European Medicines Agency
Evaluation of Medicines for Human Use

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ASSESSMENT OF THE PAEDIATRIC NEEDS
RHEUMATOLOGY

DISCLAIMER

The Paediatric Working Party (PEG) is working to identify the needs in the different therapeutic areas where there should be research and development of medicinal products for children, either old (i.e. off patent) or new ones (including those under development). Products on the list are not in any order of priority.

The lists should not be viewed as a prescription tool nor as recommendations for treatment. Accuracy of data including in particular authorised doses cannot be guaranteed.

Information on existing marketing authorisations is very limited and therefore information under "authorised" includes the indication in broad term, the lower age group authorised in at least one Member State, the authorised dose(s) and formulation(s) in at least in one Member State.

Comments from third parties are expected especially to complete and or update the list as necessary.

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NSAIDS (NON-STEROIDAL ANTI-INFLAMMATORY DRUGS)*	
IBUPROFEN	
Authorised indication	Juvenile Idiopathic Arthritis (JIA)
Authorised age group	> 1 year *(Finland)*
Authorised dose	30- 40 mg/kg/day
Authorised formulation	Liquid formulation, suppositories, tablets, micro granules, sugar-free formulation Capsules
Needs[1]	Indication for JIA and age appropriate formulation to be made available in all Member States (MSs)
NAPROXEN	
Authorised indication	JIA
Authorised age group	> 1 year (Finland)
Authorised dose	10-15 mg/kg/day
Authorised formulation	Granules and scored coated tablets (250 and 500 mg), suppositories (500 mg), capsules, liquid formulation 25 mg/ml (Finland) and 50 mg/ml (Switzerland)
Needs	Indication for JIA and age appropriate formulation to be made available in all Member States (MSs)
DICLOFENAC	
Authorised indication	Arthritis
Authorised age group	>1 year (Finland)
Authorised dose	0.5-3 mg/kg/day (b.i.d or t.i.d.)
Authorised formulation	Tablets, suppositories (100 and 25 mg) solution for intramuscular use, dispersible tablets 25mg
Needs	Data on efficacy, safety and dose in the indication for JIA Age appropriate formulation in all MSs
INDOMETHACIN	
Authorised indication	JIA
Authorised age group	> 6 years
Authorised dose	1-4 mg/kg/day (t.i.d)
Authorised formulation	Capsules (25 and 50 mg), slow release capsules 75 mg and suppositories (100 mg) 1 mg vial for injection (United Kingdom)
Needs	Extension of indication to children 2 to 6 years Age appropriate formulation to be made available in all MSs (including slow release)
MELOXICAM	
Authorised indication	JIA
Authorised age group	>15 years
Authorised dose	15 mg per day
Authorised formulation	Tablets (7.5 and 10 mg), suppositories (7.5 and 10 mg), i.v.-solution (10 mg / ml)
Needs	Extension of the indication to children > 2 years [efficacy and long term

[1] The list will specify which kind of data would be needed but neither the design, nor the number of studies (e.g. PK, efficacy). The lists will indicate the need for 'age-appropriate' formulations, without specifying which one, to keep options open and room for innovation.

	safety data, dose (empirical dose of 0.125 – 0.250 mg/kg/day to be confirmed] Age appropriate formulation to be made available in all MSs
PIROXICAM	
Authorised indication	Rheumatoid polyarthritis
Authorised age group	> 15 years
Authorised dose	10 – 40 mg per day
Authorised formulation	Capsules (10 and 20 mg), dispersible scored tablet (20 mg), injectable (20 mg i.m), suppositories (20 mg), "melt" (United Kingdom), granules (20 mg) (Germany)
Needs	Data on efficacy, safety and dose in the indication for JIA Age appropriate formulation to be made available in all MSs
COX-II INHIBITORS *	
Authorised indication	Arthritis
Authorised age group	>18 years
Authorised dose	-
Authorised formulation	-
Needs	If safety acceptable, data on efficacy, safety (particular long-term data for cardiovascular and serious skin disease immunological risks) and dose in the indication for JIA for children > 2 years might still be needed. Age appropriate formulation
BIOLOGICAL AGENTS	
INFLIXIMAB	
Authorised indication	Rheumatoid arthritis
Authorised age group	>18 years
Authorised dose	3mg/kg i.v. at 0, 2, and 6 weeks, then every 8 weeks intravenously
Authorised formulation	Powder for concentration for solution for infusion (10 mg/ml)
Needs	Data on efficacy, safety including long-term (known safety concerns: e.g. oncogenic risk and opportunistic infectious diseases such as tuberculosis) and dose (including maximal maintenance dose for incomplete response) in the indication for JIA for children > 1 years Age appropriate formulation (lower strength)
ADALIMUMAB	
Authorised indication	Rheumatoid arthritis
Authorised age group	> 18 years
Authorised dose	40 mg/every 2 weeks subcutaneously
Authorised formulation	Solution for injection
Needs	Data on efficacy, safety including long term, and dose in the indication for JIA for children > 6 years Age appropriate formulation
ETANERCEPT	
Authorised indication	Rheumatoid arthritis after treatment failure with methotrexate
Authorised age group	> 4 years
Authorised dose	400 micrograms/kg twice weekly
Authorised formulation	Solution for s.c. injection
Needs	Extended indication for JIA oligoarthritis > 2 years Extension of the indication for TNF-mediated tumor necrosis factor associated periodic syndrome (TRAPS) Efficacy of weekly vs. twice weekly dosing in paediatric age groups

	Age appropriate formulation Data on long-term safety
ANAKINRA	
Authorised indication	JIA in combination with methotrexate
Authorised age group	> 18 years
Authorised dose	100 mg s.c. daily
Authorised formulation	Solution for injection
Needs	Data on efficacy, tolerability at the site of injection, safety including long-term safety, Dose in the indication of SJIA Extension of (IL-1 mediated) Cryopyrin-Associated Periodic Syndrome (CAPS) Extension of the indication in all age groups including newborns
DMARD* (DISEASE MODIFYING ANTIRHEUMATIC DRUGS) AND IMMUNOSUPPRESSIVE AGENTS	
SULFASALAZINE	
Authorised indication	JIA
Authorised age group	> 6 years
Authorised dose	Max. daily dose 2 g
Authorised formulation	Gastro-resistant coated tablets (500 mg), suppositories (500 mg) Tablets (Italy)
Needs	Data on efficacy, safety and dose in the indication for enthesitis- related arthritis [empirical dose (loading dose: 100-150 mg/kg/day maintenance dose: 30-50-75mg/kg/day) to be confirmed] Age appropriate formulation
CICLOSPORIN A	
Authorised indication	Rheumatoid polyarthritis, , uveitis
Authorised age group	>18 years
Authorised dose	-
Authorised formulation	Capsules (25, 50 and 100 mg), i.v. solution (50 mg/ml), oral solution (100 mg/ml)
Needs	Data on efficacy, safety including long-term data (nephrotoxicity particularly in combination with NSAIDs and risk of lymphoproliferative disorders) and dose for the indications dermatomyositis – uveitis - lupus nephritis and JIA. (empirical dose of 2 – 5 mg/kg/d or more to be confirmed) Drug level monitoring needs to be evaluated Age appropriate oral low strength formulation
METHOTREXATE	
Authorised indication	JIA
Authorised age group	Unspecified age group
Authorised dose	10 mg/m2/week. Can be increased to 20 mg/m2/week
Authorised formulation	i.m. and s.c. solution, tablets 2.5 and 10 mg, i.v. solution 7.5 mg/ml
Needs	Extension of indication for children > 2 years , [data on efficacy data, empirical dose to be confirmed (10 – 20 mg/qm KOF/week or 0.5 – 0.6 (1.0) mg/kg/week but < 30 mg and long-term safety)] Low strength oral formulation
LEFLUNOMIDE	
Authorised indication	Rheumatoid arthritis and psoriatic arthritis
Authorised age group	>18 years

Authorised dose	Initial dose 100mg for 3 days then maintenance with 20mg/day for adults
Authorised formulation	Tablets (10, 20, 100 mg)
Needs	Data on efficacy, safety including long-term data (known liver toxicity and -mutagenicity) and dose in the indications for Polyarthritis and JIA in children > 6 years
CYCLOPHOSPHAMIDE	
Authorised indication	Rheumatoid arthritis Autoimmune diseases
Authorised age group	> 6 years
Authorised dose	3 – 6 mg/kg once daily as maintenance
Authorised formulation	Coated tablet (50 mg) i.v.-solution (100, 200 and 500 mg/ 10ml)
Needs	Data on efficacy, safety including long-term (known mutagenicity and oncogenetic risk, plus risk for male and female infertility) and dose in the indications for severe systemic lupus erythematosus (SLE) and SLE nephritis and vasculitis (data on optimal dose or iv pulses of up to 30mg/kg, 2 monthly for 6 months) Age appropriate oral formulation
MYCOPHENOLATE MOFETIL	
Authorised indication	Transplant rejection
Authorised age group	> 2 years
Authorised dose	10 – 20 mg/kg/day
Authorised formulation	Liquid formulation (1g/5ml), capsules (250 mg), i.v.-solution (6 mg/ml)
Needs	Data on efficacy, safety, including long term and dose in the indications for SLE nephritis – JIA and polyarthritis in children > 6 years Evaluation of the need of drug level monitoring
AZATHIOPRINE	
Authorised indication	Rheumatoid arthritis- dermatomyositis – SLE
Authorised age group	> 6 years
Authorised dose	1 – 3 mg/kg/day once daily as maintenance
Authorised formulation	Tablets (25 and 50 mg)
Needs	Age appropriate formulation
HYDROXYCHLOROQUINE	
Authorised indication	SLE JIA
Authorised age group	> 6 years
Authorised dose	3 – 6.5 mg/kg/d max. 400 mg
Authorised formulation	Coated tablet (200 mg)
Needs	Data on efficacy, safety (known ocular toxicity) and dose in the indication for antinuclear antibody positive arthritis Age appropriate formulation to be made available in all MSs
GLUCOCORTICOIDS	
PREDNISOLONE	
Authorised indication	SLE - peri-/myocarditis - dematomyocitis
Authorised age group	Unspecified
Authorised dose	0.5 mg to 2 mg/kg followed by 0.25 to 0.5 mg/kg
Authorised formulation	Coated tablets (1, 2, 2.5, 5, 6, 20 and 50 mg), soluble tablets, oral liquid formulations (France), soluble tablets (United Kingdom)

Needs	Data on efficacy, safety and dose in the indication for JIA in children > 2 years Age appropriate formulation to be made available in all MSs
LOCAL THERAPY	
TRIAMCINOLONE-HEXACETONIDE (INTRA-ARTICULAR)	
Authorised indication	Arthritis
Authorised age group	> 16 years
Authorised dose	1mg/kg per knee (max 40 mg)
Authorised formulation	20% suspension for injection
Needs	Data on efficacy, safety (including long-term data on effect on the bone) and dose in the indication for JIA in children > 2 years Product to be made available in all MSs