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

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Currently on EML</th>
<th>Addition</th>
</tr>
</thead>
<tbody>
<tr>
<td>imatinib</td>
<td>□</td>
<td>☒</td>
</tr>
<tr>
<td>dasatinib</td>
<td>□</td>
<td>☒</td>
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<tr>
<td>nilotinib</td>
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</table>

(1) Does the application adequately address the issue of the public health need for the treatment of the disease?

Yes ☒ X No ☐

Comments: convincing public health need

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

Yes ☒ X No ☐

Comments:

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

Yes ☒ X No ☐ ☒

Comments: multicentre RCT of imatinib showed improvement in disease progression from 96% to 80% compared to interferon/cytarabine. Well tolerated oral administration. Dasatinib and nilotinib are recommended for patients who are intolerant or have resistant disease. Their development is based molecular data (response to mutations) – no clinical evidence cited.
(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 ☐

Comments: blood counts must be monitored for development of neutropenia, thrombocytopenia. 15-25% of patients are intolerant. Dasatinib associated with GI bleeding (25% of patients), pulmonary complications

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 ☐

Comments: Diagnostic - need genetic tests to determine if imatinib will be effective; although 90% of patients have the translocation.

(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 ☐ ☒

Comments: imatinib is widely approved. No information on approval of dasatinib or nilotinib provided.

(7) Comment briefly on issues regarding cost and affordability of treatment.
Formal CE for imatinib is $43,000 per QUALY but will be coming off patent. Imatinib branded and generics available. No information on costs of dasatinib or nilotinib provided.

(8) Any additional comments on the application?

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

Add imatinib. Unclear whether dasatinib and nilotinib should be added as alternatives given efficacy not demonstrated, greater risk of harm, potential availability issues.