25 September 2014
EMA/PDCO/381728/2014
Human Medicines Research & Development Support Division

Draft inventory of paediatric therapeutic needs

Paediatric oncology

Event	Date
Adopted by PDCO for release for consultation	September 2014
Start of public consultation	7 October 2014
End of consultation (deadline for comments)	30 November 2014
Adoption by PDCO for final release	

Comments should be provided using this template. The completed comments form should be sent to paediatrics@ema.europa.eu

Objective of the inventory

Based on Article 43 of the European Union Paediatric Regulation the Paediatric Committee at the European Medicines Agency (PDCO) is working to establish an inventory to identify the needs in the different therapeutic areas where there should be research and development of medicinal products for children. The inventory is based on the results of a survey of all paediatric uses of medicines in Europe and on the existing list of paediatric needs established by the former Paediatric Working Party; it will be published progressively by therapeutic area. Further information can be found on the EMA website.

Disclaimer

The lists should neither be viewed as a prescription tool nor as recommendations for treatment.

The authorised indication(s) and formulation(s) of the medicinal products were taken into account; however, this information is not available for all European Member States. Users of this inventory are therefore advised to check the authorisation details of nationally authorised medicinal products of interest and any intellectual property protections in order to seize opportunities. The EMA is not competent to provide information in this regards. Some information may be publicly available such as in the Community Register of orphan medicinal products for human use.

The methodology used to establish the inventory was based as much as possible on evidence. It is acknowledged that identification of needs for research into medicinal products for paediatric use is

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

partly based on subjective criteria and may change over time and according to region. This may also be the case should further information of which the PDCO is not aware become available (e.g. on pharmacokinetics, safety and efficacy, submission of Paediatric Investigation Plans).

The PDCO prepared this inventory of anti-cancer medicines by identifying priority areas of therapeutic needs of children with cancer, considering information from the following sources:

- EMA Paediatric Working Party (PEG) Assessment of the paediatric needs - Chemotherapy products (Part I).
- Best Pharmaceuticals for Children Act (BPCA) Priority List of Needs in Pediatric Therapeutics 2012.
- Survey of all paediatric uses of medicinal products in Europe (EMA/794083/2009).
- WHO Model Lists of Essential Medicines CHILDREN, 4th edition, Rev. October 2013.
- EMA Revised priority list for studies on off-patent paediatric medicinal products Rev. 2013/2014.
- EMA Decisions on a PDCO Opinion agreeing a Paediatric investigation plan (PIP)[1].
- WHO: Priority life-saving medicines for women and children 2012.
- Information on submissions and assessments of paediatric data under Articles 45 and 46 of Regulation (EC) No. 1901/2006[2].
- Information on Member states on off label use[3].
- Information from specific publications[4].
- PDCO experience from evaluating requests to confirm applicability of EMA class waivers.

Notes

For the designation of the products International Non-proprietary Names (INN) are used whenever possible. Products are listed in alphabetical order within the product classes, not in any order of priority.

For age-appropriate pharmaceutical forms, the guideline on pharmaceutical development of medicines for paediatric use should be considered (EMA/CHMP/QWP/805880/2012).

The shaded active substances represent those for which a Paediatric Investigation Plan (PIP) has been agreed.

For further information please consult the EMA website[5].

[1] http://www.ema.europa.eu:80/ema/index.jsp?curl=pages/medicines/landing/pip_search.jsp&mid=WC0b01ac058001d129
[2] For certain nationally authorsed anti-cancer medicinal products, see http://www.hma.eu/187.html
[3] For example, in Italy „Lista farmaci Oncologia pediatrica (Allegato 2 - aggiornamento aprile 2011, L. 648/96)"
[4] Vassal 2013 Eur J Cancer; Paolucci et al. 2008 Lancet Onc
[5] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000023.jsp

Inventory paediatric oncology

1. Therapeutic needs for medicines with mechanisms of action relevant for paediatric diseases / subgroups

The marketing authorisations of the active substances do not include a paediatric use at this time even though the medicines are used in paediatric oncology practice, for which some data support the relevance of their mechanism(s) of action.

Active substance	**Malignancy/ies**	**Paediatric target population**	**Type of data**
Arsenic trioxide	Acute myeloid leukaemia	All paediatric age ranges; targeting one of the listed malignancies (left)	Paediatric data on: • PK, PD, safety, toxicity, dosing • anti-tumour activity • efficacy (as necessary for establishing a use when assessing all existing data)
Axitinib	Neuroblastoma, hepatoblastoma, medulloblastoma, Wilms tumour, ependymoma		
Bortezomib	Acute lymphoblastic leukaemia, graft versus host disease		
Cabazitaxel	CNS tumours		
Crizotinib	Anaplastic large cell lymphoma, inflammatory myofibroblastic tumour		
Fludarabine	As part of full and reduced-intensity conditioning regimens before haematopoietic stem cell transplantation		
Irinotecan	Neuroblastoma, pineoblastoma, glioblastoma, brainstem glioma, osteosarcoma, hepatoblastoma, central nervous system rhabdoid tumour		
Isotretinoin*	Neuroblastoma		
Liposomal cytarabine	Acute leukaemias, intrathecal treatment		
Liposomal doxorubicin	Acute myeloid leukaemia, CNS tumours		
Ruxolinitib	Precursor B- cell acute lympho-blasticleukaemia, precursor T-cell acute lymphoblastic leukaemia		
Anti-CD 20 monoclonal antibodies	Post-transplant lymphoproliferative disorder		
Tretinoin	Acute myeloid leukaemia		

* See also section 3

2. Therapeutic needs to address off label use

The marketing authorisation includes a paediatric use, but a wider use occurs in paediatric oncology practice (other types of tumours and lines of treatment), for which additional data are needed.

Active substance	Paediatric target population	Type of data
Carboplatin Clofarabine Ifosfamide Thiotepa Vinorelbine	All paediatric age ranges in a specific tumour type or a set of related tumour types	• Data on PK, PD, safety, toxicity, dosing • Anti-tumour activity; efficacy (to the extent necessary for establishing a use when assessing all relevant data, which need to be described and preliminarily analysed in the proposal) • Long-term safety (e.g., register set-up and first data available)

3. Therapeutic needs for oral-administration forms

Active substance	Paediatric target population	Therapeutic needs
Crizotinib Cyclophosphamide Etoposide Imatinib Isotretinoin Mercaptopurine Methotrexate Sorafenib Sunitinib Temozolomide Thioguanin Topotecan Vinorelbine	Children 3 months to less than 6 years of age, and older patients if likely unable to swallow existing pharmaceutical forms	Solid or liquid pharmaceutical form(s) appropriate for age: • Composition (excipients) as appropriate for long-term use and curative treatment intention • Dose flexibility and / or dose-banding as appropriate for necessary dose-precision • Data in target population including on PK, PD, toxicities
Vincristine		Age-appropriate parenteral form

4. Therapeutic needs for improving dosing recommendations for young patients

Recommendations for use in young patients need to be generated or improved, with a view to optimise the benefit / risk relationship, including long-term safety.

Active substance	Paediatric target population	Therapeutic needs
Cytarabine Lomustine Melphalan Oxaliplatin Temozolomide	Children less than 3 - 6 years of age (age subset to be proposed based on pharmacological characteristics, quantity and quality of available pharmacologically-relevant data across this age range)	• Exposure predictions from PBPK model before first trial and to be used for dosing in trial, • Data on PK, PD, safety, toxicity • Anti-tumour activity, obtaining relevant existing data from other uses / populations, joint modelling and analyses including how suggestions for improved dosing will be derived (plan has to be part of proposal and PIP Opinion)