Proposed medicines(s) for treatment of Early Stage Rectal 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>calcium folinate (= leucovorin, folinic acid (INN))</td>
<td>☒</td>
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<tr>
<td>fluorouracil</td>
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<tr>
<td>oxaliplatin</td>
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<td>☒</td>
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<tr>
<td>capecitabine</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: Exec summary – “neoadjuvant is ..standard of care”. This is only the case for patients with T4 and clinically node positive disease; and for some T3 patients with low rectal tumours. The comments made on the colon adjuvant apply here.

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

Yes ☐ No ☒

Comments: Need to add the refs below because both PETACC-6 and CAO/ARO include adjuvant oxaliplatin.


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

Yes ☐ No ☒

Comments: Yes for 5FU and capecitabine but not for oxaliplatin. Oxaliplatin doesn’t have a role in neoadjuvant treatment. Use as adjuvant treatment not yet been resolved. PETACC-6 (Schmoll 2014, Xelox vs cap) – DFS not statistically significantly different; CAO/ARO (Rodel C 2012/2014, Bolus 5fu vs FOLFOX) DFS at 3yrs – 75.9% vs 71.2% HR 0.79, CI 0.64-0.98). OS no difference between the two groups. Phase II ADORE trial in Lancet did show significant benefit in DFS – but this isn’t sufficient evidence to add oxaliplatin as standard of care. I think jury is still out. Its not wrong to use FOLFOX or Xelox but it may not be delivering benefit.

(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: Same comments as for colon adjuvant.

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: see colon adjuvant

(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:

(7) Comment briefly on issues regarding cost and affordability of treatment.
Relatively cheap
(8) Any additional comments on the application?

Neoadjuvant – 825mg/m² not 1000mg/m² (use lowest effective dose and data is good for 825mg/m²).

(9) Please summarise the action(s) you propose the Expert Committee take. Recommend the inclusion of capecitabine but not oxaliplatin in the essential medicines list.