Proposed medicines(s) for treatment of Early Stage Breast Cancer (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>cyclophosphamide (oral &amp; IV)</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>doxorubicin</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>paclitaxel</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>docetaxel</td>
<td>✗</td>
<td></td>
</tr>
<tr>
<td>methotrexate</td>
<td>✗</td>
<td></td>
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<tr>
<td>fluorouracil</td>
<td>✗</td>
<td></td>
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<tr>
<td>trastuzumab (HER2 positive)</td>
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<td>☑</td>
</tr>
<tr>
<td>tamoxifen</td>
<td>✗</td>
<td></td>
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<tr>
<td>☐ anastrozole (HR positive)</td>
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<td>☑</td>
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</tbody>
</table>

(1) Does the application adequately address the issue of the public health need for the treatment of the disease?  
Yes ☑ No ☐

Comments:

(2) Have all important studies that you are aware of been included in the application?  
Yes ☐ No ☐

Comments: All relevant studies have been included. However, in the references the San Gallen guidelines should be included, since in most countries these guidelines are used to decide the treatment in patients with early breast cancer.

(3) Does the application provide adequate evidence of efficacy/effectiveness of the proposed treatment regimen(s)?  
Yes ☑ No ☐

Comments: Possibly it should be stated more clearly that the switch from Tamoxifen to Anastrozole has led just to a small incremental improvement in the outcome and
that also based on these considerations, a treatment with Tamoxifen alone is still justifiable today.

(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  X  No  

   Comments:

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  X

   Comments:

(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  X

   Comments:

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

   See above.

(8) Any additional comments on the application?

   1) It should be stressed that inflammatory breast cancer should never be operated in the first treatment.

   2) In overview of regimens:
   - In HR positive /HER2 negative tumours the combination of Tamoxifen plus LHRH (or oophorectomy) should be discussed in patients at high risk.
   - The last sentence should be corrected: the use of hormone therapy instead of chemotherapy is sometimes possible but only in post-menopausal women (never in pre-menopausal women).
In standard hormone regimens:
- Add again Tamoxifen plus LHRH as above.
- In post-menopausal women 5 years of Tamoxifen followed by 5 years of an Aromatase inhibitor should be advised, if at all, only in patients at high risk, not for node negative patients.

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

Accept the addition of Anastrozole with possibly indication of the fact that under constrained circumstances Tamoxifen alone is still justifiable.