I.10	Update of the application about chemotherapy(Platinum based chemotherapy) for head and neck cancer
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: na
Briefly summarize the role of the proposed medicine(s) relative to other therapeutic agents currently included in the Model List, or available in the market.	Platinum based chemotherapy (cisplatin and carboplatin) is recommended for induction or concurrent chemotherapy of many head and neck cancers in early and locally advanced setting . For head and neck cancers various substitutions including targeted agents such as cetuximab have shown inferior local regional control and overall survival.
Have all important studies and all relevant evidence been included in the application?	☐ Yes ☒ No ☐ Not applicable If no, please provide brief comments on any relevant studies or evidence that have not been included: Most of the data presented was for early stage disease of which the OS and gains are minimal, works as a sensitizer for radiotherapy , more of local control gains . Other studies for locally advanced show significant gains.
Does the application provide adequate evidence of efficacy/effectiveness of the medicine for the proposed indication?	☐ Yes ☒ No ☐ Not applicable Briefly summarize the reported benefits (e.g. hard clinical versus surrogate outcomes) and comment, where possible on the actual magnitude and clinical relevance of benefit associated with use of the medicine(s). This application was to remove this drug from the list for head and neck cancer In the studies provided based on their metanalysis, they seemed to settle on OS as an important endpoint and show just a 2 month benefit, which weighed against AE may be considered harmful. Of note, the benefit of chemort is for local control and dfs with HR that are significant provided below. Secondly in all studies they has been no survival advantage to the addition of chemotherapy to radiotherapy for early disease. MACH-NC update in 2017 showed survival benefit of cisplatin vrs RT alone, risk of death HR 0.81[0.78-0.86]. 6.5% BENEFIT for concomitant arm. Same benefit in induction chemo cisplatin based. RTOG 91-11 induction and concurrent cisplatin HR FOR LFS 0.75. HR for failure of 0.58 for concomitant . Distant control HR 0.69. OS no difference. GORTEC showed accelerated RT was inferior to platinum based Chemort.

	Facts of De-Escalate HPV were distorted , chemort showed superior results Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? IN CHILDREN AND PREGNANT WOMEN NOTRECOMMENDED NOR IN ELDERLY CONCURRENT WITH RADIOTHERAPY .
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☒ No ☐ Not applicable Comments: it concentrated on the toxicity as a point for argument , but was not correct in assertion Carboplatin has less neurotoxicity, nephrotoxicity, thrombocytopenia better results when combined with 5FU Cisplatin is more associated with grade 3 toxicities, mucositis, nausea and vomiting especially in bolus administration and now substituted with weekly doses and confirmed by phase 3 trials JCG1008 , Baul et al JN atl Cancer INST. 2019.111(5):490
Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☒ No ☐ Not applicable Comments: Myelosuppression Oral mucositis Renal toxicity These do not require highly specialized care, however in patients with added toxicity from radiotherapy these must be continuously monitored.
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	The overall benefit to risk is favourable with no other drugs matching the same benefit
Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	The quality of evidence provided even though moderate was skewed in favour of early disease,
Are there any special requirements for the safe, effective and appropriate use of the medicine(s)**?** (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	☒ Yes ☐ No ☐ Not applicable Comments: haematological and chemistries must be checked during the treatment

Are you aware of any issues regarding the registration of the medicine by national regulatory authorities? (e.g. accelerated approval, lack of regulatory approval, off-label indication)	☒ Yes ☐ No ☐ Not applicable Comments: Cisplatin was replaced by Carboplatin as an essential drug for ovarian cancer on EML in 2009 due to lower renal, neuropathies, toxicity , emesis and improved tolerability.
Is the proposed medicine recommended for use in a current WHO Guideline approved by the Guidelines Review Committee? (refer to: https://www.who.int/publications/who-guidelines)	☒ Yes ☐ No ☐ Not applicable Comments: Yes it is recommended for various cancers . It is listed in EML for urological, lung and gynaecological and other malignancies either alone or in combinations for various phases of treatment . these drugs have been contributory to improved outcomes in the listed tumours
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	Cisplatin and Carboplatin are accessible worldwide , and part of several treatment protocols for several cancer. Generic brands are available worldwide.
Any additional comments	This application is to remove the indication but , there is benefit of this medication in locally advanced head and neck cancer. The benefit in early stage is limited to local control and DFS . not OS. Contrarily to this assertion a recent update of MACH-NC was performed in 2017 with over 19000 patients proving benefit.
Based on your assessment of the application, and any additional evidence / relevant information identified during the review process, briefly summarize your proposed recommendation to the Expert Committee, including the supporting rationale for your conclusions, and any doubts/concerns in relation to the listing proposal.	Arguments for removing this indication are null and void and based on wrong assertions. There has not been any significant OS benefit to concomitant chemo RT even in the advanced stages rather a significant local disease control and DFS . Chemotherapy is not recommended generally for early head and cancer , Inspite relatively high grade 3 toxicity for cisplatin, carboplatin in high doses or with 5FU in small studies show similar efficacy and higher tolerability. I will not recommend removal of these drugs from the EML as they are effective in local control and DFS,
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