Proposed medicines(s) for treatment of Nasopharyngeal Carcinoma (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>cisplatin</td>
<td>☐</td>
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<tr>
<td>oxaliplatin</td>
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<tr>
<td>carboplatin</td>
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<tr>
<td>fluorouracil (=calcium folinate, folinic acid (INN))</td>
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<tr>
<td>Paclitaxel</td>
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(1) Does the application adequately address the issue of the public health need for the treatment of the disease?

Yes ☒  No ☐

As per the application:
1. Only 0.7% of cancers worldwide
2. 1 per 100,000 people per year.
3. Globally, there are 80,000 new cases per year.
4. NPC the 23rd most common of all new cancers worldwide.
5. There is a disparity in geographical distribution: Much more common in certain parts of Asia and North Africa, particularly in southern China
   - It is a rare tumour: EML “priority healthcare needs of the majority of population”
   - Early diagnosis will lead to diagnose at Stage 0 /1 which require only radiation

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

Yes ☒  No ☐

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

Yes ☐  No ☒

1. Meta-analysis: Pooling six studies using disease-free/progression-free survival as the endpoint demonstrated that the addition of chemotherapy to radiation therapy increased disease-free/progression-free survival by 37% at 2 years, 40% at 3 years, and 34% at 4 years after treatment (Published in 2002, Names of chemotherapeutic agents not stated)
2. Meta-analysis done to determine the additional value of neoadjuvant, concurrent, and/or adjuvant chemotherapy to radiation in the treatment of locally advanced nasopharyngeal
carcinoma (NPC) with regard to the overall survival (OS) and the incidence of local-regional recurrences (LRR) and distant metastases (DM). The pooled hazard ratio (HR) of death for all studies was 0.82 (95% CI, 0.71 to 0.95; P = .01) corresponding to an absolute survival benefit of 4% after 5 years. The largest effect was found for concomitant chemotherapy, with a pooled HR of 0.48 (95% CI, 0.32 to 0.72), which corresponds to a survival benefit of 20% after 5 years (published in 2004, Names of chemotherapeutic agents not stated).

3. A meta-analysis which has been cited (but data not given): “Six trials in NACT group (n = 1418) and five in AC group (n = 1187) were eligible. HR of death for NACT was 0.82 [95% confidence interval (CI) 0.69–0.98, P = 0.03], corresponding to an absolute survival gain of 5.13% after 3 years. Significant reduction of DMR (P = 0.0002; RR 0.69, 95% CI 0.56–0.84) was also found from NACT. But no decrease in LRR (P = 0.49; RR 0.90, 95% CI 0.66–1.22) was observed. Patients receiving additional AC had lower LRR (P = 0.03; RR 0.71, 95% CI 0.53–0.96). But no benefit of OS and DMR were seen in AC”. Conclusion: ACT can effectively enhance OS and reduce DMR, not LRR in NPC. And AC only helps to better control locoregional recurrence of NPC.


(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 ☐

The safety issues are norm with any type of cancer medicines
Nothing above the usual
All cancer medicines induced side effects require special monitoring

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 ☐

1. Oncology Services
2. Laboratory facilities to monitor harmful effects
3. Diagnostic facilities
4. Radiology services
5. Cancer radiotherapy as chemotherapy is given together with RT

(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 ☑

Paclitaxel is a relatively new drug and recently listed in EML
(7) Comment briefly on issues regarding cost and affordability of treatment.
   Not discussed in the application

(8) Any additional comments on the application?

(9) Please summarise the action(s) you propose the Expert Committee take.
   - Application requests to replace carboplatin* to Cisplatin* and Oxaliplatin
   - Evidence submitted (as reviewed in above questions) is inadequate to add Cisplatin* as an essential medicine in the treatment of NPC