European Medicines Agency
Evaluation of Medicines for Human Use

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ASSESSMENT OF THE PAEDIATRIC NEEDS CHEMOTHERAPY PRODUCTS (PART I)

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.

ALKYLATING AGENTS	
MELPHALAN	
Authorised indication	Lymphoma (HD; NHL; AL), neuroblastoma
Authorised age group	No lower age limit mentioned
Authorised dose	-
Authorised formulation	Powder and solvent for solution for IV injection 50 mg/10 ml, tablets 2 mg
Needs	Age appropriate formulation, Update of information in the Summary of Product Characteristics (SPC) to include existing data on pharmacokinetics and data from existing studies AL + neuroblastoma: Data > 3 months
CYCLOPHOSPHAMIDE	
Authorised indication	Seminomas and testicular embryonic carcinomas, solid tumours, sarcomas, neuroblastoma, HD, NHL, AL (varies by Member States)
Authorised age group	No lower age limit mentioned
Authorised dose	100-200 mg/m^2/day (i.e. 2.5-5 mg/kg/day) up to 4g/m^2 (in haemapoeitic stem cell)
Authorised formulation	Powder and solvent for solution for IV injection, tablets 500 mg, 1000 mg and film coated tablets 50 mg
Needs	Indications to be made available in all Member States Age appropriate formulation, Data on pharmacokinetics (PK), efficacy and safety in children < 1 year needed
CHLORAMBUCIL	
Authorised indication	HD; NHL in some Member States (e.g. France and UK)
Authorised age group	>3 years
Authorised dose	Dosing per kg bodyweight , doses similar to adults
Authorised formulation	2 mg film-coated tablets
Needs	Indications to be made available in all Member States Data on long tem safety in children needed Age appropriate formulation
ACTINOMYCIN D	
Authorised indication	Wilms, Rhabdomyosarcoma, Ewing sarcoma, non-seminomatous testicular carcinoma
Authorised age group	> 6 month (Spain)
Authorised dose	Varies by indication
Authorised formulation	Lyophilized powder
Needs	Efficacy and Safety in children < 6 month
IFOSFAMIDE	
Authorised indication	Soft tissue sarcomas, osteogenic sarcoma, NHL, relapsed testicular carcinoma, relapsed AL
Authorised age group	Children
Authorised dose	Varies by indication
Authorised formulation	Powder for solution for IV infusion 0.5, 1g, 2g vials
Needs	Define lower age limit based on data on efficacy and safety and investigate where needed

DACARBAZINE	
Authorised indication	Metastatic Melanoma, HD, Sarcoma
Authorised age group	No lower age limit mentioned
Authorised dose	-
Authorised formulation	Powder and solvent for solution for IV and intra-arterial infusion - 100 mg, 200 mg, 500 mg, 1 g vials
Needs	In HD, define lower age limit based on data on efficacy and safety and investigate where needed
TEMOZOLOMIDE	
Authorised indication	Glioblastoma multiforms, anaplastic astrocytoma
Authorised age group	> 3 years
Authorised dose	200 mg/m^2 (Dosing as adults)
Authorised formulation	5 mg, 20 mg, 100 mg and 250 mg capsules
Needs	Age appropriate formulation Data for efficacy and safety children < 3 years
CARMUSTINE	
Authorised indication	Brain tumours, multiple myeloma, NHL, HD, melanoma (in some Member States)
Authorised age group	> 5 years, *(Note contraindicated < 5 years in France)*
Authorised dose	No recommendation
Authorised formulation	Powder and solvent for solution for IV infusion 100 mg, implantate 7.7 mg
Needs	Indication and age appropriate formulation to be made available in all MSs
LOMUSTINE	
Authorised indication	Brain tumours (in some Member States)
Authorised age group	No lower age limit mentioned
Authorised dose	-
Authorised formulation	Capsules 40 mg
Needs	Define lower age limit based on data on efficacy and safety and investigate where needed Age appropriate formulation
CISPLATIN	
Authorised indication	Testicular carcinoma (pediatrics) and in adults various other solid tumours
Authorised age group	> 6 months
Authorised dose	50 à 120 mg/m^2
Authorised formulation	Dry powder solution for IV infusion 10 mg, 50 mg, 100 mg
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety
CARBOPLATIN	
Authorised indication	Advanced ovarian carcinoma, lung carcinoma, advanced bladder carcinoma.
Authorised age group	
Authorised dose	-
Authorised formulation	Solution for IV infusion 10mg/ml solution vial sizes: 5 ml, 15 ml, 45ml, 60 ml
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety PK data in children

OXALIPLATIN	
Authorised indication	Colon carcinoma
Authorised age group	> 18 years
Authorised dose	
Authorised formulation	Powder for solution for IV infusion 50 mg, 100 mg vials
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety
DNA CLEAVING AGENTS	
BLEOMYCIN	
Authorised indication	Squamous cell carcinoma, HD, NHL, testicular carcinoma (in some Member States)
Authorised age group	Children
Authorised dose	The dosage should be based on that recommended for adults and adjusted to body surface area or body weight
Authorised formulation	Powder for solution for SC or IV injection and for IV infusion 15,000 iv/vial
Needs	Define lower age limit based on data on efficacy an safety and investigate efficacy and safety where needed
ANTIMETABOLITES (ANTIFOLATES, PURINE ANALOGUES, PYRIMIDINE ANALOGUES)	
METHOTREXATE	
Authorised indication	AL, Choriocarcinoma, NHL, T-cell NHL, OS
Authorised age group	Children
Authorised dose	Varies by indication
Authorised formulation	Solution for injection 2.5 mg/ml, 25 mg/ml (2-200 ml vials), 1g/10 ml, 5g/50 ml, tablets 2.5 mg, 10 mg
Needs	Age appropriate oral formulation Data on PK, efficacy and safety in infants below 6 months Update SPC (specify lower age limit for OS)
THIOTEPA	
Authorised indication	Pre-BMT (High-dose therapy)
Authorised age group	> 12 years
Authorised dose	Not specified
Authorised formulation	Solution for injection 15mg/ml
Needs	Data on PK, efficacy and safety in neuroblastoma, brain tumours, also in children < 12 years
FLUDARABINE	
Authorised indication	B-cell chronic lymphocytic leukaemia (CLL)
Authorised age group	> 18 years
Authorised dose	-
Authorised formulation	For IV injection and for IV infusion 50 mg vial; 10 mg tablet
Needs	Data on PK, efficacy and safety in children (for relapsed leukemias), allogeneic stem cell transplantation

MERCAPTOPURINE	
Authorised indication	ALL
Authorised age group	Children
Authorised dose	Initial dose 2.5 mg/kg
Authorised formulation	10 (FI), 50 mg tablets
Needs	Define lower age limit based on data on efficacy and safety Age appropriate formulation Need for pharmacogenetic data, prospective evaluation of value of the TPMT genotype
THIOGUANINE	
Authorised indication	AML, ALL, CML
Authorised age group	Children
Authorised dose	100-200 mg/m^2 (possibly 60-75 mg can be tried)
Authorised formulation	40 mg scored tablets
Needs	Age appropriate formulation Define lower age limit based on data on efficacy and safety Need for pharmacogenetic data, prospective evaluation of value of the TPMT genotype
CYTARABINE	
Authorised indication	AML, ALL (acute transformation of CML and myelodysplasia)
Authorised age group	> 3 years
Authorised dose	100 mg/m^2/day
Authorised formulation	For IV infusion 100 mg, 500 mg, 1g
Needs	Update of SPC (dose) Data on efficacy and safety from birth to 3 years
LIPOSOMAL CYTARABINE	
Authorised indication	Meningiosis carcinomatosa
Authorised age group	> 18 years
Authorised dose	
Authorised formulation	Intrathecal 50 mg/vial
Needs	Data on PK, efficacy and safety in children
5-FLUOROURACIL	
Authorised indication	Gastro-intestinal carcinoma, breast carcinoma, ovarian carcinoma, head and neck squamous cell carcinoma
Authorised age group	> 18 years
Authorised dose	
Authorised formulation	For infusion 25 mg/ml: 10 ml, 20 ml, 100 ml
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety
CAPECITABINE	
Authorised indication	Colon, breast carcinoma
Authorised age group	>18 years
Authorised dose	
Authorised formulation	Coated tablets 150 mg, 500 mg
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety

TOPOISOMERASE 1 INHIBITORS	
IRINOTECAN	
Authorised indication	Advanced colorectal carcinoma
Authorised age group	>18 years
Authorised dose	-
Authorised formulation	For IV infusion 40 mg, 100mg vials
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety
TOPOTECAN	
Authorised indication	Metastatic ovarian carcinoma
Authorised age group	> 18 years
Authorised dose	-
Authorised formulation	For IV infusion 1 mg, 4 mg vials
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety
TOPOISOMERASE II INHIBITORS	
DOXORUBICIN	
Authorised indication	Breast carcinoma, HD, NHL, lung carcinoma, CLL, carcinoma of the bladder, ovarian and stomach, AL, "childhood solid tumour",
Authorised age group	Children
Authorised dose	No mention of dose
Authorised formulation	For IV infusion 10 mg, 50 mg
Needs	Define dose and lower age limit based on data on efficacy and safety and investigate where needed, including newborns.
LIPOSOMAL DOXORUBICIN	
Authorised indication	Breast carcinoma, Ovarian carcinoma, Kaposi sarcoma
Authorised age group	>18 years
Authorised dose	-
Authorised formulation	For IV infusion 20 mg, 50 mg
Needs	Data on efficacy and safety in same indications as doxorubicin
DAUNORUBICIN	
Authorised indication	HD and NHL, AL, CML
Authorised age group	Children
Authorised dose	Dose in mg/kg
Authorised formulation	For IV infusion 20 mg
Needs	Define dose and lower age limit based on data on efficacy and safety and investigate where needed, including newborns.
EPIRUBICIN	
Authorised indication	Various solid tumours in adults
Authorised age group	> 18 years
Authorised dose	-
Authorised formulation	For IV infusion 10 mg 50 mg vials
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety
IDARUBICIN	
Authorised indication	AML, ALL

Authorised age group	Children
Authorised dose	10 mg/m^2 daily for 2 days
Authorised formulation	IV infusion 5 mg; 10 mg, capsules 5 mg; 10 mg; 25 mg
Needs	Define dose and lower age limit based on data on efficacy and safety, and investigate where needed
MITOXANTRONE	
Authorised indication	Breast carcinoma, AML, NHL
Authorised age group	> 0 years (*Spain*)
Authorised dose	Information not available
Authorised formulation	For IV infusion 20 mg, 30 mg vial
Needs	Age appropriate formulation
ETOPOSIDE	
Authorised indication	Small cell lung carcinoma, AML, germcell carcinoma
Authorised age group	> 2 years
Authorised dose	100-200 mg/m²
Authorised formulation	for IV infusion 100 mg; capsules 25, 50 and 100 mg
Needs	Age appropriate formulation Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety
MITOTIC SPINDLE POISONS (VINCA ALKALOIDS AND TAXANES)	
VINCRISTINE	
Authorised indication	ALL, HD, NHL, lung carcinoma, breast carcinoma and cervical carcinoma, myeloma, rhabdomyosarcoma, neuroblastoma, nephroblastoma, embryonic tumours of childhood, Ewing's sarcoma, osteosarcoma, idiopathic thrombocytopenic purpura
Authorised age group	< 10 kg
Authorised dose	1 to 2 mg/m^2 and for those < 10 kg starting dose 0.05 mg/kg once a week
Authorised formulation	For IV injection 2 mg, 1 mg vials
Needs	Define dose and lower age limit based on data on efficacy and safety, and investigate where needed
VINBLASTINE	
Authorised indication	HD, NHL, testicular carcinoma, Kaposi's sarcoma, choriocarcinomas, carcinoma of the ovarian, breast, kidney and bladder, certain types of histiocytosis
Authorised age group	> 0 years (*Spain*)
Authorised dose	6 mg/m^2 average dose; Paediatric indication: dose 2.5 mg/m^2 week 1, 3.75 week 2, 5 week 3, 6.25 week 4, 7.5 week 5 and 12.5 week 6
Authorised formulation	For IV injection 10 mg vial
Needs	Data on efficacy and safety in brain tumours

VINDESINE	
Authorised indication	ALL, lymphomas, certain solid tumours (e.g breast, oesophagus, head and neck, bronchopulmonary carcinoma)
Authorised age group	Children
Authorised dose	4 mg/m^2 /week
Authorised formulation	For IV injection 5 mg vial
Needs	Define dose and lower age limit based on data on efficacy and safety, and investigate where needed To define the potential efficiency of the compound on different tumours in children responsive to treatment based on its mechanism of action
PACLITAXEL	
Authorised indication	Ovarian carcinoma, non-small cell lung carcinoma, breast carcinoma
Authorised age group	> 18 years
Authorised dose	-
Authorised formulation	For IV infusion, 30 mg, 150 mg, 300 mg vials
Needs	To define the potential efficiency of the compound on different tumours in children responsive to treatment based on its mechanism of action
DOCETAXEL	
Authorised indication	Non-small cell lung carcinoma, breast carcinoma, ovarian carcinoma
Authorised age group	> 18 years
Authorised dose	Dose per m^2
Authorised formulation	For IV infusion 20 mg, 80 mg vials
Needs	Based on the mechanism of action, to define the potential effect of the product on various responsive tumours in children and where appropriate study its efficacy and safety
MONOCLONAL ANTIBODIES AND TARGETED THERAPY	
RITUXIMAB	
Authorised indication	Follicular lymphoma
Authorised age group	> 18 years
Authorised dose	-
Authorised formulation	Iv infusion
Needs	Data on PK, efficacy and safety in paediatric CD20+ NHL
OTHERS	
L-ASPARAGINASE / PEG-ASPARAGINASE	
Authorised indication	ALL
Authorised age group	Children
Authorised dose	100 IU/kg/day
Authorised formulation	i.v. infusion
Needs	Make indication available in all Member States
CRISANTASPASE	
Authorised indication	ALL, other neoplastic conditions where depletion of asparagine likely to be useful
Authorised age group	Children
Authorised dose	200 IU/kg/day
Authorised formulation	Powder for reconstitution for injection
Needs	Define dose and lower age limit based on data on efficacy and safety, and investigate where needed Availability in all Member States

PROCARBAZINE	
Authorised indication	HD
Authorised age group	Children not mentioned
Authorised dose	-
Authorised formulation	Capsules 50 mg
Needs	Define dose and lower age limit based on data on efficacy and safety, and investigate where needed Age appropriate formulation
TRETIONIN (ALL-TRANS- RETINOIC ACID)	
Authorised indication	Induction of remission in acute promyelocytic leukaemia.
Authorised age group	Children (age group not specified) *(United Kingdom)*
Authorised dose	$45/m^2$
Authorised formulation	Capsules
Needs	Based on the mechanism of action to define the effect of the product in various malignancies and where appropriate study its efficacy and safety Age appropriate formulation
ISOTRETIONIN (13-CIS-RETIONIC ACID)	
Authorised indication	Acne
Authorised age group	-
Authorised dose	-
Authorised formulation	-
Needs	Age appropriate formulation Based on the mechanism of action to define the effect of the product in neuroblastoma, juvenile myelomonocytic leukamia and where appropriate study its efficacy and safety