Proposed medicines(s) for treatment of AML and APML (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>cytarabine (AML, APML)</td>
<td>☒</td>
<td>☐</td>
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<tr>
<td>daunorubicin (AML, APML)</td>
<td>☒</td>
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<tr>
<td>ATRA (all-trans retinoic acid) (APML)</td>
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<tr>
<td>arsenic trioxide (APML)</td>
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<tr>
<td>6-mercaptopurine (APML)</td>
<td>☒</td>
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<tr>
<td>methotrexate (APML)</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 ☒
- No ☐

Comments: different subcategories of the disease have not been classified, so true incidence unknown

(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 ☐

Comments: The two additions are recommended for Acute Promyelocytic Leukemia (APML) only. 2 of 3 studies showed small improvements in survival and progressions with addition. Tallman trial showed 3% improvement in CR rate with addition of ATRA; 17% increase in 3 year survival rate. Powell showed addition of As2O3 improved 3 year EFS from 63 to 80%; 3 year OS from 81-86%.
(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: yes, see #5; treatment with dexamethasone may be required for syndrome associated with ATRA

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: laboratory access for diagnosis and monitoring; some antibiotics recommended for infection risks are not on EML. “blood products, isolation facilities, ICU support as well as hematology and molecular laboratory as well as radiology support” need to be available.

(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: Not clear if As2O3 is readily available. Neither listed in document on regulatory information, so assume use is off label?

(7) Comment briefly on issues regarding cost and affordability of treatment.

No information provided

(8) Any additional comments on the application?

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

Assuming these are readily available and affordable, add to EML. However, added benefit is small.