A.28 Toripalimab – EML 1st line esophageal squamous cell cancer / 1st and 2nd line nasopharyngeal carcinoma – EML*

Reviewer summary	☒ Supportive of the proposal for nasopharyngeal cancer ☒ Not supportive of the proposal for esophageal cancer and nasopharyngeal cancer Justification (based on considerations of the dimensions described below): Toripalimab is a PD-1 antibody Resubmission Toripalimab for esophageal squamous cell cancer: • One of five immune checkpoint inhibitor-based treatments being proposed for this indication. • More cost-effective compared to pembrolizumab, nivolumab and nivolumab combined with ipilimumab. • Against this backdrop, moderate gain in overall survival offset by cost, uncertainty in response durability, unclear role of PD-L1 expression as a predictive biomarker, potential for increased harms associated with poorer prognosis at baseline and lack of long-term data across the immune checkpoint inhibitors. Toripalimab NPC: in first line studied with chemotherapy including gemcitabine which is not on the EML
Does the EML and/or EMLc currently recommend alternative medicines for the proposed indication that can be considered therapeutic alternatives? (**https://list.essentialmeds.org/**) No checkpoint inhibitors for this indication Gemcitabine not listed on the EML for nasopharyngeal cancenr	☒ Yes ☒ No ☐ Not applicable ☐ No But gemcitabine not listed for this indication
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication? (e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;)	☒ Yes ☐ No ☐ Not applicable
Does adequate evidence exist for the safety/harms associated with the proposed medicine? (e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;) Esophageal cancer: Toripalimab + chemo versus chemo**:** the gains in overall survival are moderate in size (17 vs 11 months). They were offset by the unclear role of PD-L1 expression as a predictive biomarker**,** the potential threshold at PD-L1 CPS≥1, the potential for increased harm associated with poorer prognosis at baseline, and the lack of long-term data across the immune checkpoint inhibitors. No QoL data. Nasopharyngeal cancer: First-line Toripalimab modest effect on OS. The treatment arm in the pivotal randomized trial also included the chemotherapeutic gemcitabine, requiring its listing to be expanded to malignant neoplasms of the nasopharynx, beyond indications in the ovary, bronchus, and lung, which are already on the EML.	☒ Yes ☐ No ☐ Not applicable
Overall, does the proposed medicine have a favourable and meaningful balance of benefits to harms?	☒ Yes ☐ No ☐ Not applicable

Are there any special requirements for the safe, effective and appropriate use of the medicines? (e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc) As done for PD-1 antibodies	☒ Yes ☐ No ☐ Not applicable
Are there any issues regarding price, cost-effectiveness and budget implications in different settings?	☒ Yes ☐ No ☐ Not applicable
Is the medicine available and accessible across countries? (e.g. shortages, generics and biosimilars, pooled procurement programmes, access programmes) Yes, relatively less expensive than other PD_1 inhibitors	☒ Yes ☐ No ☐ Not applicable
Does the medicine have wide regulatory approval? <u>Esophageal cancer:</u> EMA approved, and NMPA (China) approved, FDA not approved <u>Nasopharyngeal cancer + chemo:</u> FDA, EMA, NMPA, Hong Kong, India approved <u>Nasopharyngeal cancer post-chemo:</u> FDA, NMPA, Hong Kong, India approved approved for marketing in over 30 countries and regions across 3 continents worldwide drug applications are under review by regulatory authorities in the UK, Australia, Singapore, South Africa, Chile and Jordan The most cost-effective option as the first-line therapy for advanced ESCC patients in China. The lower cost of toripalimab (USD 1.46 per mg) compared to other immune checkpoint inhibitors (e.g., USD 25.35 per mg for pembrolizumab), based on cost estimates derived from the YAOZH database, may result in better cost-effectiveness. Toripalimab + chemotherapy, when compared to chemotherapy, was cost-effective in China (incremental cost-utility ratio: USD 25,576/QALY) and US (incremental cost-effectiveness ratio: USD 74,004/QALY).	☒ Yes, for the proposed indication ☐ Yes, but only for other indications (off-label for proposed indication) ☐ No ☐ Not applicable