Proposed medicines(s) for treatment of Hodgkin Lymphoma (refer to application for specific protocols):

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Currently on EMLc</th>
<th>Addition to EMLc</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>for other indications</td>
<td>for Hodgkin Lymphoma</td>
</tr>
<tr>
<td>vincristine</td>
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<tr>
<td>doxorubicin</td>
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<tr>
<td>cyclophosphamide</td>
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<td>prednisone</td>
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<tr>
<td>etoposide</td>
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<tr>
<td>bleomycin</td>
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<tr>
<td>dacarbazine</td>
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</tbody>
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(1) Does the application adequately address the issue of the public health need for the treatment of the disease?

Yes ☒ No ☐

Hodgkin lymphoma is one of the more common pediatric malignancies, particularly in adolescents. It is also one of the most curable of childhood cancers. A variety of regimens have proven to be effective for management of this disease.

(2) Have all important studies that you are aware of been included in the application?

Yes ☐ No ☒

The application focuses on regimens utilized by the Children’s Oncology Group in North America, and of the GPOH in Europe. While these regimens are highly effective, multiple less toxic regimens (Stanford V, ABVD) are also effective and may be more suitable for use in developing countries where therapies of shorter duration may be beneficial and where facilities for management of acute toxicities or therapy (eg fever and neutropenia) may be less available. Two highly effective drugs for Hodgkin lymphoma (vinblastine and mechlorethamine) are not included in the application, but would be important components of alternative regimens.
Does the application provide adequate evidence of efficacy/effectiveness of the proposed treatment regimen(s)?

Yes ☒ No ☐

Without specific therapy, virtually all children with Hodgkin lymphoma will die of disease. Fortunately, a variety of regimens have proven to be very effective in this disease, such that the overwhelming majority of children with Hodgkin lymphoma are now cured. The efficacy of the proposed regimens (and other analogous regimens) is indisputable. The focus of modern studies is to refine therapy to identify those elements necessary for cure while omitting elements that contribute only to toxicity. Long term toxicities are of particular concern.

Does the application provide adequate evidence of safety for the proposed treatment regimen(s)? Are there any adverse effects of concern, or that may require special monitoring?

Yes ☒ No ☐

The regimens used for this tumor incorporate drugs that have been in use for decades. The acute and late toxicities of therapy are well known and are well described in the “Harms and Toxicity Considerations” section of the application.

ADDITIONAL CONSIDERATIONS:

Are there special requirements or training needed for the safe, effective and/or appropriate use of the proposed treatment(s)?

Yes ☐ No ☒

The relative rarity of the tumor mandates that therapy should be undertaken in centers with appropriate diagnostic and therapeutic expertise and the availability of suitable supportive care facilities and specialists able to manage chemotherapy complications. Toxicities of therapy and potential complications have been well described and are manageable in centers with appropriate experience.

Are there any issues regarding the registration of the proposed medicines by regulatory authorities? (e.g., recent registration, new indications, off-label use)

Yes ☐ No ☒

Drugs utilized for treatment of Hodgkin lymphoma are relatively old, off-patent with well-described acute and late toxicities. As is true for many of the older chemotherapeutic agents used in children, it is unclear that any of these drugs are labelled specifically for use in childhood Hodgkin lymphoma.
(7) **Comment briefly on issues regarding cost and affordability of treatment.**

The proposed drugs are off patent and relatively inexpensive.

(8) **Any additional comments on the application?**

(9) **Please summarise the action(s) you propose the Expert Committee take.**

Addition of vincristine, doxorubicin, cyclophosphamide, prednisone, etoposide, bleomycin, and dacarbazine to the List of Essential cytotoxic and adjuvant medicines for use in children with Hodgkin lymphoma. Vincristine, doxorubicin and cyclophosphamide are already on the WHO Model List of Essential medicines for other pediatric cancers. Etoposide, bleomycin, and dacarbazine are already on the List of Essential cytotoxic and adjuvant medicines for use in adults. Prednisone is, surprisingly, not yet on the List of Essential cytotoxic and adjuvant medicines for either adult or pediatric cancers, although it should be. Other synthetic corticosteroids (methylprednisolone, prednisolone, dexamethasone) are on the List of Essential cytotoxic and adjuvant medicines for adults and children. It is surprising that prednisone is not listed among the choices.