Proposed medicines(s) for treatment of mCRC (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>leucovorin (= calcium folinate, folic acid (INN))</td>
<td>☒</td>
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<tr>
<td>fluorouracil</td>
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<tr>
<td>oxaliplatin</td>
<td>☐</td>
<td>☒</td>
</tr>
<tr>
<td>irinotecan</td>
<td>☐</td>
<td>☒</td>
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<tr>
<td>capecitabine</td>
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</tbody>
</table>

(1) Does the application adequately address the issue of the public health need for the medicine?
   Yes  ✓  No  ☐

Please provide brief details:
It is a common and deadly malignancy, 1.2 million new cases a year, It is an important cause of morbidity and mortality, it is also the fourth most common cause of cancer death in men and third in women. (320,600 men and 288,100 women).
Patients with advanced disease are the ones who need the drug and they are more in number both in developing and developed countries.

(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:

Survival was 21.5 months and 20.6 for FOLFIRI and 20.6 months for FOLFOX.
There is a high response rate from 45-50% (FOLFIRI) with a median overall survival 15-20 compared with 5FU and folic acid and a median overall survival 15-20 compared with 5FU and folic acid.
For FOLFOX there is a median survival 19.5 months. FOLFOX regimen improves response rate, median progression free survival and overall survival.

(4) Is there evidence of efficacy in diverse settings and/or populations?
   Yes ☐ No  √

Please provide brief details:
Only studies from Europe and America. None from Asia, Africa and South America were included.

(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:
Both FOLFOX and FOLFIRI cause increased myelosuppression and nausea. Palmar-plantar erythrodythesia (hand-foot) syndrome is also common. Oxaliplatin can cause serious neuropathy in approximately 18% of patients.

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:
There is need for I.V ambulatory infusion and laboratory backup for adverse effects.

(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 Oxaliplatin, Irinotecan**

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

Yes ✔ No ☐

Please provide brief details:

In NICE guidelines

(9) **Please comment briefly on issues regarding cost and affordability of this medicine.**

*Very expensive and not affordable in the low income countries.*

(10) **Any additional comments?**

*It should be made available for people who can afford it.*

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

*Oxaliplatin, Capecitabine and Irinotecan should be included in the Essential Medicine List*