Proposed medicines(s) for treatment of Early Stage Colon Cancer (refer to application for specific protocols):

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Currently on EML</th>
<th>Addition</th>
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<tbody>
<tr>
<td>calcium folinate (= leucovorin, folinic acid (INN))</td>
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<tr>
<td>fluorouracil</td>
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<tr>
<td>oxaliplatin</td>
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<tr>
<td>capecitabine</td>
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(1) Does the application adequately address the issue of the public health need for the medicine?
   Yes ☑ No ☐

Please provide brief details:

*It is the 4th most common cause of cancer related death and there are 1.2 million new cases a year worldwide.*

*Early stage colon is the cause of 320,600 and 288,000 death annually for men and women respectively.*

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

Please provide brief comments on any relevant studies that have not been included:

(3) Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed use?
   Yes ☑ No ☐

Briefly summarise the reported outcomes (e.g. clinical, surrogate, other) and comment, where possible, on the magnitude of clinical benefit associated with use of the medicine:

*Oxaliplatin in folfox4 improved survival by 20% compared to 5-FU/ calcium folinate.*
The 5 year overall survival was more (76.5%) for FLOX as against 73.8% for FULV. Capeox regimen improved progression free survival compared to 5-FU/ calcium folinate. The three year disease free survival was 70.9% with Capeox and 66.5% 5FU/Calcium folinate. Overall survival at 5 years was 77.6% with Capeox and 66.5% with 5FU.

(4) Is there evidence of efficacy in diverse settings and/or populations?

Yes √ No □

Please provide brief details:
Evidence of efficacy exist for different geographical location e.g. Asian/ Europe/North America
There is also evidence of benefit for different age group, sex etc.

(5) Has the application adequately considered the safety and adverse effects of the medicine? Are there any adverse effects of concern, or that may require special monitoring?

Yes √ No □

Please provide brief details:
Diarrhea is seen in 50% of patients treated with 5-FU or Capecitabine and can be so severe as to require IV fluid replacement.
Up to 60% of patients on 5-FU and capecitabine can develop palmar-plantar erythrodysesthesia (hand foot syndrome) and may require treatment interruption.
Neutropenia with overwhelming infection is also a serious challenge.

ADDITIONAL CONSIDERATIONS:

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

Yes √ No □

Please provide brief details:
For 5-FU based combination (FLOX and FOLFOX6), intravenous catheter access and 46 hour continuous infusion is needed.
Lab facilities for follow up are needed

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

Yes □ No √

Please provide brief details:
FDA approved.

(8) Is the medicine recommended for use in a current WHO GRC-approved Guideline (i.e., post 2008)?

Yes √ No □

Please provide brief details:
ESMO and NICE guidelines.

(9) Please comment briefly on issues regarding cost and affordability of this medicine.
Oxaliplatin and capecitabine are very expensive and may not be affordable in resource poor setting.

(10) Any additional comments?

It should be available for people who can afford it.

(11) Please summarise the action you propose the Expert Committee takes.

Oxaliplatin and capecitabine should be added to the essential medicine list.