabeth A. Farley Prater, MD, Reena N. Rupani, MD, Michael Siegel, PhD, Benjamin Stoff, MD, MA, Bruce E. Strober, MD, PhD, Emily B. Wong, MD, Jashin J. Wu, MD, Avidhya Hariharan, PhD, And Craig A. Elmets, MD (Co-Chair)

Dallas, Texas; San Francisco, California; Rochester, Minnesota; Boston, Massachusetts; Chicago, Illinois; Los Angeles, California; Birmingham, Alabama; Philadelphia, Pennsylvania; Milwaukee, Wisconsin; New York, New York; Pittsburgh, Pennsylvania; San Diego, California; Cleveland, Obio; St Louis, Missouri; Detroit, Michigan; Bethesda, Maryland; Sumter, South Carolina; Centennial, Colorado; Oklaboma City, Oklaboma; Indianapolis, Indiana; Atlanta, Georgia; Cromwell and New Haven, Connecticut; San Antonio, Texas; Irvine, California; and Rosemont, Illinois

PEDIATRIC PSORIASIS

- A CHRONIC, MULTISYSTEM INFLAMMATORY DISEASE THAT AFFECTS 1% OF CHILDREN
- MOST COMMON TIME OF ONSET: ADOLESCENCE
- ONE THIRD OF CASES OF PSORIASIS START IN CHILDHOOD
- MULTIPLE COMORBIDITIES: PSORIATIC ARTHRITIS HAS LARGEST EVIDENCE BASE

AAD GUIDELINES: Journal American Academy of Dermatology 2020

COMORBIDITIES IN PEDI PSORIASIS

- PSORIATIC ARTHRITIS
- OBESITY
- HYPERLIPIDEMA
- DIABETES MELLITUS
- RHEUMATOID ARTHRITIS
- INFLAMMATORY BOWEL DISEASE



> JAMA Dermatol. 2017 Jul 1;153(7):698-704. doi: 10.1001/jamadermatol.2017.0499.

Pediatric Psoriasis Comorbidity Screening Guidelines

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Affiliations + expand

PMID: 28514463 PMCID: PMC5748031 DOI: 10.1001/jamadermatol.2017.0499

Free PMC article

PSORIATIC ARTHRITIS: SCREEN FOR UVEITIS





Children (Basel). 2021 Nov; 8(11): 1057.

Published online 2021 Nov 16. doi: 10.3390/children8111057

PMCID: PMC8619705

PMID: 34828770

Skin Disease in Children: Effects on Quality of Life, Stigmatization, Bullying, and Suicide Risk in Pediatric Acne, Atopic Dermatitis, and Psoriasis Patients

Katherine A. Kelly, 1,* Esther A. Balogh, 1 Sebastian G. Kaplan, 2 and Steven R. Feldman 1,3,4,5



The Crutchfield-Brownstone-Lebwohl

Biologic Medication Quick Reference Sheet for Psoriasis

Brand Name	Generic Name	Ages	Loading Dose	Maintenance Dose	TNF	IL-4	IL-12	IL-13	IL-17	IL-23
Enbrel*	Etanercept	PsA 18 yrs + PsO 4 yrs +	50 mg SQ Twice Weekly for 12 wks	50 mg SQ q wk	,					
			PEDS: 0.8 mg/kg q wk (max-dose 50 mg q wk)		√					
Humira*	Adalimumab	PsO / PsA 18 yrs +	80 mg SQ on Day 1 and then 40 mg SQ on Day 8	40 mg SQ q2 wks	✓					
Remicade*	Infliximab	PsO / PsA 18 yrs +	5 mg/kg IV wk 0, 2, and 6	5 mg/kg IV q8 wks	✓					
Cimzia*	Certolizumab Pegol	PsO / PsA 18 yrs +	>90 kg: No Loading Dose	400 mg SQ q2 wks	√					
			<90 kg: 400 mg SQ at wk 0, 2 and 4	200 mg SQ q2 wks						
Stelara*	Ustekinumab	PsO 6 yrs + PsA 18 yrs +	<100 kg: 45 mg SQ at wk 0 and 4	45 mg SQ q12 wks			1			✓
			>100 kg: 90 mg SQ at wk 0 and 4	90 mg SQ q12 wks]					
			PEDS: Weight-based dosing recommended at initial Less than 60 kg = 0.75 mg/kg 60 kg to 100 kg = 4	al dose, 4 weeks later, then q12 weeks. 45 mg Greater than 100 kg = 90 mg						
Cosentyx*	Secukinumab	PsA 2 yrs + PsO 6 yrs +	300 mg SQ at wk 0, 1, 2, 3, and 4	300 mg SQ q4 wks						
			PEDS: Dosage based on body weight and administered by SQ at wks 0, 1, 2, 3, and 4 and q4 wks Less than 50 kg = 75 mg Greater than or equal to 50 kg = 150 mg						✓	
Taltz*	lxekizumab	PsA 18 yrs + PsO 6 yrs +	160 mg at wk 0, then 80 mg at wk 2, 4, 6, 8, 10, and 12	80 mg SQ q4 wks						
			PEDS: Greater than 50 kg = 160 mg at wk 0 then 80 mg q4 wks 25 to 50 kg = 80 mg at wk 0 then 40 mg q4 wks Less than 25 kg = 40 mg at wk 0 then 20 mg q4 wks						✓	
Siliq	Brodalumab	PsO 18 yrs +	210 mg SQ at wk 0, 1, and 2	210 mg SQ q2 wks					✓	
Tremfya*	Guselkumab	PsO / PsA 18 yrs +	100 mg SQ at wk 0 and 4	100 mg SQ q8 wks						✓
llumya	Tildrakizumab	PsO 18 yrs +	100 mg SQ at wk 0 and 4	100 mg SQ q12 wks						√
Skyrizi*	Risankizumab	PsO / PsA 18 yrs +	150 mg SQ at wk 0 and 4	150 mg SQ q12 wks						✓

Only 5 FDA medications approved for pediatric patients

(one listed = different formulation)

• Biologics:

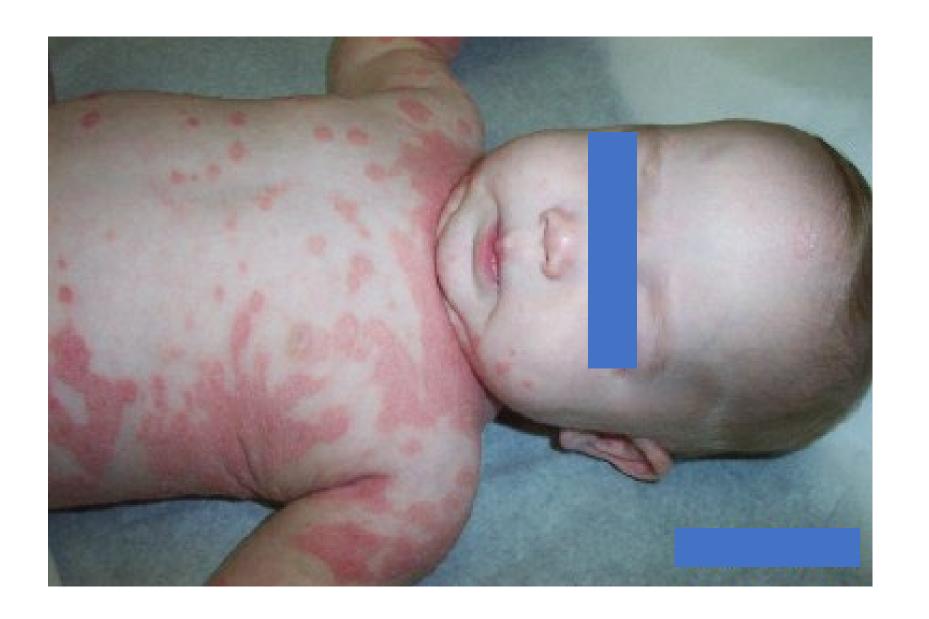
- Etanercept: ≥ 6 years
- Ustekinumab : ≥ 6 years
- Ixekizumab: ≥ 6 years
- Secukinumab: ≥ 6 years (May 2021)
- **Topicals:** Roflumilast cream 0.3% ≥ 6 years
 - Calcipotriene Foam 0.005%: ≥ 4 years scalp and body
 - Calcipotriene 0.005% and betamethasone 0.064% **foam**:
 - ≥12 years: mild to severe plaque psoriasis
 - Calcipotriene 0.005% and betamethasone 0.064%

suspension: scalp and body: ≥ 12 years

Mimickers of Pediatric Psoriasis

Mimickers:

- Sodium valproate-induced psoriasiform drug eruption
- Sanitizing hand and diaper wipes containing:
 - -Methylchorothiazolinone
 - periorificial or perineal psoriasisform distribution







CONCLUSION

- MANY CHALLENGES WHEN MANAGING PEDIATRIC PSORIASIS
- FAR FEWER MEDICATIONS
- REMEMBER COMORBIDITIES
- NAIL DISEASE: WORSE PROGNOSIS