A.35	Tislelizumab – Platinum refractory locally advanced or metastatic urothelial cancer
Does the application adequately address the issue of the public health need for the medicine?	☒ Yes ☒ No ☐ Not applicable Comments: Urothelial cancers are likely to present at advanced stages and at risk of metastases and mortality. Information here is skewed toward china
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.	Available immunotherapy drugs include Pembrolizumab, atezolizumab, nivolumab and many newly developed drugs . Many of these drugs following high quality evidence are indicated for metastatic/locally advanced are most effective in the presence of high PD-1 expression by immune cells or tumour. In spite of clinical evidence supporting efficacy of immunotherapies in advanced cancer and their incorporation in protocols , only pembrolizumab and nivolumab are included in the model list . Tislelizumab is a new PD-1 monoclonal antibody , an immunotherapy drug currently undergoing clinical evaluation for efficacy in Platinum refractory urothelial. Other options to immunotherapy are paclitaxel, docetaxel, gemcitabine and doxorubicin with poor response rates.
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: A phase 3 trial RATIONALE 307 confirms efficacy of tislelizumab in the management of locally advanced squamous cell lung cancer. This may support the argument for safety .
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). All evidence in the literature for this indication is gleaned from phase 1 and 2 with very few cohorts or small non randomised trials with short follow up periods. Phase 3 trial quoted here is for hodgkins lymphoma. Table. 9-1 conclusion shows an ORR od 24% but non inferior OS and mPFS compared to other immunotherapy drugs . There currently no comparator studies ..

	Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Most of the data presented here on the drug is derived from Chinese data not readily accessible. Cannot confirm any phase 3 trials being done in China. It use is contraindicated in pregnant women, children under 18yrs as a precaution and in older persons following low grade evidence . .
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☐ Yes ☒ No ☐ Not applicable Comments: The quality of the evidence is low and therefore could not be admitted for evaluation. Anaemia and pyrexia the most common AE, only 18% discontinue treatment . 6 of 106 patients dies within the study period but not much information is given about the cost of death, It categorically states there is not much information about toxicities in certain groups of people
Are there any adverse effects of concern, or that may require special monitoring?	☒ Yes ☐ No ☐ Not applicable Comments: Pneumonitis, colitis, severe liver failure, endocrinopathies
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	There is insufficient evidence to make a decision on this , most likely an uncertain 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 for this application is low and the strength is very weak.
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: PD -1 testing . Standard adoption of reporting recommendation must be adopted. Patients must be clinically monitored by highly skilled personnel to recognise and manage AE.

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: This drug is currently only approved in China for this indication.
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:
Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	There are no cost effective analysis done , however in direct cost comparison, this medication is relatively cheaper in comparison to existing immunotherapy drugs. Following the necessary clinical trial applications , when established , this may be a cost effective PD-1 alternative for many LMIC.
Any additional comments	This drug has not been rigorously evaluated for efficacy and safety for the requested application. They is very little data to support this application
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.	I have genuine concerns about the quality of evidence to support listing of this drug for the intended purpose. For now I recommend rejection of application until further information is available whilst results are reproducible.
References (if required)	