I.5 Erythropoiesis stimulating agents – EML and EMLc

Reviewer summary	☐ Supportive of the proposal ☒ Not supportive of the proposal Justification (based on considerations of the dimensions described below): The application proposes a therapeutic group of different erythropoiesis-stimulating agents (ESAs) for supportive management in patients experiencing anemia <10g/dL during chemotherapy for cancer. The idea of having these as a therapeutic group is justified by their common mechanism of action, their demonstrated efficacy in clinical trials, the ability to titrate the drugs to clinical effect (ie level of hemoglobin) and their uniform toxicity profiles. ESAs are approved for this indication in many high income countries, but they are not subsidized in all high income jurisdictions. These drugs have been considered cost-effective in countries with high willingness-to-pay thresholds. Their judicious use (as in trials, and in practice following guidelines) improves hemoglobin levels, can reduce transfusions (but often not eliminate them), and may improve quality of life. They do not improve overall survival, and indeed there have been signals in trials for potential reduction in survival. The application prosecutes a case for filling a gap in LMICs where access to transfusions is limiting. While reasonable, no evidence as to the degree of benefit in those circumstances (eg redirection of the blood supply, more effective use of chemotherapy) is provided. The data and the application make the case that these drugs are desirable to have, but not the case that these are essential, in the absence of higher survival and/or major reduction in use of more expensive care. It is acknowledged that the increasing availability of biosimilars will likely aid in reducing their cost, which is the major barrier to uptake. However, it is also sobering to recognise a point made in the application that "prices can be higher in LMICs due to import and supply chain costs". In any future application, it would be helpful to know what proportion of ESA use in LMICs (or indicative countries) will be for this indication as compared with the existing EML listings for chronic anemia of renal failure. Will an expansion of the ESA market reduce unnecessary import and supply chain costs?
Does the EML and/or EMLc currently recommend alternative medicines for the proposed indication that can be considered therapeutic alternatives? (**https://list.essentialmeds.org/**)	☐ Yes ☐ No ☐ Not applicable
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;)	☐ 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?	☐ Yes ☐ No ☐ Not applicable

(e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)	
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 ☐ No ☐ Not applicable
Does the medicine have wide regulatory approval?	☐ Yes, for the proposed indication ☐ Yes, but only for other indications (off-label for proposed indication) ☐ No ☐ Not applicable