European Medicines Agency
Evaluation of Medicines for Human Use

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ASSESSMENT OF THE PAEDIATRIC NEEDS
NEPHROLOGY

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 (only related to chemotherapy), the lower age group authorised in at least one Member State, the authorised dose(s) (if authorised for use in patients less than 18 years of age) and formulation(s) in at least in one Member State.

Please refer to the EMEA/PEG procedure for identifying the paediatric needs for further information.

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

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As the treatment of renal diseases in children includes medicinal products from various therapeutic areas (e.g. immunology, cardiology, anti-infectives etc.) the following list focuses on products not already sufficiently covered by previous lists. It should be noted that particular emphasise is put on diuretics. The PEG however acknowledges that not all medicinal products for the treatment of paediatric renal disease can be covered in this list.
If not stated separately the need for availability in all Member States of the Community applies to all products included in this list.

DIURETICS	
THIAZIDES	
BENDROFLUMETHIAZIDE	
Authorised indication	Oedema and hypertension
Authorised age group	Children *(United Kingdom)*
Authorised dose	1 month – 2 years: 50-100 µg/kg/daily adjusted according to response 2-12 years: initially 50-400 µg/kg/daily then 50-100 µg/kg
Authorised formulation	Tablets 2.5 and 5 mg
Needs	Data on PK, safety and efficacy in indication tubulopathies in children < 18 years Age-appropriate formulation
CHLOROTHIAZIDE	
Refer to list of paediatric needs Cardiovascular products	
HYDROCHLOROTHIAZIDE	
Authorised indication	Oedema and hypertension
Authorised age group	No age limit specified
Authorised dose	12.5 - 25 mg daily
Authorised formulation	Tablets 25 mg
Needs	Define lower age limit and investigate where needed Data on PK, efficacy and safety in indication tubulopathies in children < 18 years Age-appropriate formulation
METOLAZONE	
Authorised indication	Oedema and hypertension
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, efficacy and safety < 18 years Age-appropriate formulation
POTASSIUM SPARING DIURETICS	
AMILORIDE	
Authorised indication	Adjunct to thiazide and loop diuretics in oedema (not available as monosubstance in all Member States)
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children > 3 months Availabililty of monosubstance in all Member States Data on PK, efficacy and safety in indication monotherapy in congenital tubulopathies *(e.g. nephrogenic diabetes insipidus, primary hypomagnesemia with secondary hypocalcemia (TRPM-defect), thiazide-like salt losing tubulopathies (Bartter-Gitelman syndromes), Liddle-*

	syndrome (monogenetic hypertension with hypokalemia))
TRIAMTEREN	
Authorised indication	Adjunct to thiazide and loop diuretics in oedema (not available as monosubstance in all Member States)
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on safety and efficacy in children > 3 months Availabililty of monosubstance in all Member States Extension of the indication to monotherapy in congenital tubulopathies *(e.g. nephrogenic diabetes insipidus, primary hypomagnesemia with secondary hypocalcemia (TRPM-defect), thiazide-like salt losing tubulopathies (Bartter-Gitelman syndromes), Liddle-syndrome (monogenetic hypertension with hypokalemia))*
LOOP DIURETICS	
FUROSEMIDE	
Authorised indication	Oedema and hypertension
Authorised age group	All age groups (*France*)
Authorised dose	400-600 µg/kg/day in all age groups *(Finland)*
Authorised formulation	Solution for injection, Tablets, Oral solution
Needs	Data on PK, efficacy and safety in indications renal failure and renal hypertension
BUMETAMIDE	
Authorised indication	Oedema
Authorised age group	> 12 years *(United Kingdom)*
Authorised dose	1-2 mg (i.v. injection)
Authorised formulation	Tablets, solution for injection
Needs	Data on PK, safety and efficacy in children < 12 years
ALDOSTERONE ANTAGONISTS	
SPIRONOLACTONE	
Authorised indication	Diuresis in ascites and oedema
Authorised age group	No age limit specified
Authorised dose	By mouth: Neonate: 1-2 mg/kg daily in 1-2 divided doses Child 1 month-12 years 1-3 mg/kg 2-3 daily in 1-2 divided doses Child 12-18 years 50-100mg daily in 1-2 divided doses
Authorised formulation	Tablets, Oral suspension
Needs	Data on PK, safety and efficacy in premature infants Data on safety in long-term use Age appropriate formulation
OSMODIURETICS	
MANNITOL	
Authorised indication	Oliguric acute renal failure, cerebral oedema, elevated intracranial pressure
Authorised age group	No age limit specified in indication renal insufficiency *(Finland)*
Authorised dose	Test dose 1.3 ml/kg, Treatment dose 13 ml/kg
Authorised formulation	Solution for infusion *(Finland)*
Needs	Availability in all Member States

ANGIOTENSIN RECEPTOR BLOCKERS	
IRBESARTAN (CA)	
Authorised indication	Renal disease in patients with hypertension and type-2 diabetes mellitus as part of an antihypertensive drug regimen
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children < 18 years with chronic kidney diseases associated with hypertension and proteinuria Data on PK, safety and efficacy in children < 18 years with type 1 diabetes to prevent and treat diabetic nephropathy Age-appropriate formulation
LOSARTAN (NA)	
Authorised indication	Renal insufficiency in patients with type-2 diabetes with proteinuria
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children < 18 years with chronic kidney diseases associated with hypertension and proteinuria Data on PK, safety and efficacy in children with type-1-diabetes to prevent and treat diabetic nephropathy Age-appropriate formulation
VALSARTAN	
Authorised indication	Essential hypertension
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children < 18 years with chronic kidney diseases associated with hypertension and proteinuria Data on PK, safety and efficacy in children with type-1-diabetes to prevent and treat diabetic nephropathy Age-appropriate formulation
CANDESARTAN	
Authorised indication	Essential hypertension
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children < 18 years with chronic kidney diseases associated with hypertension and proteinuria Data on PK, safety and efficacy in children with type-1-diabetes to prevent and treat diabetic nephropathy Age-appropriate formulation
TELMISARTAN	
Authorised indication	Essential hypertension
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children < 18 years with chronic kidney diseases associated with hypertension and proteinuria Data on PK, safety and efficacy in children with type-1-diabetes to prevent and treat diabetic nephropathy

	Age-appropriate formulation
ACE-INHIBITORS	
CAPTOPRIL	
Authorised indication	Proteinuria in nephritis or type I diabetic nephropathy
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children < 18 years with chronic kidney diseases associated with hypertension and proteinuria Data on PK, safety and efficacy in children < 18 years with type 1 diabetes to prevent and treat diabetic nephropathy Age-appropriate formulation
ENALAPRIL	
Authorised indication	Proteinuria in nephritis, diabetic nephropathy
Authorised age group	Children > 20 kg (Austria)
Authorised dose	-
Authorised formulation	-
Needs	Define lower age limit in both indications and investigate where needed (data on PK, safety and efficacy) Liquid formulation known to be challenging – Need for information on extemporaneous formulation in Summary of Product Characteristics
PARENTERAL SOLUTIONS AND ORAL PREPARATIONS FOR FLUID AND ELECTROLYTE IMBALANCE	
ETHERIFIED STARCH (E.G. PENTASTRACH – HAES)	
Authorised indication	Low blood volume
Authorised age group	No age limit specified
Authorised dose	-
Authorised formulation	-
Needs	Define lower age limit and investigate where needed (data on PK, efficacy and safety in children < 18 years)
ETHERIFIED STARCH – HYPERTONIC SOLUTION (HYPER-HAES)	
Authorised indication	Low blood volume
Authorised age group	Adults *(France)*
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, efficacy and safety in children < 18 years
SODIUM-BICARBONATE	
Authorised indication	Renal metabolic acidosis
Authorised age group	No age limit specified *(Germany, United Kingdom)*
Authorised dose	By mouth: Neonate: 1-2 mmol/kg daily in 1-2 divided doses Child 1 months-2 years 1-2 mmol/kg daily in 1-2 divided doses Child 2-18 years: 70 mmol/m^2 in 1-2 divided doses
Authorised formulation	Capsules, Tablets, Solution for infusion
Needs	Define lower age limit and investigate where needed Oral age appropriate formulation
SODIUM-CHLORIDE	
Authorised indication	Sodium chloride substitution
Authorised age group	No age limit specified *(Germany, United Kingdom)*
Authorised dose	By mouth:

	Neonate: 1-2 mmol/kg daily
Authorised formulation	Capsules, Tablets
Needs	Date on PK, safety and efficacy in indications renal tubular disorders Age appropriate formulation
POTASSIUM CHLORIDE	
Authorised indication	Compensation of potassium loss
Authorised age group	No age limit specified
Authorised dose	By mouth: 0.5-1 mmol/kg K+ twice daily adjusted to plasma potassium concentration
Authorised formulation	Syrup, Tablets, Solution for injection, Capsules
Needs	Oral age appropriate formulation
PHOSPATE	
Authorised indication	Hypophosphataemia
Authorised age group	No age limit specified
Authorised dose	By mouth: 1 mmol/kg daily in 1-2 divided doses
Authorised formulation	Tablets, Solution for infusion, Solution for injection
Needs	Oral age appropriate formulation
ANTICHOLINERGIC DRUGS	
OXYBUTYNINE	
Authorised indication	Detrusor hyperactivity, urinary frequency, urgency and incontinence, neurogenic bladder
Authorised age group	> 2 years (*Germany*)
Authorised dose	0.3-0.4 mg/kg > 5 years: 2.5mg 2-3 times daily
Authorised formulation	Tablets 2.5 and 5 mg
Needs	Data on PK, efficacy and safety in children 3 months to 2 years for indication neurogenic bladder Data on PK, efficacy and safety for intravesical installation
OTHER	
LEVAMISOLE	
Authorised indication	Not authorised in nephrotic syndrome
Authorised age group	-
Authorised dose	-
Authorised formulation	-
Needs	Any formulation Data on PK, safety and efficacy in children < 18 years in steroid resistent nephrotic syndrome
CINACALCET	
Authorised indication	Treatment of secondary hyperparathyroidism (HPT) in patients with end-stage renal disease (ESRD) on maintenance dialysis therapy
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Safety and efficacy data in children Age appropriate formulation
BISPHOSPHONATES	
Authorised indication	Osteogenesis imperfecta and other forms of osteoporosis in children Not authorised in hypercalcaemia, osteopenia in renal failure or post renal transplant

Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children in hypercalcaemia and/or osteopenia in children with renal failure or post renal transplant. Age appropriate formulation
PYRIDOXINE	
Authorised indication	Pyridoxine-dependent disturbances (e. g. cerebral seizures, hyperoxaluria Typ I, and others)
Authorised age group	> 1 year (*Germany*)
Authorised dose	10 - 250 mg (1 year: 2 – 15 mg) ,
Authorised formulation	Tablets 100 mg
Needs	Data on PK, safety and efficacy in indication hyperoxaluria in children < 1 year Age-appropriate formulation
TIOPRONINE	
Authorised indication	Cystinuria
Authorised age group	> 18 years
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children Age-appropriate formulation
HYPOLIPIDAEMICS	
REFER TO ASSESSMENT OF PAEDIATRIC NEEDS CARDIOVASCULAR PRODUCTS	
IMMUNOSUPPRESSANTS	
AZATHIOPRINE	
Authorised indication	Suppression of transplant rejection, Treatment of autoimmune conditions when corticosteroid therapy alone has proved inadequate
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Extension of the indication to nephrotic syndrome Age appropriate formulation
CYCLOPHOSPHAMIDE	
Authorised indication	Authorised in ALL, non-hodgkin lymphoma and other malignancies Not authorised for treatment of nephrotic syndrome, vasculitis and lupus
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Extension of indication: Safety and efficacy data in nephrotic syndrome, vasculitis and lupus Age appropriate formulation
MYCOPHENOLATE MOFETIL	
Authorised indication	Prevention and treatment of rejection in kidney transplants
Authorised age group	Children > 2 years
Authorised dose	600 mg/m² BID via oral route
Authorised formulation	250 mg capsules, 500 mg tablets 1g/5ml powder for oral suspension. 500 mg Powder for concentrate for solution for infusion (adult only)
Needs	Extension of indication to nephrotic syndrome

TACROLIMUS	
Authorised indication	Prophylaxis of transplant rejection in liver, kidney or heart allograft recipients Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products
Authorised age group	No age limit specified
Authorised dose	0.30 mg/kg/day
Authorised formulation	0.5,1,5mg capsules, 5mg/ml solution for infusion
Needs	Data on PK, safety and efficacy in indication nephrotic syndrome Age appropriate formulation
RITUXIMAB	
Authorised indication	Prevention of acute rejection after de novo allogenic kidney transplantion, lymphoma
Authorised age group	> 18 years
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in children in indication nephritic syndrome
SIROLIMUS	
Authorised indication	Prevention of rejection after renal transplant
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	Data on PK, safety and efficacy in Children < 18 years Data on PK, safety and efficacy data in children in indication nephrotic syndrome Age appropriate formulation
NSAIDS	
NSAIDS (INDOMETHACIN AND OTHER)	
Authorised indication	Pain, Arthritis Not authorised for nephrologic indications
Authorised age group	-
Authorised dose	-
Authorised formulation	-
Needs	Full paediatric development for the following indications: congenital salt losing tubulopathies (SLTs) of the furosemide-types (NKCC2-, ROMK-, Barttin- and combined C1C-Ka and b defect) and the thiazide-types (NCCT- and isolated C1C-Kb-defect) as well as for nephrogenic diabetes insipidus, reduction of proteinuria in congenital nephrotics Data on long-term safety
ANTITHROMBOTICS	
REFER TO ASSESSMENT OF PAEDIATRIC NEEDS CARDIOVASCULAR PRODUCTS	

UNMET MEDICAL NEEDS
The PEG considers that for the new class of aquaretics (AVP-receptor antagonists) a full development for all paediatric populations in indication hyponatremia, associated chronic heart failure, cirrhosis and SIADH including oliguric hyponatraemia in preterm infants with PDA during NSAIDS-treatment is needed.

The following products were considered by the PEG to be devoid of interest in the paediatric population:
DEXTRAN
TROPSIUM
PROPIVERIN
TOLTERODINE
AMINO/THEOPHYLLINE

PK = pharmacokinetics