I.9 Cancer medicines for children – new indications for currently listed EMLc medicines

Does the application adequately address the issue of the public health need for the medicine?

☒ Yes

☐ No

☐ Not applicable

Comments:

Being already listed on the EMLc for other indications, and included on many national essential medicines lists, the budget impact to health systems of endorsing these medicines for new indications on the EMLc is likely to be small, considering the relatively small burden of disease.

Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.

The applicants identified cancer medicines included in standard arms of European paediatric oncology treatment protocols, for which efficacy is supported by literature, that are not currently included on the EMLc for the indications proposed.

Medicine	Proposed new indication(s)
Carboplatin	Ovarian and testicular germ cell tumours Nephroblastoma
Cyclophosphamide	Nephroblastoma
Dactinomycin	Ewing sarcoma
Dexamethasone	Burkitt lymphoma
Etoposide	Acute myeloid leukaemia Osteosarcoma Nephroblastoma
Hydrocortisone	Burkitt lymphoma
Ifosfamide	Burkitt lymphoma Nephroblastoma
Imatinib	Acute lymphoblastic leukaemia
Irinotecan	Nephroblastoma Rhabdomyosarcoma
Methotrexate	Burkitt lymphoma
Methylprednisolone	Burkitt lymphoma

Have all important studies and all relevant evidence been included in the application?	☐ Yes ☐ No ☒ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included: No specific clinical data were presented in the application.
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☐ Yes ☐ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). These are medicines that are considered as standard treatment for the proposed new indications. All medicines are currently included on the EMLc for various other indications. It is proposed that inclusion of the proposed new indications will lead to a more accurate picture of treatment strategies for childhood cancers, and would support better availability and access to cancer medicines for children. No specific clinical data were presented in the application. However, all medicines involved have been previously considered and recommended for the EML and EMLc for other indications so extrapolation of efficacy and safety can be made in this case. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)?
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☐ No ☒ Not applicable Comments: No specific clinical data were presented in the application. However, all medicines involved have been previously considered and recommended for the EML and EMLc for other indications so extrapolation of efficacy and safety can be made in this case.
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☐ No ☒ Not applicable Comments: No specific clinical data were presented in the application. However, all medicines involved have been previously considered and recommended for the EML and EMLc for other indications so extrapolation of efficacy and safety can be made in this case.

Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Being already listed on the EMLc for other indications, and included on many national essential medicines lists, the budget impact to health systems of endorsing these medicines for new indications on the EMLc is likely to be small, considering the relatively small burden of disease.
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	No specific clinical data were presented in the application. However, all medicines involved have been previously considered and recommended for the EML and EMLc for other indications so extrapolation of efficacy and safety can be made in this case.
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☐ Yes ☒ No ☐ Not applicable Comments:
Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☐ Yes ☒ No ☐ Not applicable Comments:
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	No specific clinical data were presented in the application. However, all medicines involved have been previously considered and recommended for the EML and EMLc for other indications so extrapolation of efficacy and safety can be made in this case.
Any additional comments	
Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	These medicines are all used in standard, multi-modal chemotherapy protocols for the proposed new indications. Expanding the EMLc indications for these medicines would support the goals of WHO Global Paediatric Cancer initiative and contribute towards the achievement of the best possible cancer care for children. I support the expansion the listings on the EMLc for the proposed cancer medicines for the proposed new indications. The availability of clinical evidence in the paediatric context is limited but considered that obtaining the usual level of evidence required for EML listings was unlikely. In this case, efficacy and safety could be accepted based on of extrapolation of the well-known benefits and harms from use of these medicines in adults, for other indications in children, and as part of standard cancer care in children.

References (if required)	