Overview of Paediatric Investigation Plan (PIP) in Paediatric Rheumatology

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Paediatric Investigation Plan (PIP) Applications

CONDITION	APPLICATIONS	OPINIONS	UNDER EVALUATION	STUDIES	UNDER EVALUATION
JIA	11	8	3	18	5
SLE	2	1	1	1	1
AUTOINFLAMMATORY DISEASE	1	1	0	5	0

Discrepancies Between Initially Proposed and Finally Agreed Conditions

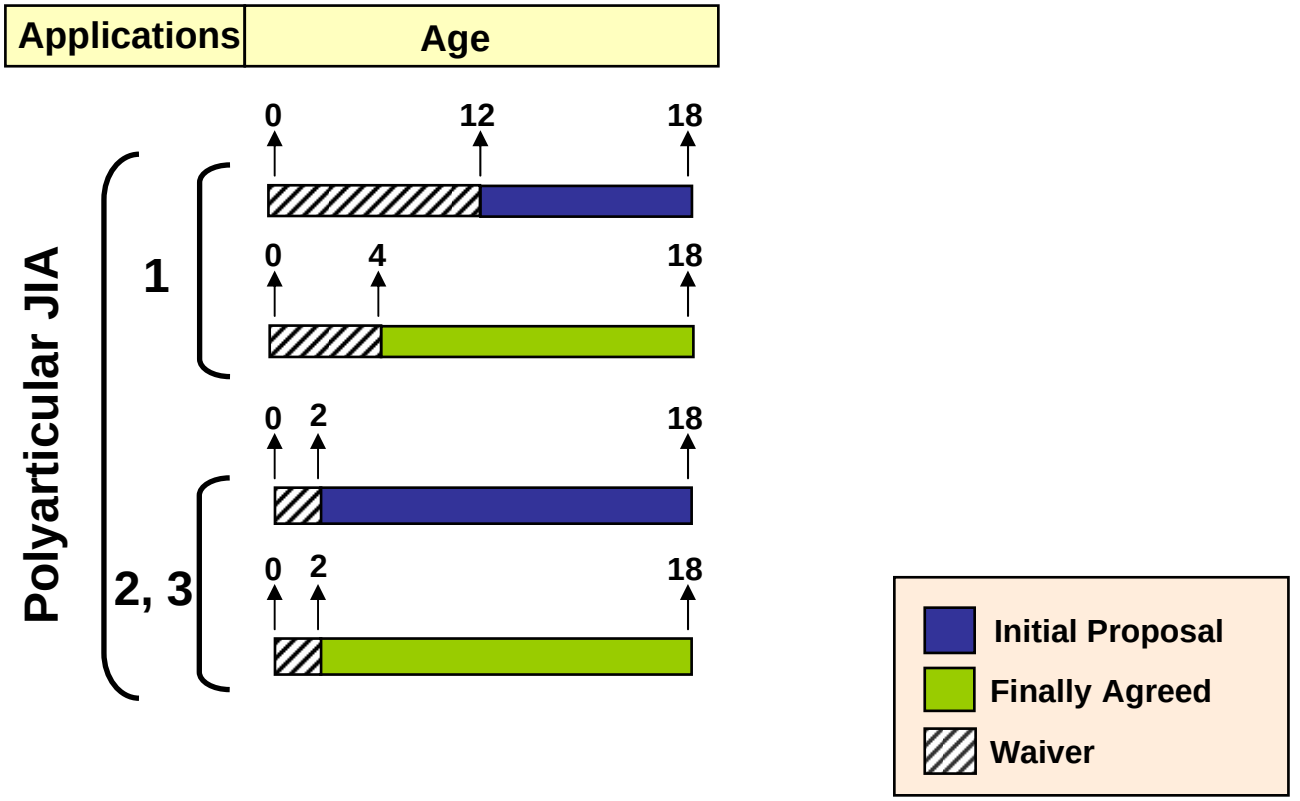
Initial Proposed Condition	
JIA	1
Poly JIA	1
Systemic JIA	2
RA	6

Discrepancies Between Initially Proposed and Finally Agreed Conditions

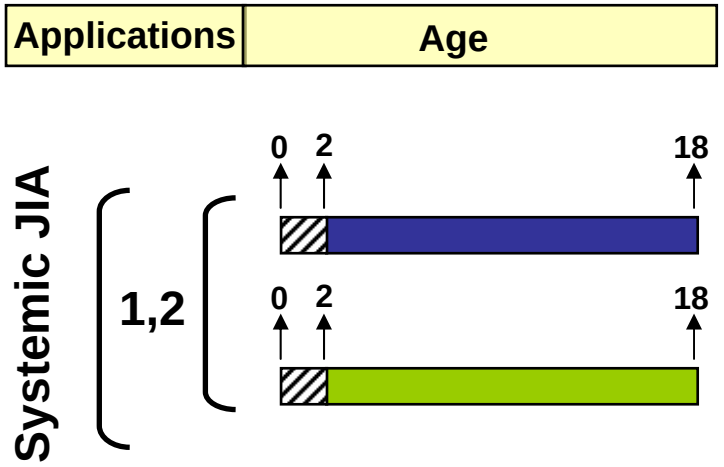
Initial Planned Condition	
JIA	1
Poly JIA	1
Systemic JIA	2
RA	6

Finally Approved by PDCO	
JIA	4
PsA	1
ERA	1
RA	2
AA	3

Age and Waiver Analysis in Polyarticular JIA PIPs



Age and Waiver Analysis in Systemic JIA PIPs

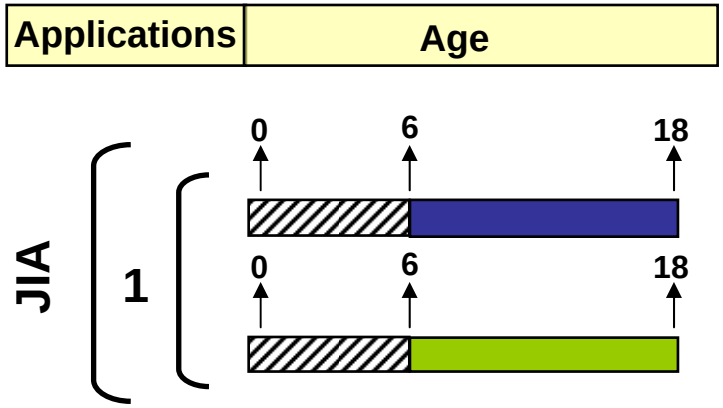


Initial Proposal

Finally Agreed

Waiver

Age and Waiver Analysis in JIA PIPs

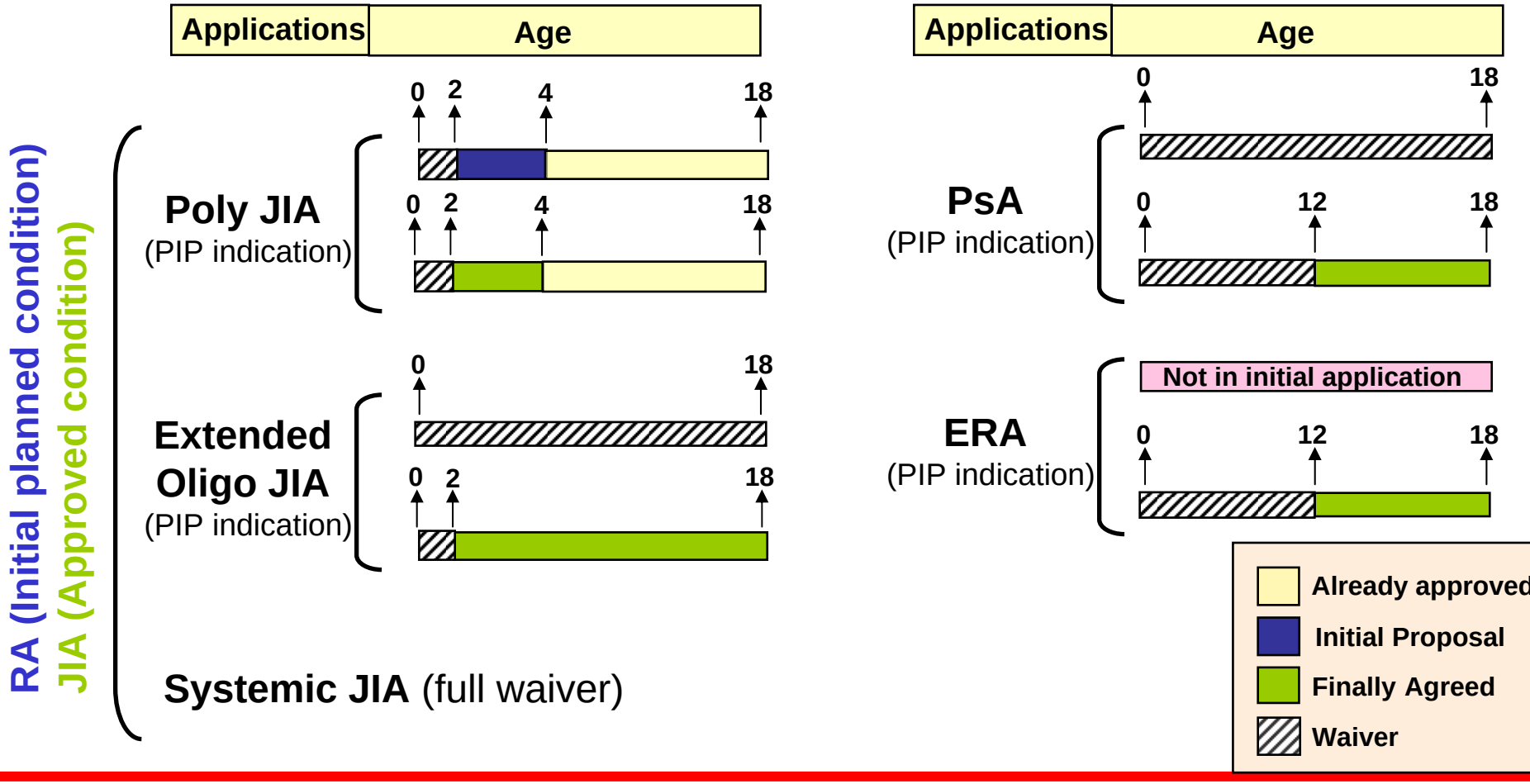


Initial Proposal

Finally Agreed

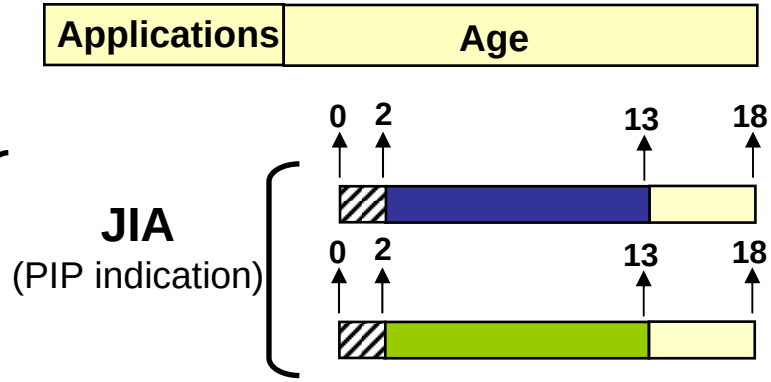
Waiver

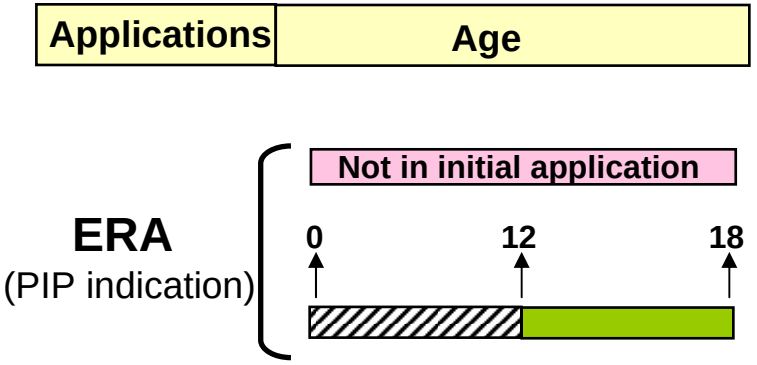
Age and Waiver Analysis in RA (initial planned condition) PIPs



Age and Waiver Analysis in RA (initial planned condition) PIPs

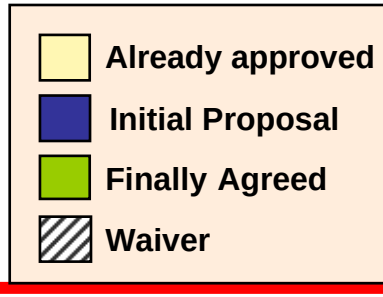
RA (Initial planned condition)
RA (Approved condition)





PsA (full waiver)

Ankylosing spondylitis (full waiver)



Denosumab
EMEA-000145-PIP01-07

CONDITION: JIA
PIP Indication: poly JIA, from **4 to less 18 years.**
WAIVER: JIA, from **birth to less than 4 years of age.**

Clinical	Pharmacokinetics	2	Phase 1 study in patients in children from 12 years to less than 18 years of age with polyarticular juvenile idiopathic arthritis (RF+) evaluating safety and PK/PD of denosumab. Phase 1 study in patients in children from 4 years to less than 12 years of age with polyarticular juvenile idiopathic arthritis (RF+) evaluating safety and PK/PD of denosumab.
	Efficacy and safety	2	Phase 2 study in patients from 12 to less than 18 years of age with polyarticular juvenile idiopathic arthritis (RF+), evaluating inhibition of progression of structural damage by denosumab in combination with disease modifying anti rheumatic drugs (DMARDs). Phase 2 study in patients from 4 to less than 12 years of age with polyarticular juvenile idiopathic arthritis (RF+) evaluating inhibition of progression of structural damage by denosumab in combination with DMARDs.

Abatacept
EMEA-000118-PIP01-07

CONDITION: JIA **PIP Indication: Poly JIA,** from **6 to less than 18 years.** **WAIVER: JIA**, from **birth to less than 6 years of age.**			
Clinical	Pharmacokinetic, efficacy and safety	1	A Phase 3 multi-centre, multi-national, randomised, withdrawal study to evaluate the safety and efficacy of abatacept in children and adolescents with active polyarticular juvenile rheumatoid arthritis

Tocilizumab
EMEA-000309-PIP01-08

CONDITION: Autoimmune Arthritis
PIP indication: **Systemic JIA** and **Active polyarticular-course JIA** (RF+/RF- poly-JIA and extended oligo-JIA), both from **2 to less than 18 years**.
WAIVER: JIA, from **birth to less than 2 years of age.**

Clinical		2	Randomised, double-blind, placebo-controlled, parallel-group, 2-arm 12 week study to evaluate the efficacy and safety of tocilizumab in patients aged from 2 years to less than 18 years with active systemic juvenile idiopathic arthritis with 92-week single-arm open-label extension. Open-label, multi-centre withdrawal study to evaluate the efficacy and safety of tocilizumab in patients aged from 2 years to less than 18 years with active polyarticular-course juvenile idiopathic arthritis, with open -label extension.

Golimumab
EMEA-000265-PIP01-08

CONDITION: Autoimmune Arthritis **PIP indication: Moderately to severely active polyarticular-course JIA**, from **2 to less than 18 years**. **WAIVER: JIA**, from **birth to less than 2 years of age.**			
Clinical		1	Double-blind, randomized, multi-centre, multiple-dose, dose-ranging, placebo-controlled trial to evaluate pharmacokinetics, safety and efficacy of golimumab in combination with methotrexate in children from 2 years to less than 18 years of age with inadequate response to methotrexate.

Etanercept

EMEA-000299-PIP01-08

CONDITION: JIA

PIP indication: **Extended oligo JIA and poly JIA,** both from **2 to less than 18 years**; **PsA and ERA,** both from **12 to less than 18 years.**

WAIVER: JIA: **sJIA, Full waiver**, **Oligo JIA,** from **birth to < 2 years**; **Poly JIA**, from **birth to < 2 years**; **PsA,** from **birth to < 12 years**; **ERA,** from **birth to < 12 years**.

Clinical		3	Open-label nonrandomized multi-centre registry study of children with polyarticular course or systemic onset JIA from 1 year to less than 18 years for evaluation of long-term safety of etanercept compared to patients receiving methotrexate (Study 20021626). Open-label multi-centre extension study for evaluation of long-term efficacy and safety in patients with RA and JIA involved in previous studies (Study 20021618). Single-treatment open-label multi-centre study of patients with oligoarticular JIA from 2 years to less than 18 years and psoriatic arthritis or enthesitis related arthritis from 12 to less than 18 years to evaluate efficacy and safety of etanercept in comparison with historical control cohort of placebo treated patients (Study 0881A1-3338-WW).

Adalimumab
EMEA-000366-PIP01-08

CONDITION: RA
PIP indication: JIA, from **2 to less than 18 years**;
ERA, from **12 to less than 18 years.**
WAIVER: RA, from **birth to < 2 years**
ERA, from **birth to < 12 years**.

Clinical		3	A Multi-centre, Randomised, Double-Blind, Placebo-Controlled Study of the Safety, Efficacy, and Pharmacokinetics of the Human Anti-TNF Monoclonal Antibody Adalimumab in Children With Polyarticular Juvenile Rheumatoid Arthritis. Compassionate Use Study of Adalimumab in Children from 2 to less than 4 Years Old or Age 4 and Above Weighing Less Than 15 kg with Active Juvenile Idiopathic Arthritis (JIA). A double-blind, placebo-controlled, multi-centre study of the efficacy and safety of the human anti-TNF monoclonal antibody adalimumab in paediatric patients with enthesitis-related arthritis.

Rituximab
EMEA-000308-PIP01-08

CONDITION: **Autoimmune Arthritis** **WAIVER:** **Autoimmune Arthritis:** **Full waiver**.			
Clinical		0	NO STUDIES

Canakimumab
EMEA-000060-PIP02-07

CONDITION: JIA
PIP indication: JIA, from **2 to less than 18 years**;
WAIVER: sJIA, from **birth to < 2 years**

Clinical		4	A multi-centre, open label, repeated dose range finding study to evaluate the safety, tolerability, immunogenicity and pharmacokinetics of canakinumab given subcutaneously in paediatric subjects with active systemic juvenile idiopathic arthritis. A randomized, double-blind, placebo controlled, single-dose study to assess the efficacy of canakinumab in patients from 2 years to less than 20 years of age with Systemic Juvenile Idiopathic Arthritis (sJIA) and active systemic manifestations. A randomized, double-blind, placebo controlled, withdrawal study of flare prevention of canakinumab in patients from 2 years to less than 20 years of age with Systemic Juvenile Idiopathic Arthritis (sJIA) and active systemic manifestations. An open-label extension study canakinumab in patients with Systemic Juvenile Idiopathic Arthritis (sJIA) and active systemic manifestations.

CONCLUDING REMARKS

- Paediatric regulation impact
- Definition of condition/indication
- Age groups
- Study design
- Outcome measures
- What is the need for further JIA studies?