RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

4th Annual National Conference

September 21–23, 2023

New Kids on the Block

Ingrid Pan, Pharm.D, BCPPS
Ambulatory Rheumatology Pharmacist
Children's Hospital Colorado

Accreditation Statement

- All individuals in control of the content of continuing education activities provided by the Annenberg Center for Health Sciences at Eisenhower (ACHS) are required to disclose to the audience all relevant financial relationships related to the content of the presentation or enduring material. Full disclosure of all relevant financial relationships will be made in writing to the audience prior to the activity. All other staff at the Annenberg Center for Health Sciences at Eisenhower and RhAPP have no relationships to disclose.

Faculty Disclosures

Ingrid Pan, PharmD:

- Consultant: Wolters Kluwer Clinical Drug Information, Inc.

Objectives

1. Review the different FDA approval processes for pediatric indications

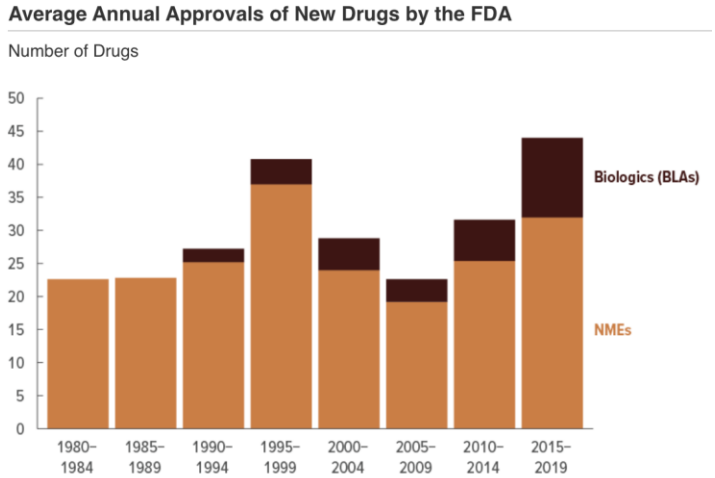
2. Evaluate the literature for recent FDA approvals of medications for pediatric rheumatic conditions

Key Abbreviations

- bDMARD = biologic DMARD
- CANDLE = Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature
- jPsA = Juvenile psoriatic arthritis
- PsO = Plaque psoriasis
- SAVI = STING-associated vasculopathy with onset in infancy
- TAK = Takayasu’s Arteritis

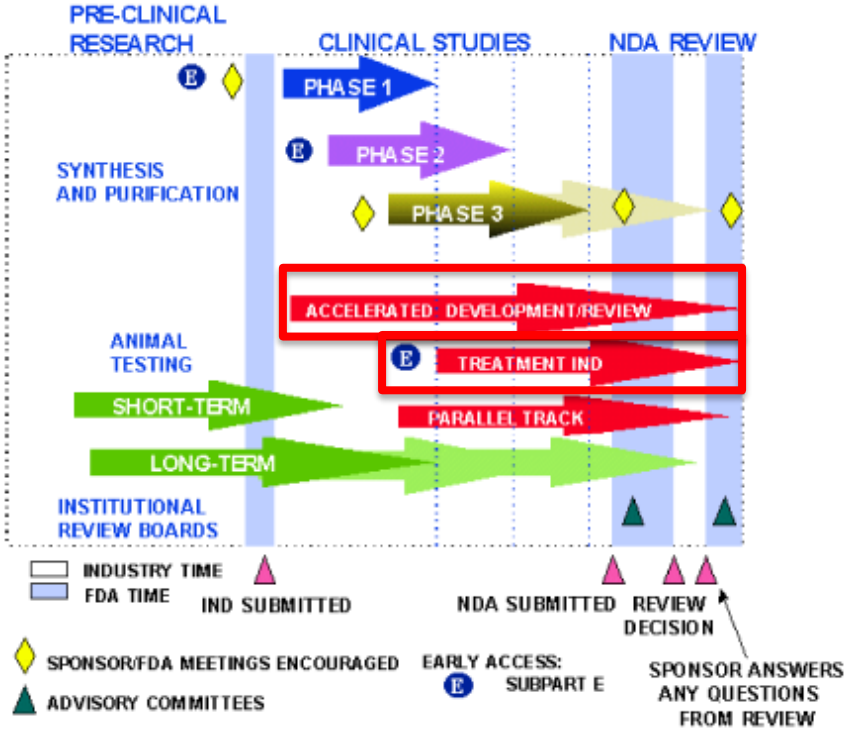
Current State of Drug Development

- ~ $83 billion has been spent in R&D by the pharmaceutical industry
- From 2010-2019, there was a 60% in drug approvals compared to the previous decade



https://www.cbo.gov

Overview of the Drug Development Process



https://www.fda.gov

Best Pharmaceuticals for Children Act (BPCA)

- Became federal law in 2002 and was recently renewed in 2022
- Role: To improve the efficacy and safety of drug use and dosage in pediatric patients
- Goals of legislation
  1. Encourage the pharmaceutical industry to conduct additional studies in the pediatric population to improve patent labeling and be awarded an additional 6 months of patent exclusivity
  2. Allow the NIH to determine which therapeutic areas should be prioritized sponsoring of clinical trials of medications currently used off-label
- Example: Abatacept (Orencia)

https://www.nichd.nih.gov
https://www.fda.gov/drugs/development-resources

Pediatric Research Equity Act (PREA)

- Became federal law in 2003 and reauthorized in 2017
- Role: Authorizes FDA to require additional clinical studies for certain drugs and biological products submitted for application
- Goals of legislation
  1. Evaluate the efficacy and safety of the product for the claimed indications in the pediatric population
  2. Provide adequate dosing and administration capability for each pediatric subpopulation
  3. Addresses integration of pediatric evaluation of molecularly targeted agents
- Examples: belimumab (Benlysta®), golimumab (Simponi®), secukinumab (Cosentyx®)

https://www.fda.gov/drugs/development-resources

A Closer Look at Pediatric Clinical Studies

Current State

- Off-label use of medications in pediatric population
  - Non-neonates: ~40%
  - Neonates: ~ 90%
- Barriers to clinical pediatric studies
  - Limited number of patients
  - Physiological changes in pediatric population
  - Ethical considerations

Solution: Extrapolation

- Assumes diseases and treatment responses are similar in the population in question
- 3 types

JAMA. 2012; 307:1914–1915.
Ther Innov Regul Sci. 2017;2017:1-7.
Paediatr Drugs. 2022 Nov;24(6):699-714.

The Concept of "Extrapolation of Efficacy"

Type of Extrapolation from Adult Data	Assumptions	Purpose of Pediatric Study	Supportive Evidence Requested from Pediatric Studies
No extrapolation	Disease/condition and/or treatment response to intervention are not similar	Demonstrate efficacy and safety in target population	• 2 well-controlled, efficacy and safety trials AND • PK data
Partial extrapolation	Disease/condition and/or treatment response to intervention are similar, but there is uncertainty in strength of assumption	Confirmation of efficacy and assessment of safety	• 1 well-controlled efficacy and safety trial + PK data • 1 controlled or un-controlled efficacy and safety trial + PK data • Single exposure – response trial + PK data
Complete extrapolation	Disease/condition and/or treatment response to intervention are similar with a high degree of certainty of assumption	Exposure data to confirm age-appropriate dose and assessment of safety	Safety and/or PK data

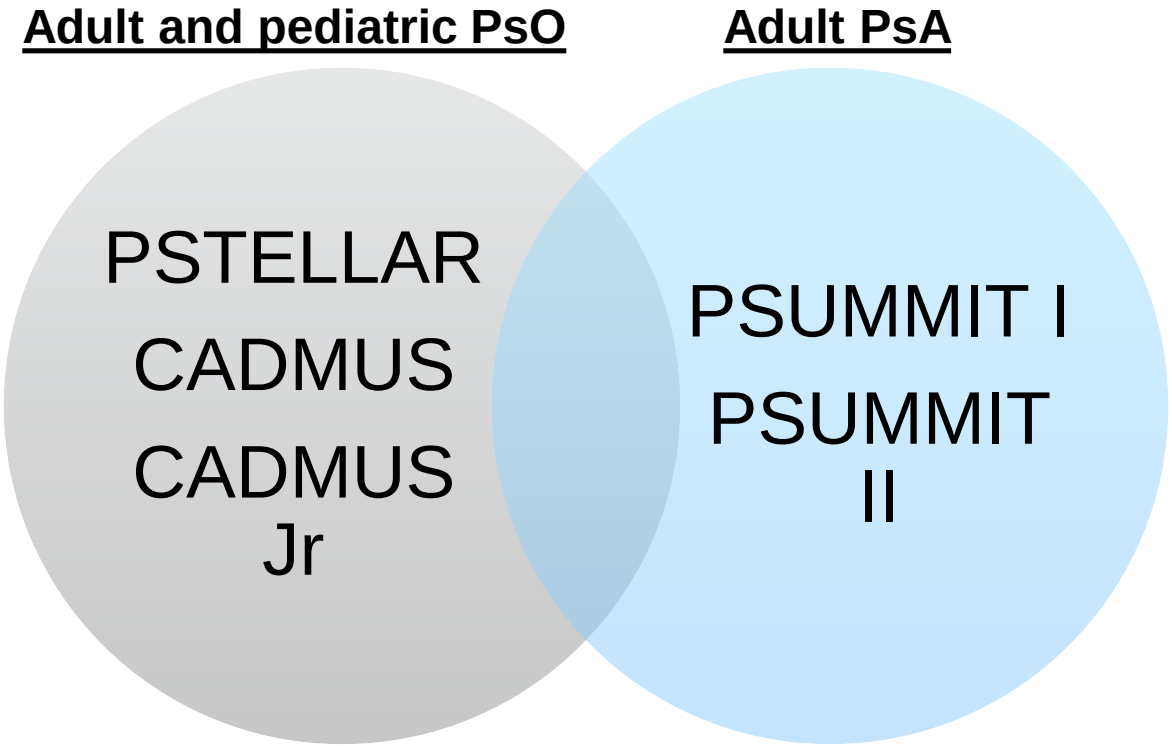
Pediatrics. 2011 Nov;128(5):e1242-9.

Extrapolation of Efficacy in Pediatric Rheumatology

- PREA requires bDMARDs approved for RA to be studied in JIA
- FDA issued waivers for studies in jPsA after previous approval in adult PsA
  - Assumptions made:
    - Underlying mechanisms, comorbidities, and clinical presentations of PsA overlap with RA and PsO
    - Data from pc-JIA, RA, adult and pediatric PsO, and adult PsA can be extrapolated to jPsA **without a PK study**

https://www.fda.gov

Case Study: Stelara® (Ustekinumab)



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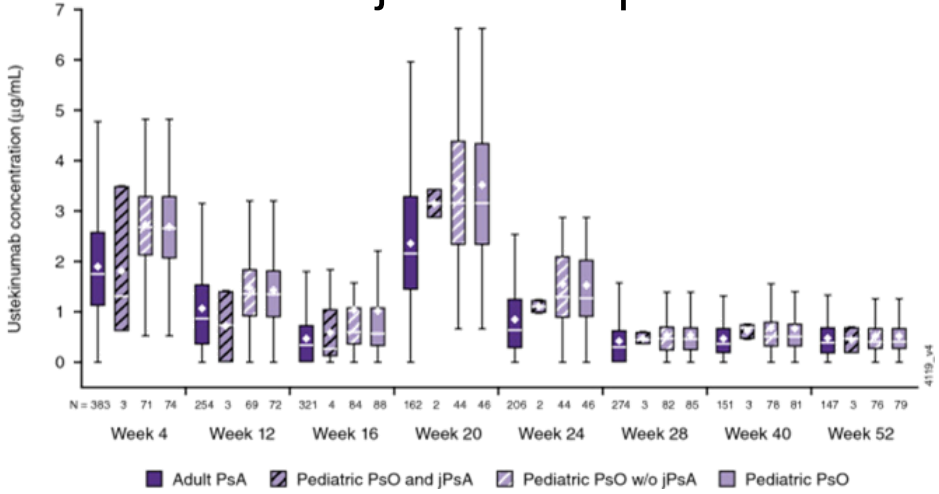
Ustekinumab PK Data for jPsA

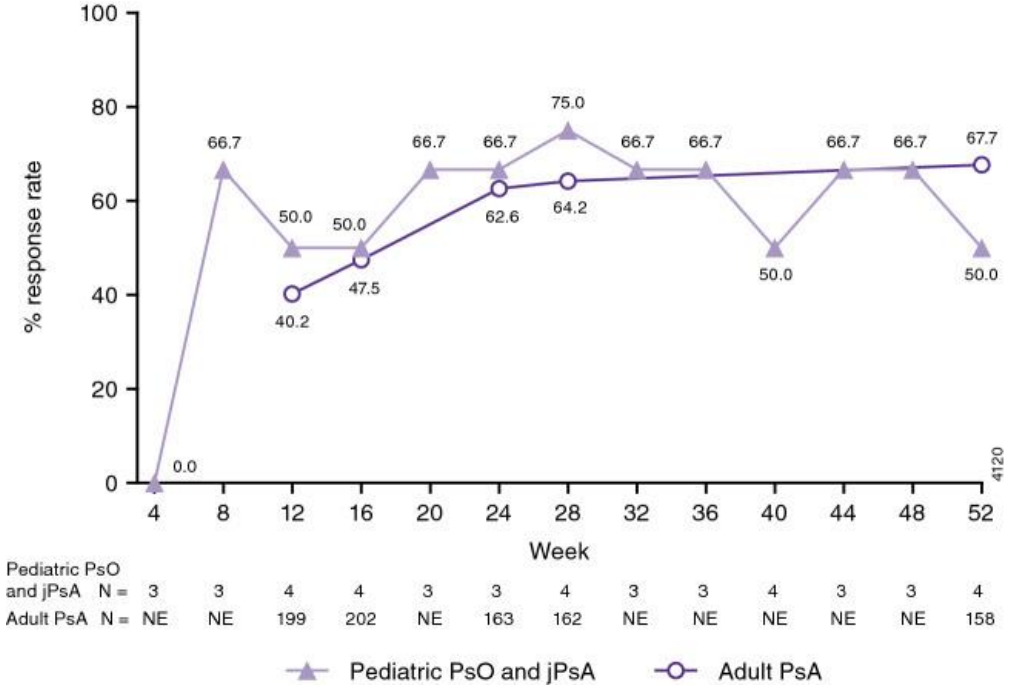
4 pediatric patients with PsO and jPsA + 91 patients with PsO without jPsA



CONCLUSION: Serum concentrations comparable between pediatric patients with PsO with OR without jPsA

Paediatr Drugs. 2022 Nov;24(6):699-714.

Ustekinumab Efficacy Data for jPsA



Conclusion:
PASI75 response rate in 4 pediatric patients with PsO and jPsA had similar responses to adult PsA

Paediatr Drugs. 2022 Nov;24(6):699-714.

FDA Approval of Ustekinumab for jPsA

At the time of approval for adult PsA in September 2013, a full waiver for Pediatric Research Equity Act (PREA)-required pediatric studies was granted due to the rarity of pediatric PsA. The waiver was granted based on the justification that dedicated clinical studies to establish efficacy of products in pediatric PsA would be impossible or highly impracticable to conduct because there are too few children with the disease/condition to study. On October 2, 2019, the FDA/M-CERSI (University of Maryland Center of Excellence in Regulatory Science and Innovation) public workshop, titled "Accelerating Drug Development for Polyarticular Juvenile Idiopathic Arthritis (pJIA)," brought together academia, industry, regulators, and patients to discuss the cumulative experience with drug development for pJIA. From these discussions, the Agency reconsidered the approach to the pediatric assessment for PsA. Specifically, the Agency considered the high degree of similarity between adults with PsA and pediatric patients with PsA to support a scientific rationale for a pediatric extrapolation of efficacy, meaning that efficacy established in adequate and well-controlled studies in adults with PsA could be extrapolated to pediatric patients with PsA based on matching of the pharmacokinetic (PK) exposures between the 2 populations. This extrapolation of efficacy is based on appropriate scientific justification and data provided by the Applicant to support the expectation of similarity in exposure-response (E-R) between the 2 populations which could be product-specific. However, safety and immunogenicity, if relevant, in pediatric patients cannot be extrapolated from the studies in adults and would need to be supported by a reasonable safety database in pediatric patients with PsA or, with appropriate justification, a relevant

[1] Ravelli A and Martini A. Juvenile idiopathic arthritis. *Lancet*. 2007; 369(9563): 767-78.
[2] Stoll ML and Punaro M. Psoriatic juvenile idiopathic arthritis: a tale of two subgroups. *Curr Opin Rheumatol*. 2011; 23(5): 437-443.

pediatric patient population. The Applicant seeks approval of ustekinumab for the treatment of pediatric PsA by providing support in this supplement for this approach to extrapolate efficacy of ustekinumab from adult PsA to pediatric PsA. The supplement includes the following: (1) information to support the similarity of adult PsA and adult PsO with respect to the target, the similarity of adult and pediatric PsO with respect to PK, safety, and response to treatment with ustekinumab, the similarity between adult PsA and pediatric PSA, and the similarity between pediatric PsA and pediatric PsO; (2) justification that the pharmacokinetics (PK) of ustekinumab are expected to be similar in pediatric psoriasis and pediatric PsA and that the therapeutic target and primary mechanism of action are relevant to the 2 indications; (3) rationale for PK bridging (comparable exposure) between adult PsA and pediatric PsA; (4) justification and relevant information to support the extrapolation of efficacy from adult PsA to pediatric PsA; (5) justification of the relevance of the safety data from adult psoriasis, pediatric psoriasis, and adult PsA to pediatric PsA. While ustekinumab is the first-in class product for PsA, additional contextual information on the relevance of the target and mechanism of action is provided by the established efficacy of ustekinumab, at similar exposures, in the related indication of adult and pediatric PsO, further supporting the PK-based extrapolation approach.

FDA U.S. FOOD & DRUG ADMINISTRATION

BLA 125261/S-158
BLA 761044/S-009

SUPPLEMENT APPROVAL

Janssen Biotech, Inc.
Attention: Jessica Miller, MS, RAC
Manager, Global Regulatory Affairs, Immunology
Welsh & McKean Roads, PO Box 776
Spring House, PA 19477

Dear Ms. Miller:

Please refer to your supplemental biologics license application (sBLA), dated and received September 17, and 22, 2023, respectively, submitted under section 351(a) of the Public Health Service Act for Stelara (ustekinumab).

This Prior Approval supplemental biologics application provides for addition of the adverse reaction of hypersensitivity vasculitis into the Postmarketing Experience section of the label.

APPROVAL & LABELING

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, you are exempt from this requirement.

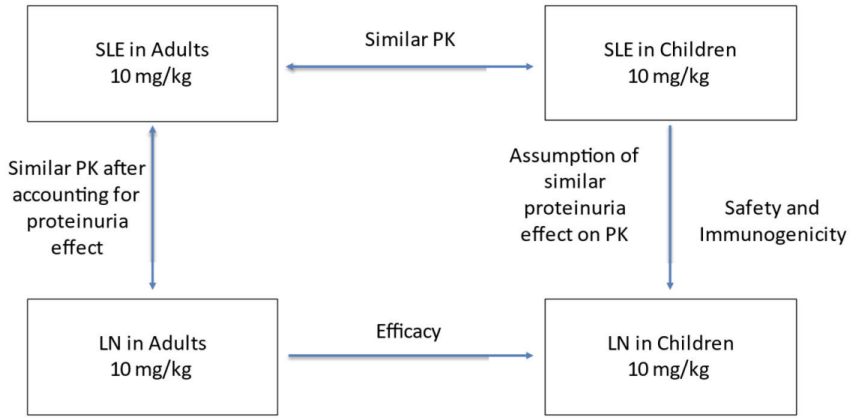
https://www.fda.gov/
https://www.accessdata.fda.gov/

What’s New Since Last Year?

New FDA Approvals: Intravenous Belimumab for Pediatric Lupus Nephritis

- Approval date: July 2022
- Method of data extraction: extrapolation of efficacy

Figure 1 Full Extrapolation Schematic for Intravenous Belimumab



https://www.fda.gov/drugs
https://www.fda.gov/media

Extrapolation of Efficacy: Belimumab

Efficacy: Pharmacokinetics of Belimumab 10 mg/kg IV

Parameter	Summary	Baseline Age 5-11 Years (Cohort 2) N=10	Baseline Age 12-17 Years (Cohorts 1 and 3) N=43	Total Pediatric 5-17 Years (Cohorts 1-3) N=53	Adult N=563
Cmax,ss (µg/mL)	Geo. Mean (%CV)	305 (22.1%)	317 (33.1%)	315 (31.2%)	311 (20.3%)
	95% CI	267 - 350	288 - 350	290 - 342	306 - 316
	Range	193 - 403	81 - 587	81 - 587	173 - 573
Cmin,ss (µg/mL)	Geo. Mean (%CV)	42 (61.8%)	52 (69.7%)	50 (68.3%)	46 (57.1%)
	95% CI	30 - 60	43 - 63	42 - 59	44 - 48
	Range	15 - 95	4 - 146	4 - 146	4 - 222
Cavg,ss (µg/mL)	Geo. Mean (%CV)	92 (42.9%)	112 (42.8%)	108 (43.2%)	100 (34.6%)
	95% CI	71 - 118	99 - 126	96 - 120	98 - 103
	Range	49 - 142	21 - 238	21 - 238	34 - 308
AUC,ss (day µg/mL)	Geo. Mean (%CV)	2569 (42.9%)	3126 (42.8%)	3012 (43.2%)	2811 (34.6%)
	95% CI	1992 - 3314	2765 - 3533	2695 - 3367	2734 - 2890
	Range	1381 - 3988	589 - 6654	589 - 6654	954 - 8627

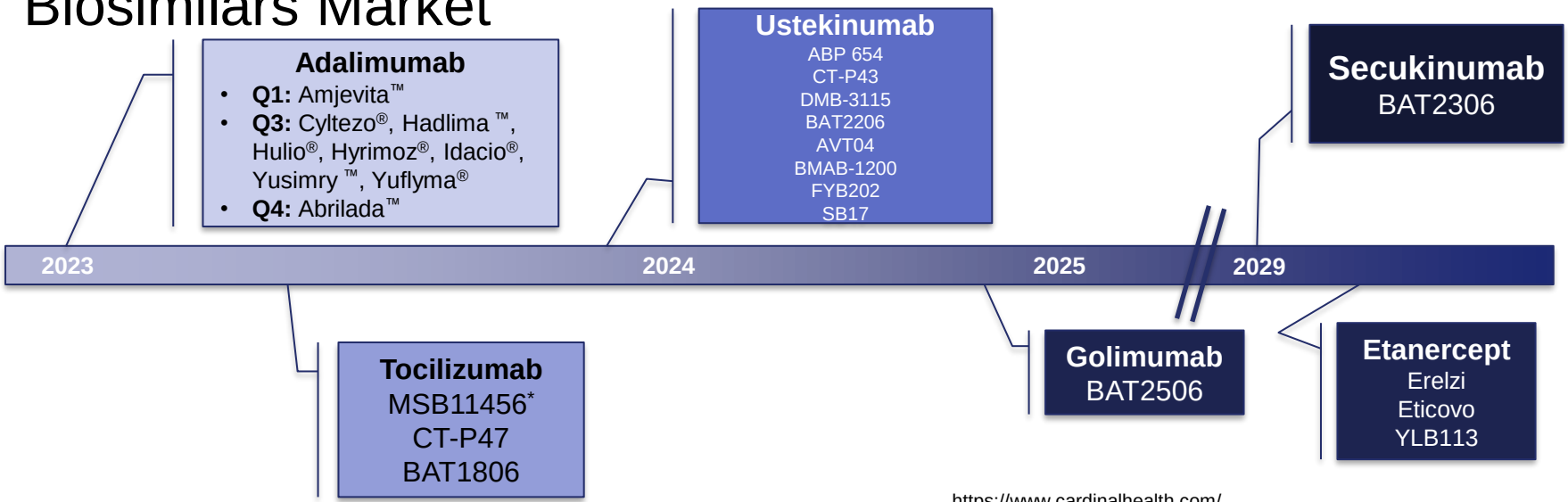
Safety

- 109 pediatric SLE patients used to extrapolate safety for pediatric LN
- Post-Marketing Surveillance from March 2021 – March 2022: no new safety signals or patterns observed seen

https://www.fda.gov/media

Honorable Mention: Biosimilars

- Biologics Price Competition and Innovation Act (BPCIA) of 2009
- Biosimilars Market



https://www.cardinalhealth.com/

Safety Signal Updates

Medication	Package Insert Update
Hydroxychloroquine *Updated 7/27/23*	Suicidal ideation and other neuropsychiatric events have occurred within the first month of treatment
Secukinumab (Cosentyx®) *Updated 7/27/23*	• Hypersensitivity reaction: anaphylaxis, urticaria • Post-marketing surveillance: Severe eczematous eruptions, such as atopic dermatitis-like eruptions, dyshidrotic eczema, and erythroderma

https://www.accessdata.fda.gov

Ongoing Clinical Trials: JIA

Medication	Patient Population and Clinical Trial
Abatacept	2 – ≤ 16.5 years old with arthritis ≤ 4 joints
Apremilast	5 – 17 years old with juvenile PsA
Baricitinib	1 – 17 years old with JIA
Camoteskimab	6 – 75 years old with SJIA/AOSD
Certolizumab pegol	2- 17 years old with severe polyarticular JIA and ≥ 10 kg
Etanercept	2 – 65 years old with JIA or RA with BMI ≥ 30 kg/m^2
Guselkumab (vs. ustekinumab)	5 – 17 years old with jPsA
Ixekizumab	≥ 2 years old with active ERA or juvenile PsA and ≥ 10 kg
Sarilumab	1 – 17 years old with SJIA and ≥ 10 kg
Tofacitinib	2 – 17 years old with SJAI
Upadacitinib (vs. tocilizumab IV/SC)	1 – 17 years old with active SJIA and ≥ 10 kg
Upadacitinib	2 – 17 years old with polyarticular JIA
Ustekinumab	5 – 17 years old with jPsA

https://classic.clinicaltrials.gov

Ongoing Clinical Trials: SLE

Medication	Patient Population and Clinical Trial
Anifrolumab	5 – 17 years old with SLE
Belimumab SC	≥ 5 -17 years old with active SLE and ≥ 15 kg
Dapirolizumab pegol (CDP-7657)	16 years old with active SLE
Ianalumab SC (VAY736)	≥ 12 years old with active SLE and ≥ 35 kg
Telitacicept	≥ 12 years old with moderate – severe SLE and on standard of care immunosuppressants
Obinutuzumab	12 – 17 years old with Class III or IV LN + SLE
Voclosporin	12 – 17 years old with active SLE + LN
Autologous SCT	8 – < 25 years old with severe SLE (and systemic sclerosis)

https://classic.clinicaltrials.gov

Ongoing Clinical Trials: Other Indications

Disease State	Medication	Patient Population and Clinical Trial
Behçet's Disease	Apremilast	2 – 17 years old with BD and had prior treatment with ≥ 1 non-biologic BD therapy and ≥ 2 oral ulcers
Castleman Disease	Sirolimus	2 – 80 years old with refractory disease to IL-6 antagonists
MAS	Emapalumab	6 months – 80 years old presenting with MAS with SLE or SJIA/AOSD
SAVI, NNS/CANDLE, AGS	Baricitinib	≥ 6 months with systemic signs and symptoms of inflammation
Systemic scleroderma	Autologous HSCT	Up to 75 years old with SSc who have failed at least 4 months of MMF/MPA or CYC
Uveitis	Baricitinib (vs. Adalimumab)	≥ 2 years old with active anterior uveitis, inadequate response or intolerance to MTX
Vasculitis	Abatacept	GPA: ≥ 12 years old with GPA
	Upadacitinib	≥ 15 years old with TAK

https://classic.clinicaltrials.gov

Agents in Development

- AbbVie: https://www.abbvie.com/science/pipeline.html
- Amgen: https://www.amgenpipeline.com/
- AstraZeneca: https://www.astrazeneca.com/our-therapy-areas/pipeline.html
- BMS: https://www.bms.com/researchers-and-partners/in-the-pipeline.html
- Eli Lily: https://www.lilly.com/discovery/clinical-development-pipeline
- Genentech: https://www.gene.com/medical-professionals/pipeline
- GSK: https://www.gsk.com/en-gb/innovation/pipeline/
- Johnson and Johnson: https://www.investor.jnj.com/pharmaceutical-pipeline
- Pfizer: https://cdn.pfizer.com/pfizercom/product-pipeline/Pipeline_Update_02MAY2023_0.pdf?so7sLOHZhv6wg5Nez9aAo9.FrRlGpcRO
- Novaritis: https://www.novartis.com/research-development/novartis-pipeline
- Sanofi: https://www.sanofi.com/minisites/pipeline/en/index.html
- Sobi: https://www.sobi.com/en/pipeline
- UCB: https://www.ucb.com/our-science/pipeline

Summary

- The BCPA and PREA provide additional financial incentives for drug manufacturers in order to expand the availability of FDA-approved medications in the pediatric population
- Extrapolation of efficacy is commonly used to overcome barriers associated with completing clinical studies in the pediatric population
- There has been minimal new FDA approved medications for pediatric patients with rheumatic conditions from Q3 2022 to Q3 2023
- There are numerous ongoing clinical trials evaluating the efficacy and safety of established medications in pediatric rheumatic conditions

References

1. Research and Development in the Pharmaceutical Industry. Congressional Budget Office. Accessed July 28, 2023. https://www.cbo.gov/publication/57126.
2. New Drug Development and Review Process. U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/new-drug-development-and-review-process.
3. Best Pharmaceuticals for Children Act. National Health Institute. Accessed July 28, 2023. https://www.nichd.nih.gov/research/supported/bpca/about.
4. Reviews of Pediatric Studies Conducted under BPCA and PREA from 2012 – present. U.S. Food Drug Administration. Accessed July 28, 2023. https://www.fda.gov/drugs/development-resources/reviews-pediatric-studies-conducted-under-bpca-and-prea-2012-present.
5. Pediatric Research Equity Act | PREA. U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.fda.gov/drugs/development-resources/pediatric-research-equity-act-prea.
6. Sachs AN, Avant D, Lee CS, Rodriguez W, Murphy MD. Pediatric information in drug product labeling. *JAMA*. 2012; 307:1914–1915.
7. Sun H, Temeck JW, Chambers W, Perkins G, Bonnel R, Murphy D. Extrapolation of Efficacy in Pediatric Drug Development and Evidence-based Medicine: Progress and Lessons Learned. *Ther Innov Regul Sci*. 2017;2017:1-7.
8. Leu JH, Shiff NJ, Clark M, Bensley K, Lomax KG, Berezny K, Nelson RM, Zhou H, Xu Z. Intravenous Golimumab in Patients with Polyarticular Juvenile Idiopathic Arthritis and Juvenile Psoriatic Arthritis and Subcutaneous Ustekinumab in Patients with Juvenile Psoriatic Arthritis: Extrapolation of Data from Studies in Adults and Adjacent Pediatric Populations. *Paediatr Drugs.* 2022 Nov;24(6):699-714.
9. Dunne J, Rodriguez WJ, Murphy MD, Beasley BN, Burckart GJ, Filie JD, Lewis LL, Sachs HC, Sheridan PH, Starke P, Yao LP. Extrapolation of adult data and other data in pediatric drug-development programs. *Pediatrics.* 2011 Nov;128(5):e1242-9.
10. Accelerating Drug Development for Polyarticular Juvenile Idiopathic Arthritis (pJIA). U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/accelerating-drug-development-polyarticular-juvenile-idiopathic-arthritis-pjia-10022019-10022019.

References

11. NDA/BLA Multi-Disciplinary Review and Evaluation – BLA 125433 IV Golimumab (Simponi Aria) for pJIA. U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.fda.gov/media/143318/download.
12. Primary Review, Cross Discipline Team Leader Review, Division Director Summary – BLA 125261/s161 Ustekinumab for juvenile psoriatic arthritis. U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.fda.gov/media/167751/download.
13. BLA 125261/S-158 – Supplement Approval. U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2023/125261Orig1s158,761044Orig1s009ltr.pdf.
14. New Drug Therapy Approvals 2022. U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/new-drug-therapy-approvals-2022#:~:text=In%202022%2C%20CDER%20approved%20Vidaza,for%20this%20type%20of%20leukemia.
15. Novel Drug Approvals for 2023. U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2023.
16. BLA 12537s-078 and BLA 761043/s-021 Multi-Disciplinary Review and Evaluation Benlysta® (belimumab) for intravenous infusion in Children 5 to less than 18 years old with Lupus Nephritis. U.S. Food & Drug Administration. Accessed July 28, 2023. https://www.fda.gov/media/160711/download.
17. New and upcoming biosimilar launches. Cardinal Health. Accessed July 28, 2023. https://www.cardinalhealth.com/content/dam/corp/web/documents/Report/cardinal-health-biosimilar-launches.pdf.
18. Drug Safety-related Labeling Changes – Hydroxychloroquine. Accessed July 28, 2023. https://www.accessdata.fda.gov/scripts/cder/safetylabelingchanges/index.cfm?event=searchdetail.page&DrugNameID=2714.
19. Drug Safety-related Labeling Changes – Secukinumab. Accessed July 28, 2023. https://www.accessdata.fda.gov/scripts/cder/safetylabelingchanges/index.cfm?event=searchdetail.page&DrugNameID=1276.
20. Preventing Extension of Oligoarticular Juvenile Idiopathic Arthritis JIA (LIMIT-JIA). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT03841357?intr=%22Abatacept%22&age=0&draw=3&rank=3.

References

21. Apremilast Pediatric Study in Children with Active Juvenile Psoriatic Arthritis (PEAPOD). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04804553?recrs=abdf&intr=%22Antirheumatic+Agents%22&age=0&draw=3.
22. A Study of Baricitinib in Participants From 1 Year to Less Than 18 Years Old with Juvenile Idiopathic Arthritis (JUVE-X).). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT03773965?recrs=abdf&cond=%22Psoriatic+Juvenile+Idiopathic+Arthritis%22&age=0&draw=2&rank=8.
23. A Study to Evaluate Camoteskimab in Participants with Still's Disease (AOSD/sJIA). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04752371?recrs=abdf&cond=%22Systemic+Onset+Juvenile+Idiopathic+Arthritis%22&age=0&draw=2&rank=5.
24. Pediatric Arthritis Study of Certolizumab Pegol (PASCAL). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT01550003?recrs=abdf&intr=%22Antirheumatic+Agents%22&age=0&draw=2&rank=53.
25. Pharmacokinetics and Pharmacodynamics of Biologic Drugs in Obese Patients with Arthritis (PRECISE). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04585711?recrs=abdf&intr=%22Antirheumatic+Agents%22&age=0&draw=7&rank=577.
26. A Study of Ustekinumab or Guselkumab in Pediatric Participants with Active Juvenile Psoriatic Arthritis (PSUMMIT-Jr). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05083182?recrs=abdf&cond=%22Psoriatic+Juvenile+Idiopathic+Arthritis%22&age=0&draw=2&rank=5.

References

27. A Study of Ixekizumab (LY2439821) in Children with Juvenile Idiopathic Arthritis Categories of Enthesitis-related Arthritis (Including Juvenile Onset Ankylosing Spondylitis) and Juvenile Psoriatric Arthritis.). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04527380.
28. A Safety, Efficacy, and Pharmacokinetics Study of Tofacitinib in Pediatric Patients with sJIA. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023.. https://classic.clinicaltrials.gov/ct2/show/study/NCT03000439?recrs=abdf&cond=%22Systemic+Onset+Juvenile+Idiopathic+Arthritis%22&age=0&draw=2&rank=11.
29. A Repeated Dose-Finding Study of Sarilumab in Children and Adolescents with Systemic Juvenile Idiopathic Arthritis (SKYPS). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT02991469?recrs=abdf&cond=%22Systemic+Onset+Juvenile+Idiopathic+Arthritis%22&age=0&draw=2&rank=7.
30. Study of Oral Upadacitinib and Subcutaneous/Intravenous Tocilizumab to Evaluate Change in Disease Activity, Adverse Events and How Drug Moves Through the Body of Pediatric and Adolescent Participants with Active Systemic Juvenile Idiopathic Arthritis. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05609630?recrs=abdf&intr=%22Antirheumatic+Agents%22&age=0&draw=2&rank=28.
31. A Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of Upadacitinib in Pediatric Subjects with Polyarticular Course Juvenile Idiopathic Arthritis. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT03725007?recrs=abdf&intr=%22Antirheumatic+Agents%22&age=0&draw=2&rank=32.
32. A Study of Ustekinumab in Pediatric Participants (U-POPS) with Juvenile Psoriatic Arthritis or Psoriasis (U-POPS). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05252533.
33. An Efficacy and Safety Study of Intravenous Anifrolumab to Treat Systemic Lupus Erythematosus in Pediatric Participants (SLE). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05835310?recrs=abdf&cond=%22Lupus+Erythematosus%2C+Systemic%22&age=0&draw=2&rank=3

References

34. Study of Subcutaneous (SC) Belimumab in Pediatric Participants with Systemic Lupus Erythematosus (SLE). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/study/NCT04179032.
35. A Study to Evaluate the Safety and Tolerability of Dapirolizumab Pegol in Study Participants with Systemic Lupus Erythematosus. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04976322?recrs=abdf&cond=%22Lupus+Erythematosus%2C+Systemic%22&age=0&draw=2&rank=16.
36. Phase 3 Study to Evaluate Two Regimens of Ianaumab to Top of Standard-of-care Therapy in Patients with Systemic Lupus Erythematosus (SIRIUS-SLE 1). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05639114.
37. A Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Obiutuzumab in Adolescents with Active Class III or IV Lupus Nephritis (POSTERITY). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05039619?recrs=abdf&cond=%22Lupus+Nephritis%22&age=0&draw=2&rank=4.
38. A Study of Telitacicept for the Treatment of Moderately to Severely Active Systemic Lupus Erythematosus. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05306574?recrs=abdf&cond=%22Lupus+Erythematosus%2C+Systemic%22&age=0&draw=2&rank=19.
39. Voclosporin in Adolescents with Lupus Nephritis (VOCAL). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05288855?recrs=abdf&cond=%22Lupus+Nephritis%22&age=0&draw=2&rank=1.
40. Autologous Stem Cell Transplant (ASCT) for Autoimmune Diseases. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05029336?recrs=abdf&cond=%22Lupus+Erythematosus%2C+Systemic%22&age=0&draw=2&rank=31.

References

41. Apremilast Pediatric Study in Children With Active Oral Ulcers Associated with Behcet's Disease (BEAN). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04528082?recrs=abdf&intr=%22Antirheumatic+Agents%22&age=0&draw=3.
42. A Study of Baricitinib (LY3009104) in Adult and Japanese Participants with NNS/CANDLE, SAVI, and ACS. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04517253?cond=%22STING-associated+Vasculopathy+With+Onset+in+Infancy%22&draw=2&rank=1.
43. A Study of Baricitinib (LY3009104) in Participants From 2 Years to Less than 18 Years Old with Active JIA-Associated Uveitis or Chronic Anterior Antinuclear Antibody-Positive Uveitis.). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04088409?recrs=abdf&intr=%22Adalimumab%22&age=0&draw=2&rank=6.
44. Abatacept for the Treatment of Relapsing, Non-Severe, Granuloatosis with Polyangiitis (Wegener's). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT02108860?recrs=abdf&intr=%22Abatacept%22&age=0&draw=2&rank=12.
45. Evaluate Efficacy, Safety, and Tolerability, PK and PD of Emapalumab in Children and Adults with MAS in Still's or SLE (EMERALD). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT05001737?recrs=abdf&cond=%22Macrophage+Activation+Syndrome%22&age=0&draw=2&rank=4.
46. Scleroderma Treatment with Autologous Transplant (STAT) Study. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT01413100?recrs=abdf&cond=%22Systemic+Scleroderma%22&age=0&draw=2&rank=1.
47. Sirolimus in Previously Treated Idiopathic Mutilcentric Castleman Disease. U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT03933904?recrs=abdf&cond=%22Multicentric+Castleman+Disease%22&age=0&draw=2&rank=1
48. A Study to Evaluate the Efficacy and Safety of Upadacitinib in Participants with Takayasu Arteritis (TAK) (SELECT-TAK). U.S. National Library of Medicine – Clinical Trials.gov. Accessed July 28, 2023. https://classic.clinicaltrials.gov/ct2/show/NCT04161898?recrs=abdf&intr=%22Antirheumatic+Agents%22&age=0&draw=7&rank=591.