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

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Currently on EMLc for other indications</th>
<th>Addition to EMLc for Retinoblastoma</th>
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<tbody>
<tr>
<td>vincristine</td>
<td>☒</td>
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<tr>
<td>carboplatin</td>
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<td>☒</td>
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<td>cisplatin</td>
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<td>etoposide</td>
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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 ☐

Retinoblastoma is a very rare tumor of young children, more than ¼ of which are inherited through germline mutation of the \( Rb1 \) gene. Management of children presenting with early stage disease is focused on preserving vision as well as saving life. The efficacy of chemotherapy with careful ophthalmologic monitoring and intervention has been clearly demonstrated. Unfortunately, in developing countries, many children still present with advanced tumors where chemotherapy can be essential to preserve vision.

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

Yes ☒ No ☐

Comments:

(3) Does the application provide adequate evidence of efficacy/effectiveness of the proposed treatment regimen(s)?

Yes ☒ No ☐

The efficacy of chemotherapy in retinoblastoma has been demonstrated. For patients with more advanced disease, the application of chemotherapy and/or irradiation is
instrumental in improving survival. In those with less advanced disease, chemotherapy and irradiation may allow for preservation of vision.

(4) 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. Expertise in administration of chemotherapy and in ophthalmologic monitoring of treatment are required for optimal outcome.

ADDITIONAL CONSIDERATIONS:

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

Yes ☒ No ☐

The 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 provide local control therapies. Toxicities of therapy and potential complications have been well described and are manageable in centers with appropriate experience.

(6) 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 in the regimen 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 retinoblastoma.

(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, cisplatin, carboplatin, and etoposide to the List of Essential cytotoxic and adjuvant medicines for use in retinoblastoma. Vincristine is already on the WHO Model List of Essential medicines for other pediatric cancers. Carboplatin and etoposide are already on the List of Essential cytotoxic and adjuvant medicines for use in adults. Cisplatin is not on the List of Essential cytotoxic and adjuvant medicines for use in adults or children, but it should be.