



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. 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. Information on the off-patent and authorisation status is not guaranteed by EMEA. Users of this list are therefore advised to check the patent status and the 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) No1901/2006 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, currently 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 (PUMA) (Art. 30, http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2006_1901/reg_2006_1901_en.pdf). The agreement on the specific content of a PUMA application will eventually be through a Paediatric Investigation Plan (PIP).

The revision of the priority list provides the basis for the Fourth Call of the 7th Framework Programme of the European Commission. It ensures that funds are directed into research of medicinal products with the highest needs in the paediatric population.

The following list of off-patent products has been revised by the Paediatric Committee (PDCO) and was agreed on 03/07/2009.

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	(refer also to 'nephrology')		
	adrenaline	Shock, cardiac failure	Data on efficacy in neonates.*
	amiodarone	Supraventricular and ventricular arrhythmia	Data on long-term safety.
	dobutamine	Shock, cardiac failure	Data on efficacy in neonates.*
	dopamine	Shock, cardiac failure	Data on efficacy in neonates.*
	milrinone	Cardiac failure	Data on PK, efficacy and safety.*
	propranolol	Hypertension, supraventricular tachycardia	Data on PK, efficacy and safety.
* Please note that there is a need for international consensus on the definition of 'shock' in neonates, and any medicine development should take this into consideration.			
Child & adolescent psychiatry			
	fluoxetine	Major depressive disorder (MDD) with psychotic symptoms, General anxiety disorder (GAD), obsessive compulsive disorder (OCD)	Data on short and long term-safety. Data on short and long term-safety and efficacy.
Dermatology	(refer to immunology)		
Endocrinology			
	androstanolone gel	Micropenis/severe hypospadias	Data on PK, efficacy and safety.
	cholestyramine	Hypercholesterolaemia	Data on efficacy and safety in children from 6 years. Palatable formulation.
	glibenclamide	Diabetes mellitus type II	Data on PK, efficacy and safety in children from 10 years.
	hydrocortisone	Adrenal insufficiency	Age-appropriate oral formulation; age group 0-2 years.

Therapeutic field	Product	Condition(s)	Specific needs
	metformine	Diabetes mellitus type II SGA children with precocious/early/rapidly progressing puberty Polycystic Ovary Syndrome	Data on PK and efficacy in DM II in children from 10 years. Data on PK, efficacy and safety. Data on PK, efficacy and safety.
	carbimazole	Hyperthyroidism	Data on safety.
Gastroenterology	(refer also to immunology)		
	bisacodyl	Constipation	Data on long-term efficacy, safety, all age groups; age-appropriate formulation.
	macrogol	Constipation	Data on long-term efficacy, safety, all age groups.
Haematology			
	deferiprone	Thalassaemia	Data on PK, efficacy and safety; age from 2 years to less than 10 years.
	unfractionated heparin	Anticoagulation	Data on PK, efficacy and safety.
Immunology	(refer also to oncology, gastroenterology and rheumatology)		
	azathioprine	Chronic rejection in transplantation Crohn's disease Severe atopic dermatitis	Data on efficacy in infants. Age appropriate oral formulation. Data on efficacy and safety in combination with biologicals such as anti TNF; age-appropriate formulation. Data on efficacy and safety.
	etopophos	Before allogenic and autologous hematopoietic stem cell transplantation (HSCT) for various conditions.	Data on PK, short and long term safety in all paediatric age groups.
	fludarabine	Before allogenic HSCT for various conditions.	Data on PK, short- and long-term safety; in all paediatric age groups.

Therapeutic field	Product	Condition(s)	Specific needs
	melphalan	Before allogenic and autologous HSCT for various conditions.	Data on PK, efficacy, short- and long-term safety; in all paediatric age groups.
	methotrexate	Crohn's disease Juvenile dermatomyositis, childhood scleroderma, JIA-related uveitis	Data on efficacy and safety [including combination with biologicals such as anti-TNF]. Data on PK, efficacy and safety-
	mycophenolate mofetil	Short and long term immunosuppression for prevention of graft rejection and GVD after allogenic HSCT Systemic Lupus Erythematosus (SLE) nephritis Renal, heart and liver transplantation	Data on PK, efficacy and safety. Data on PK, efficacy and safety. Data on PK, efficacy and safety in children from 0-2 years.
Infections			
	amphotericin B	Mycotic infections	Data on efficacy and safety in immuno-compromised patients in all age groups, including neonates and preterm infants.
	azithromycin	Neonatal <i>chlamydia</i> infections; infections caused by <i>mycoplasma</i> , <i>bordetella pertussis</i> , <i>ureaplasma</i> .	Data on PK, efficacy and safety.
	clindamycin	Osteomyelitis; infections caused by MR <i>Staphylococcus aureus</i> and MR <i>Staphylococcus epidermidis</i>	Data on PK (unless available) in all age groups; relevant tissue and fluid levels; short- and long-term efficacy and safety.
	ganciclovir	CMV infection	Data on PK, efficacy and safety in immuno-compromised patients in all age groups, neonates, and preterm infants.

Therapeutic field	Product	Condition(s)	Specific needs
	itraconazole	Invasive mycotic infections, aspergillosis, chronic granulomatous disease, febrile neutropenia.	Data on PK, efficacy and safety.
Intensive care/anaesthesiology	(refer also other fields such as cardiology, haematology, infections, neonatology and pain)		
	clonidine	Pain, sedation in PICU	Data on PK, efficacy and safety. Age-appropriate formulations including oral formulation.
	diclofenac	Perioperative pain	Data on PK, efficacy and safety; age-appropriate formulations (rectal, intravenous); age group 0-6 months.
	propofol	Short-term sedation, for surgical and diagnostic procedures.	Data on PK, efficacy and safety; all paediatric age groups.
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/anaesthesiology, neurology, pain)		
	morphine	Sedation, pain	Data on efficacy and safety in neonates.
	spironolactone	Bronchopulmonary dysplasia (BPD)	Data on PK, efficacy and safety. Age-appropriate formulation.
Nephrology/urology	(refer also to cardiology)		
	amiloride	Nephrogenic diabetes insipidus	Data on efficacy and long-term safety.
	ciclosporin	Idiopathic nephrotic syndrome	Data on long-term efficacy and safety.
	deflazacort	Nephrotic syndrome, and post renal transplantation.	Age-appropriate formulation.
	captopril	Cardiac failure, hypertension, chronic renal disease	Data on PK, efficacy and safety. Age-appropriate formulation.
	enalapril	Cardiac failure, hypertension, chronic renal disease	Data on PK, efficacy and safety. Age-appropriate formulation.
	lisinopril	Cardiac failure, hypertension, chronic renal disease	Data on PK, efficacy and safety. Age-appropriate formulation.

Therapeutic field	Product	Condition(s)	Specific needs
	ramipril	Cardiac failure, hypertension, chronic renal disease	Data on PK, efficacy and safety. Age-appropriate formulation.
Neurology	(refer also to neonatology)		
	allopurinol	Cerebral neuroprotection in hypoxic ischemic encephalopathy	Proof of concept – if this is shown, data on PK, efficacy and safety for intravenous formulation.
	ethosuximide	Absence seizures	Data on PK and safety.
	lidocaine	Neonatal seizures	Data on PK, efficacy and safety for intravenous formulation.
	topiramate	Neonatal seizures	Data on PK, efficacy and safety for intravenous formulation. Age-appropriate formulation.
Oncology	Data in infants are considered of high priority. (refer also to immunology)		
	cyclophosphamide	CNS tumours, Germ-cell tumours, Ewing sarcoma, retinoblastoma, soft-tissue sarcoma, neuroblastoma, Hodgkin lymphoma, non-Hodgkin lymphoma, acute lymphoblastic leukaemia	Data on long-term safety.
	cytarabine	Acute lymphoblastic leukaemia (ALL)	Data on PK and efficacy in infants.
	daunorubicin	Acute lymphoblastic leukaemia (ALL)	Data on PK and efficacy in infants.
	etoposide	Neuroblastoma, CNS tumours, germ-cell tumours, leukaemia, lymphoma, retinoblastoma, bone and soft-tissue sarcomas	Efficacy and safety data on intrathecal use for leptomeningeal disease. Age-appropriate formulation for oral use. All paediatric age groups.
	6-mercaptopurine	Acute lymphoblastic leukaemia (ALL)	Data on PK and efficacy in infants.
	topotecan	Soft-tissue and Ewing sarcoma	Data on PK and efficacy in all age groups.
<i>Anti-emetics</i>	granisetron	Vomiting post chemotherapy, post radiation or post operative	Data on efficacy and safety; all age groups.
	tropisetron	Vomiting post chemotherapy, post radiation or post-operative	Data on efficacy and safety; all age groups.
	ondansetron	Vomiting post chemotherapy, post radiation or post operative	Data on efficacy and safety; all age groups.

Therapeutic field	Product	Condition(s)	Specific needs
Pain	(refer also to intensive care, neonatology)		
	carbamazepine	Neuropathic pain	Data on efficacy and safety.
	clonidine	Pain	Data on PK, efficacy and safety. Age appropriate formulations.
	gabapentin	Neuropathic pain	Data on efficacy and safety.
	ibuprofen	Acute pain	Data on PK, efficacy and safety (including risk of infection) of parenteral formulation.
Pneumology	(refer also to infections, immunology, intensive care)		
	azithromycin	In e.g. cystic fibrosis, severe persistent asthma	Data on PK, anti-inflammatory efficacy, safety; all paediatric age groups.
	dornase alfa	Cystic fibrosis Primary ciliary dyskinesia, non-CF bronchiectasis	Data on PK, efficacy and safety; age group below the age of 5 years. Data on PK, efficacy and safety; all paediatric age groups.
Rheumatology	(refer to immunology)		

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 the revision in 2008 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.

The latest revision in 2009 took into account the projects which have been funded in the previous calls as well as comments and proposals from learned scientific and paediatric Societies, following a wide call for expression of interest.