A.31 Ustekinumab – EML and EMLc

Reviewer summary	☐ Supportive of the proposal ☒ Not supportive of the proposal Justification (based on considerations of the dimensions described below): The effectiveness and safety profile of biologics are generally better than the conventional systemic agents. Ustekinumab is also have superior efficacy and safety profile compare to TNF inhibitors like adalimumab. However, current recommendation in major guidelines place it as treatment with 2nd line label for moderate to severe psoriasis treatment after TNF inhibitors, likely due to its higher cost. Another biologic agent which is currently in the EML and EMLc is thus preferred.
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 Despite 8 options of medicine in the EML, only one is for systemic therapy.
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;) Evidence are from systematic review (incl a 2023 Cochrane SR), RCTs and real-world studies for long-term outcomes although nearly all RCTs are in western countries on a population of predominantly of European ancestry. Certainty of evidence are predominantly from moderate to high.	☒ 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;) A Cochrane systematic review reported low number of SAEs and no clear differences between the treatments for the safety profile of SAEs (low to very low or moderate certainty in the evidence for this outcome). Long-term studies and real-world studies also reported that SAEs are rare. The risk of serious infections and reactivation of TB is among the lowest compare to other biologics.	☒ Yes ☐ No ☐ Not applicable
Overall, does the proposed medicine have a favourable and meaningful balance of benefits to harms? Effectiveness has been established with favourable long-term safety than the current systematic agent in the EML.	☒ 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)	☒ Yes ☐ No ☐ Not applicable

SC injection, can be self-administered but needs proper training. The dosing schedule (12 weeks) is less frequent than adalimumab. Requires cold chain storage, typically needing to be kept refrigerated until administration. Pre-treatment recommended laboratory parameters consist of full blood count, liver enzymes, serum creatinine, urine status, pregnancy test, C-reactive protein, hepatitis-B-virus, hepatitis-C virus, human immunodeficiency virus, and an interferon-gamma release assay to exclude TB. During treatment, control of full blood count and liver enzymes is recommended every 3-6 months.	
Are there any issues regarding price, cost-effectiveness and budget implications in different settings? Cost-effectiveness studies are comparing between the biologics and besides high-income countries also include Thailand and Costa Rica. The costs are still higher compare to the conventional systemic agent. Compare to adalimumab the cost-effectiveness of Ustekinumab is higher in some studies but lower in others.	☒ Yes ☐ No ☐ Not applicable
Is the medicine available and accessible across countries? (e.g. shortages, generics and biosimilars, pooled procurement programmes, access programmes) Available in 46 countries (not available in Africa and South-east Asia region). Several biosimilars are available.	☐ Yes ☒ No ☐ Not applicable
Does the medicine have wide regulatory approval?	☒ Yes, for the proposed indication From 7 SRAs and 2 NRAs (Saudi Arabia and Singapore). ☐ Yes, but only for other indications (off-label for proposed indication) ☐ No ☐ Not applicable