The Expert Committee noted that the incidence of paediatric tumours has been steadily increasing over the past decades with the largest increases reported in youngest children. The Expert Committee recommended the extension of the current listings on the complementary list of the EMLc of the medicines outlined in the following table for the indications specified. Noting that these paediatric cancers also affect older children and adolescents, the Committee also recommended extending the listings for these medicines on the EML.

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Indication(s)</th>
<th>Cancer supportive care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboplatin</td>
<td>(Nephroblastoma, ovarian and testicular germ cell tumours)</td>
<td></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>(Nephroblastoma)</td>
<td></td>
</tr>
<tr>
<td>Dactinomycin</td>
<td>(Ewing sarcoma)</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>(Burkitt lymphoma)</td>
<td></td>
</tr>
<tr>
<td>Etoposide</td>
<td>(Acute myeloid leukaemia, nephroblastoma, osteosarcoma)</td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>(Burkitt lymphoma)</td>
<td></td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>(Burkitt lymphoma, nephroblastoma)</td>
<td></td>
</tr>
<tr>
<td>Imatinib</td>
<td>(Acute lymphoblastic leukaemia)</td>
<td></td>
</tr>
<tr>
<td>Irinotecan</td>
<td>(Nephroblastoma, rhabdomyosarcoma)</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td>(Burkitt lymphoma)</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>(Burkitt lymphoma)</td>
<td></td>
</tr>
</tbody>
</table>

The Committee noted that administration of intravenous cyclophosphamide or ifosfamide required the use of the accompanying medicine mesna to prevent haemorrhagic cystitis commonly associated with these treatments. The Committee therefore also recommended the extension of the current listing for mesna on the EML and EMLc to include the indications of nephroblastoma and Burkitt lymphoma.

**Background**

The proposed medicines are all included on the EMLc for other cancer indications.

**Public health relevance**

Cancer is a leading cause of death in children globally; the most common cancer types in children are leukaemias, lymphomas and
Cancer in children and adolescents is almost exclusively treated according to national and international treatment protocols. This is the case for first treatment and relapsed and refractory disease. Treatment regimens are devised by clinical experts from relevant tumour groups and are further developments of previous regimens. Often these treatment protocols consist of the standard arm that has proven to be effective based on previous experimental trials. All medicines proposed in this application are part of international treatment regimens and are considered the standard of care.

Benefits

Cancer in children and adolescents generally cannot be prevented or screened for, so improving outcomes for children with cancer relies on early and accurate diagnosis and access to effective treatments. In 2018, WHO launched the Global Initiative for Childhood Cancer, to provide leadership and technical assistance to Member States to build and sustain high-quality childhood cancer programmes. The goal of this initiative is to achieve at least 60% survival for all children with cancer globally by 2030 (2).

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Chemotherapy is associated with serious adverse events in the acute setting and also in the long term in cancer survivors; it therefore requires close monitoring (25–27). All proposed medicines in this application are already included on the EMLc. Their safety profiles are well known as a result of long-standing experience with their use.

Harms

Chemotherapy is associated with serious adverse events in the acute setting and also in the long term in cancer survivors; it therefore requires close monitoring (25–27). All proposed medicines in this application are already included on the EMLc. Their safety profiles are well known as a result of long-standing experience with their use.

Cost / cost effectiveness

Not reported in the application.

WHO guidelines

WHO guidelines for the treatment of paediatric cancer are not available. Burkitt lymphoma and nephroblastoma are among the six tracer cancers in the WHO Global Initiative for Childhood Cancer.

Availability

The proposed medicines are already included on the EMLc and are available in branded and generic forms.

Other considerations

The EML Cancer Medicines Working Group advised that it supported expansion of the listings on the EMLc for the proposed cancer medicines for the proposed new indications. These medicines are all used in standard, multimodal chemotherapy protocols for the
proposed indications. Expanding the EMLc indications for these medicines would support the goals of Global Paediatric Cancer initiative and contribute towards the achievement of the best possible cancer care for children. The Working Group acknowledged that the availability of clinical evidence in the paediatric context was 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 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.

15. Multicentre prospective phase III trial for extracranial malignant germ cell tumours including a randomized comparison of carboplatin and cisplatin. Amsterdam: EU Clinical Trials Register; 2012 (EudraCT number 2012-001784-36/DE, accessed 18 May 2021).