European Medicines Agency
Evaluation of Medicines for Human Use

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ASSESSMENT OF THE PAEDIATRIC NEEDS
ANAESTHESIOLOGY

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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If not stated separately, the need for availability in all Member States of the Community applies to all medicinal products included in this list

Local anaesthetics	
LIDOCAINE + PRILOCAINE	
Authorised indication	Local anaesthesia before minor skin procedures and venous cannulation/puncture (*Finland*) (topical application)
Authorised age group	Children > 1 year (*United Kingdom*) Children of all ages, limited dose and application time for newborns and young infants. Not for infants under 12 months receiving drugs that increase methaemoglobin, and preterms < 37weeks (*Finland)*
Authorised dose	Thick layer under occlusive dressing Maximal dose depending age: 0-3 mo 1.0 g/ 10 cm^2, max application time 1 h, max 1 plaster 3-12 mo 2.0 g/ 10 cm^2 1-6 yrs 10.0g/ 10 cm^2 6-12 yrs 20.0 g/ 10 cm^2 For children with atopic skin for removal of molluscs application max 30 min (*Finland*)
Authorised formulation	Cream, plaster (*Finland*)
Needs	Data in sutures and evaluation in paracentesis and zoster
ROPIVACAINE (REFER ALSO LIST OF PAEDIATRIC NEEDS PAIN)	
Authorised indication	Caudal, epidural and peripheral block; pain
Authorised age group	Children > 1 year for single dose, repeated doses > 12 years (*Finland*)
Authorised dose	Caudal peridural administration: 2mg/kg, peripheral nerve block 3 mg/kg (*Finland*)
Authorised formulation	Solution for injection 2, 5, 7.5 and 10 mg/ml (*Finland)*
Needs	Data on PK and efficacy in children < 1 year PK and Efficacy data in continous peripheral block use Additional data on intrinsic vasoconstrictous potential Data on intrathecal administration Data on continuous epidural infusion ± opioids Safety in long term infusions and repeated infusions, in combination with opioids, in intrathecal blocks in children (quoted from pain list)
BUPIVACAINE	
Authorised indication	Local, regional, lumbosacral and thoracolumbar epidural and spinal anaesthesia/analgesia (*Finland*) (especially spinal anaesthesia)
Authorised age group	No age limit specified (*Germany, Finland)*
Authorised dose	Adjusted according to child's physical status and nature of procedure: Local and peripheral blocks: children < 6 mo: max single dose 1.5 mg/kg, children > 6 mo: max single dose 2-2.5 mg/kg Epidural injection detailed recommendations fron 2 to 50 kg children in ml/kg doses, in combination with adrenalin max 2 mg/kg. Continuous epidural infusion: children < 3 mo max dose 0.2 mg/kg/h (< 4.8 mg/kg/24h), children > 3 mo max dose 0.4 mg/kg/h (< 9.6 mg/kg/day) Spinal anaesthesia: 0-5 kg bodyweight 0.5 mg/kg, 5-15 kg 0.4 mg/kg, >15 kg 0.3 mg/kg

Authorised formulation	20 mg/4ml solution for injection 2.5 and 5 mg/ml for epidural and peripheral use, 5 mg/ml for spinal use
Needs	Age appropriate formulation Studies in children < 1 month Safety in long term infusions and repeated infusions, in combination with opioids
LEVOBUPIVACAINE (Refer also to List of paediatric needs pain)	
Authorised indication	Peripheral blocks
Authorised age group	Age limit unspecified
Authorised dose	Ilioinguinal/iliohypogastric block: 1.25 mg/kg/side
Authorised formulation	Solution for injection
Needs	Data on pharmacokinetics, safety and efficacy of epidural administration Dose recommendations needed Safety in long-term infusions and repeated infusions, in combination with opioids
Premedication, hypnotics, sedatives	
Benzodiazepines	
FLUNITRAZEPAM	
Authorised indication	Premedication, general anaesthesia
Authorised age group	Children > 3 years (*France*)
Authorised dose	0.015-0.030 mg/kg for premedication and induction of general anaesthesia
Authorised formulation	Solution for injection
Needs	Age appropriate formulation
MIDAZOLAM	
Authorised indication	Premedication, sedation for procedures and during intensive care
Authorised age group	Not recommended < 6 months for premedication (*France*)
Authorised dose	Sedation (ICU): 60 micrograms/kg/hour adjusted according to response FI: Iv administration: not recommeded for children < 6 mo, children 6 mo- 5 yrs: initial bolus 0.05-0.1 mg/kg up to total dose 0.6 mg/kg, max dose not to exceed 6 mg. Children 6-12 yrs: initial bolus 0.025-0.05 mg/kg, max 0.4 mg/kg, max dose not to exceed 10 mg. children > 12 yrs as adults. Continuous iv infusion children > 6 mo: 0.06-0.12 mg/kg/h. Preterms < 32 wk 0.03 mg/kg/h, preterms > and children < 6 mo 32 wk 0.06 mg/kg/h. Rectal administration 0.3-0.5 mg/kg, not for children < 6 mo.
Authorised formulation	Solution for injection i.v. i.m., oral solution iv solution 1 and 5 mg/ml For children < 15 kg solution max 1 mg/ml, no oral solution in *Finland*
Needs	Age and route appropriate formulation Data on development of tolerance in long-term use in preterm newborn infants/long-term use in any paediatric age group PK data buccal administration
Others	
ATROPIN	
Authorised indication	Premedication, control of muscarinic side-effects
Authorised age group	Premedication in children > 1 month (s.c.) (*France*)

Authorised dose	Premedication : 0.1-0.3 mg (1-30 month)
Authorised formulation	Solution for s.c. injection (*France*)
Needs	Authorisation paediatric indication in all Member States Age appropriate formulation (only 1 mg/ml available)
GLYCOPYRROLATE	
Authorised indication	Premedication, control of muscarine side-effects during reversal of muscle relaxation
Authorised age group	No age limit specified (*United Kingdom*)
Authorised dose	0.0044 mg/kg im / iv (*Finland*)
Authorised formulation	0.2 mg/ml solution for injection
Needs	Age appropriate formulation
GLYCOPYRROLATE + NEOSTIGMINE	
Authorised indication	Control of muscarine side-effects during reversal of muscle relaxation
Authorised age group	No age limit specified (*United Kingdom*)
Authorised dose	0.02 ml/kg (max 2 ml)
Authorised formulation	0.2 mg/ml solution for injection
Needs	Age appropriate formulation
ETOMIDATE	
Authorised indication	Induction of anaesthesia
Authorised age group	Children > 2 years (contraindicated in children < 2 years) (*France*)
Authorised dose	150-300 micrograms/kg (induction of anaesthesia)
Authorised formulation	Solution of injection i.v.
Needs	Data on PK, efficacy and safety in children < 2 years.
THIOPENTAL	
Authorised indication	Induction of anaesthesia
Authorised age group	Age limit not specified (*United Kingdom*)
Authorised dose	4 mg/kg (child > 1 month)
Authorised formulation	Solution for injection
Needs	Availability in all Member States
KETAMINE	
Authorised indication	Induction and maintenance of anaesthesia
Authorised age group	Age limit not specified
Authorised dose	1-4.5mg/kg produces 5-10 minutes of surgical anaesthesia (children 12-18 years)
Authorised formulation	Solution for injection i.v., i.m. oral solution
Needs	Age appropriate formulation Data on efficacy, PK and safety in children in all age groups
S-KETAMINE (REFER ALSO TO LIST OF PAEDIATRIC NEEDS PAIN)	
Authorised indication	Emergency pain management, intensive care
Authorised age group	Not authorised for paediatric use (*Finland, United Kingdom, Germany*)
Authorised dose	-

Authorised formulation	-
Needs	Data on PK, efficacy and safety, dose in children Age appropriate formulations for use in all age groups
PROPOFOL	
Authorised indication	Induction and maintenance of anaesthesia, sedation in intensive care
Authorised age group	> 1 month for induction, > 15 years for sedation, not for children under 6 month, CI for sedation in ICU for children < 16 years
Authorised dose	3-5mg/kg (1 month – 3 years)(general anaesthesia) Induction children > 8 yrs 2,5 mg/kg, maintenance 9-15 mg/kg/h
Authorised formulation	Solution for injection 10 and 20 mg/ml
Needs	Age appropriate formulation for short term use Target controlled intravenous anaesthesia (painless during infusion) Studies in children < 1 month
SEVOFLURANE	
Authorised indication	Induction and maintenance of anaesthesia
Authorised age group	Age limit not specified (*France, United Kingdom*)
Authorised dose	Up to 5 % in oxygen or nitrous oxide-oxygen (induction in children 1 month –18 years)
Authorised formulation	Liquid for inhalation
Needs	Data in premature newborns
ISOFLURANE	
Authorised indication	Induction and maintenance of anaesthesia
Authorised age group	No age limit specified (*Germany, United Kingdom*)
Authorised dose	1-2.5% in nitrous oxide-oxygen (maintenance of anaesthesia)
Authorised formulation	Liquid for inhalation
Needs	Availability in all Member States. Safety data in children < 2 years
DESFLURANE	
Authorised indication	Induction and maintenance of anaesthesia
Authorised age group	Authorised in children in all age groups except preterms (*Finland*)
Authorised dose	MAC in 100% oxygen 0-1 yr 8.95-10.65, 1-12 yrs 7.2-9.4 MAC values also in O2/N2O
Authorised formulation	Liquid for inhalation
Needs	Authorisation for paediatric indication in all Member States Data in premature newborn infants
Opioid analgesics	
ALFENTANIL	
Authorised indication	Analgesia in short procedures; enhancement of anaesthesia
Authorised age group	No age limit specified
Authorised dose	Children 1month – 18 years: initially 30-50 micrograms/kg (by i.v. injecion over 30 seconds)
Authorised formulation	Solution for injection
Needs	Availability in all Member States

FENTANYL (SEE ALSO PAEDIATRIC NEEDS PAIN)	
Authorised indication	Induction and maintenance of anaesthesia
Authorised age group	> 2 years (*Finland*)
Authorised dose	Induction 1-3 µg/kg iv, maintenance 1-2 µg/kg/30-45 min
Authorised formulation	Solution for injection (Austria)
Needs	Data on PK, efficacy and safety in children < 2 years Age and route appropriate formulation for use in all age groups for all Member States Data on epidural use in all age groups
REMIFENTANIL	
Authorised indication	Induction and maintenance of anaesthesia, sedation in intensive care
Authorised age group	> 1 year
Authorised dose	Children 1-12 years: Initially 1 µg/kg iv over 30 seconds, then 0.05-1 µg/kg/minute adjusted according to response
Authorised formulation	Solution for injection
Needs	Data on PK, Efficacy and Safety in children < 1 year
SUFENTANYL	
Authorised indication	Induction and maintenance of anaesthesia, epidural anaesthesia
Authorised age group	No age limit specified (*France*)
Authorised dose	5-20 µg/kg (children up to 12 years) Dose recommendations in children from 2 to 12 years 10-20 ug/kg iv (*Finland*)
Authorised formulation	Solution for injection or peridural route
Needs	Age appropriate formulation Data on epidural use
Depolarising muscle relaxants	
SUXAMETHONIUM CHLORIDE	
Authorised indication	Muscle relaxation during surgery
Authorised age group	Age limit not specified (*France*)
Authorised dose	1.5 mg/kg 1-2 mg/kg (*Finland*)
Authorised formulation	Solution for injection iv, im
Needs	PK data in infants Age appropiate formulation (only 50 mg/ml available)
Non-depolarising muscle relaxants	
VECURONIUM BROMIDE	
Authorised indication	Muscle relaxation during surgery; assisted ventilation in intensive care
Authorised age group	Authorised in all age groups (*Finland)*
Authorised dose	Initially 10-20 µg/kg, then incremental doses, according to response For intubation 0.08-0.1 mg/kg. Infants < 4 mo: 0.01 -0.02 mg/kg test dose (Finland)
Authorised formulation	Solution for injection (2mg and 4mg/ml) (*Finland)*
Needs	Age appropriate formulation
ROCURONIUM BROMURE	
Authorised indication	Muscle relaxation during surgery and during intensive care
Authorised age group	Children > 1 month (*France*)

Authorised dose	Initially 600 µg/kg then 300-600 µg/kg/hour adjusted according to response
Authorised formulation	Solution for injection (10 mg/ml)
Needs	Data on efficacy and safety in children < 1 month Age appropriate formulation
ATRACURIUM BESILATE	
Authorised indication	Muscle relaxation for surgery or during intensive care
Authorised age group	Children > 3 month (*France*)
Authorised dose	Initially 300-600 µg/kg, then 300-600 µg/kg/hour adjusted according to response
Authorised formulation	Solution for injection
Needs	Data in children < 3 months
MIVACURIUM	
Authorised indication	Muscle relaxation during surgery
Authorised age group	Children > 2 months (*France*)
Authorised dose	Initially 200 µg/kg, then 8-10 µg/kg/minute adjusted if necessary every 3 minutes by 1 /minute 0.1-0.2 mg/kg, maintenance 0.1mg/kg, continuous infusion for infants aged 7-23 mo 11 µg/kg/min during halothane anestesia, children 2-12 yr 5-31 µg/kg/min during halothane of narcotic anaesthesia. Dose should be reduced during sevoflurane anaesthesia. Infants 2-6 mo 0.15 µg/kg for intubation, maintenance and infusion as older children (*Finland*)
Authorised formulation	Solution for injection or infusion
Needs	Data in children < 2 months
CISATRACURIUM	
Authorised indication	Muscle relaxation for intubation and during surgery
Authorised age group	Children 1 month to 12 years for intubation Children 2 – 12 years for maintenance during surgery
Authorised dose	Initially 150 µg/kg, then 20 µg/kg/repeated approx. every 9 minutes as necessary (Children 2-12 years for intubation and during surgery)
Authorised formulation	Solution for infusion, injection
Needs	Data in children < 2 years
Sympathomimetics	
ADRENALINE	
Authorised indication	Cardiopulmonary resuscitation, acute anaphylaxis, acute hypotension
Authorised age group	Age limit not specified
Authorised dose	Initially 100 nanograms/kg/minute i.v. (neonates) Resuscitation 0.01-0.03 mg/kg iv, anaphylaxis and angioneurotic oedema 0.01 mg/kg iv.
Authorised formulation	Solution for injection i.v., i.m. s.c. 0.1 mg/ml (iv) and 1 mg/ml (im, sc), auto-injector for children 15-30 kg
Needs	To define lower age limit and investigate where needed
DOBUTAMINE	
Authorised indication	Inotropic support in low cardiac output states, after cardiac surgery, cardiomyopathies, shock
Authorised age group	Age limit not specified (*France*)
Authorised dose	2.5 – 10 µg/kg/min 2.5-20 µg/kg/min

Authorised formulation	Solution for infusion
Needs	Extension of the indications, including in neonates (efficacy, safety data and dose) Age appropriate formulation
DOPAMINE	
Authorised indication	To correct the haemodynamic imbalance due to acute hypotension, shock, cardiac failure, adjunct following cardiac surgery
Authorised age group	Age limit not specified (*France*)
Authorised dose	2.5 – 10 µg/kg/min
Authorised formulation	Solution for injection
Needs	Extension of the indications, including in neonates (efficacy, safety data and dose) Age appropriate formulation
NORADRENALINE (PLEASE REFER ALSO TO LIST OF PAEDIATRIC NEEDS CARDIOLOGY)	
Authorised indication	Acute hypotension (septic shock) or shock secondary to excessive vasodilation
Authorised age group	Adults and children (unspecified lower age group) in the CV list
Authorised dose	0.01-0.03 mg/kg
Authorised formulation	Solution for injection
Needs	To define lower age group where there is a need
plasma substitutes	
ETHERIFIED STARCH	
Authorised indication	Low blood volume
Authorised age group	Age limit not specified
Authorised dose	According to the child's condition, age, weight Maximum of 33mL/kg/24hours for a patient of 75 kg body weigth (6% solution)
Authorised formulation	Solution for infusion
Needs	Safety data
CLONIDINE (REFER ALSO TOLIST OF NEEDS PAIN)	
Authorised indication	Concomitant medication in long-term analgosedation Potentiation of local anaesthetics in peri and rachi-anaesthesia and in peripheral blocks
Authorised age group	Not authorised in children
Authorised dose	-
Authorised formulation	Solution for infusion
Needs	Data on safety and efficacy in long-term analgosedation on ICU's Data on parenteral and epidural use in children Age appropriate formulations
PROTAMINE SULFATE	
Authorised indication	Heparin overdose
Authorised age group	Adults
Authorised dose	-

Authorised formulation	-
Needs	Extension of the indication
CHLORALHYDRATE	
Authorised indication	Postoperative nausea
Authorised age group	Not authorised in children
Authorised dose	-
Authorised formulation	-
Needs	Age apppropriate oral formulations Availability in all Member States Efficacy and safety data for indication sedation
Antiemetics	
ONDANSETRON (REFER ALSO TO ONCOLOGY LIST PART II)	
Authorised indication	Treatment and prevention of postoperative nausea and vomiting
Authorised age group	> 2 years (*France*); (*no lower age limit in United Kingdom*)
Authorised dose	i.v. 5 mg/m^2 , p.o 4 mg for children 10 -25 kg and 8 mg for children > 25mg; > 15 years as adults.
Authorised formulation	Film-coated tablets, oral lyophilisate, syrup 4 mg/5 ml; solution for IV injection UK also "Melts" 4mg, NO suppositories 16 mg (adults).
Needs	Development of rectal appropriate formulations in appropriate strength, PK, bioavailability, efficacy and safety for children under 2 years. Availability in all Member States
TROPISETRON (REFER ALSO TO ONCOLOGY LIST PART II)	
Authorised indication	Treatment of postoperative nause and vomiting
Authorised age group	Adults
Authorised dose	-
Authorised formulation	-
Needs	PK, safety and efficacy in children < 2 years Age appropriate formulation Availability in all Member States