



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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REVISED PRIORITY LIST FOR STUDIES INTO OFF-PATENT PAEDIATRIC MEDICINAL PRODUCTS

NOTE and DISCLAIMER

The list includes only products considered to be off-patent, i.e. not covered by a basic patent or a supplementary protection certificate. Information on the off-patent status is not guaranteed by EMEA. It should be noted that information on the authorisation status as well as on available paediatric formulations of medicinal products is very limited and not available for all European Member States. Users of this list are therefore advised to check the patent and authorisation status of the medicinal products of interest.

The methodology used to establish the list was based as much as possible on evidenced based medicine. It is however acknowledged that identification of priorities for research into medicinal products for paediatric use is partly based on subjective criteria and that identified priorities may change over time.

OBJECTIVE OF THE LIST

The aim of Regulation (EC) 1901/2006 of the European Parliament and the Council on Medicinal Products for Paediatric Use, as amended, is to increase availability of medicines authorised for children as well as to increase the information available on the use of medicinal products in the paediatric population. The Regulation includes provisions for funding of studies into off-patent medicinal products. This funding, provided through the EU Framework programmes, should cover the development of off patent medicinal products with a view to the submission of a Paediatric Use Marketing Authorisation (Art. 40:

http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2006_1901/reg_2006_1901_en.pdf).

The objective of the revision of the priority list is to provide the basis for the work programme for the Third Call for Framework Programme 7 of the European Commission. It ensures that funds are directed into research of medicinal products with the highest need in the paediatric population.

The following list of off-patent products has been revised by the Paediatric Committee (PDCO) and was agreed on 29/08/2008.

PRIORITY LIST FOR STUDIES INTO OFF-PATENT PAEDIATRIC MEDICINAL PRODUCTS

The products are listed according to their therapeutic field and condition(s) in alphabetical order.

Age-appropriate formulations (even if not stated explicitly for a product) and data in neonates (except for oncology) are considered to be of high priority.			
Therapeutic field	Product	Condition(s)	Specific needs
Cardiology	amiodarone	Supraventricular and ventricular arrhythmia	Data on long-term safety.
	dobutamine, dopamine, adrenaline	Shock, heart failure	Data on efficacy in neonates. Definition of endpoint "shock" in neonates.
	enalapril	Cardiac failure	Data on efficacy and safety.
	milrinone	Cardiac failure	Data on PK, efficacy and safety. Definition of endpoint "shock" in neonates.
	propranolol	Hypertension, supraventricular tachycardia	Data on PK, efficacy and safety. Comparative study to atenolol.
Child & adolescent psychiatry	fluoxetine	Major depressive disorder (MDD) with psychotic symptoms,	Data on short and long term-safety.
		general anxiety disorder (GAD), obsessive compulsive disorder (OCD)	Data on short and long term-safety and efficacy for GAD and OCD.
	risperidone	Psychosis; conduct disorders	Data on efficacy and safety in - psychosis in adolescents - conduct disorder in children (not developmentally delayed).
Dermatology	azathioprine	Atopic dermatitis	Data on efficacy and safety.
Endocrinology	cholestyramine	Hypercholesterolaemia	Data on efficacy and safety.
	glibenclamide	Diabetes mellitus type II	Data on PK, efficacy and safety in children above 6 years and adolescents.
	metformin	Diabetes mellitus type II,	Data on PK and efficacy in DM II in children above the age of 6 years.
		growth deficiency	Data on PK, efficacy and safety in small-for-gestational-age children with precocious/early/rapidly progressing puberty.
	thiamazole or carbimazole	Hyperthyroidism	Data on safety.

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Therapeutic field	Product	Condition(s)	Specific needs
Gastroenterology	azathioprine	Crohn's disease	Data on efficacy and safety in combination with biologicals such as anti TNF; age-appropriate formulation.
	baclofen	Gastro-oesophageal reflux (GER)	Data on PK, efficacy and safety.
	lactulose versus polyethylene glycol (PEG)	Constipation	Comparative study.
	methotrexate	Crohn's disease	Data on efficacy and safety [including combination with biologicals such as anti-TNF].
Immunology	azathioprine	Chronic rejection in transplantation	Data on efficacy in infants Age appropriate oral formulation.
	muronomab-CD3	Acute rejection in transplantation	Data on efficacy in relation to ATG (anti-thymocyte globulin).
Infections	amphotericin B	Mycotic infection	Data on efficacy and safety in immunocompromised patients, neonates, and preterm infants.
	azithromycin	Neonatal chlamydia infections; infections caused by <i>mycoplasma</i> , <i>bordetella pertussis</i> , <i>shigella</i> .	Data on efficacy and safety.
	clindamycin	Osteomyelitis; infections caused by resistant organisms, e.g. MR Staphylococcus Aureus and MR Staphylococcus Epidermidis	Data on PK (unless available) in all age groups; relevant tissue levels; short- and long-term efficacy and safety.
	foscarnet	CMV in immunocompromised haematology patients and in patients with resistant strains	Data on PK and efficacy.
	itraconazole	Invasive mycotic infections	Data on PK, efficacy and safety.
	meropenem	Meningitis, sepsis, neonatal sepsis.	Data on PK, efficacy and safety in children below 3 months of age. Studies ongoing in the US.
Intensive care/anaesthesiology	(refer also other fields such as cardiology, infections, neonatology and pain)		

Age-appropriate formulations (even if not stated explicitly for a product) and data in neonates (except for oncology) are considered to be of high priority.

Therapeutic field	Product	Condition(s)	Specific needs
	unfractionated heparin	Anticoagulation	Data on PK, efficacy and safety.
Metabolism	alendronate	Osteoporosis induced by immobility (e.g. severe cerebral palsy) or corticosteroids.	Data on efficacy and short- and long-term safety (oral use).
	pamidronate	Osteoporosis induced by immobility (e.g. severe cerebral palsy) or corticosteroids.	Data on efficacy and short- and long-term safety (intravenous use).
Neonatology	(refer also other fields such as cardiology, infections, intensive care, neurology, pain)		
	bumetanide	Neonatal seizures	Data on PK, efficacy and safety.
	fentanyl	Sedation, pain	Data on efficacy and safety.
	hydrochlorothiazide	Bronchopulmonary dysplasia (BPD)	Data on PK, efficacy and safety. Age appropriate formulation.
	midazolam	Neonatal seizures	Data on PK, efficacy and short- and long-term safety.
	morphine	Sedation, pain	Data on efficacy and safety.
Nephrology/urology	ciclosporin	Idiopathic nephrotic syndrome	Data on long-term efficacy and safety.
	hydrochlorothiazide	Acute renal failure	Age-appropriate formulation. Data on PK.
	levamisole	Nephrotic syndrome	Data on PK, safety and efficacy.
	oxybutynin	Organic enuresis	Data on PK.
Neurology	bumetanide	Neonatal seizures	Data on PK, efficacy and safety.
	ethosuximide	Absence seizures	Data on PK and safety.
	lamotrigine	Partial seizures	Data on efficacy in various epileptic syndromes.
	midazolam	Neonatal seizures	Data on PK, efficacy and short- and long-term safety.
Oncology	Data in infants are considered of high priority.		
	actinomycin	Nephroblastoma, soft tissue sarcoma, Ewing sarcoma.	Data on PK in children below the age of 6 years.
	asparaginase	ALL	Data on PK and efficacy in infants.

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Therapeutic field	Product	Condition(s)	Specific needs
	carboplatin	CNS tumours, germ cell tumours, hepatoblastoma, retinoblastoma, nephroblastoma, soft tissue sarcoma, Hodgkin lymphoma	Data on high dose in all age groups and on PK in children below the age of 3 years.
	cladribine	Histiocytosis, AML	Data on PK and efficacy in all age groups.
	cyclophosphamide	CNS tumours germ cell tumours Ewing sarcoma, retinoblastoma, soft tissue sarcoma, neuroblastoma, Hodgkin lymphoma, Non-Hodgkin lymphoma, acute lymphoblastic leukaemia	Data on PK of metabolites. Age appropriate oral formulation.
	cytarabine	ALL	Data on PK and efficacy in infants.
	daunorubicin	ALL	Data on PK and efficacy in infants.
	6-mercaptopurine	ALL	Data on PK and efficacy in infants.
	temozolomide	CNS tumours	Data on PK in children particularly below the age of 3 years and oral age appropriate formulation.
	topotecan	Soft tissue and Ewing sarcoma	Data on PK and efficacy in all age groups.
Pain	(refer also to intensive care, neonatology)		
	carbamazepine	Chronic pain	Data on efficacy and safety.
	clonidine	Pain	Data on PK, efficacy and safety. Age appropriate formulations.
	gabapentin	Chronic pain	Data on efficacy and safety.
	ibuprofen	Pain	Data on PK, efficacy and safety (parenteral formulation).
Rheumatology	methotrexate	Juvenile idiopathic arthritis	Data on dose and long-term safety.

METHODOLOGY

The original list 2003 had been prepared from a public health perspective prioritising **in a first step** conditions based on factors such as severity of disease, non-availability of treatment alternatives, affected paediatric age groups and paediatric prevalence data. **In a second step** for each condition medicinal off-patent products were identified according to published therapeutic reviews.

For this revision medicinal products were prioritised also taking into account the WHO list of essential medicines for children, the FDA/NICHHD list of products and further paediatric needs. Potential collaboration with FDA/NICHHD has been taken into consideration with a view to avoid duplication of efforts.