A.20 (item number)	Long-acting insulin analogues - diabetes (application title)
Does the application adequately address the issue of the public health need for the medicine?	☐ Yes ☒ No ☐ Not applicable Comments: Although it is stated in the application that diabetes affects significant number of people (463 million) globally and they might need to be treated by insulin at some point, it did not address that a large proportion of them is from LMIC where the higher cost of analogue insulin is an important factor. Besides that, the challenge of insulin largely due to affordability and access, while the price of analogue insulin is significantly higher than the human insulin (IDF, 2019)
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.	Long-acting insulin analogues are synthetic insulin used as an alternative to human insulin (currently included in the EML). It is said to be a safer and more convenient choice compare to human insulin with regards to the occurrence of hypoglycaemia as a common adverse event of insulin treatment.
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:

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). Many studies show small benefit of LA insulin analogues and containing high risk of bias resulting in low evidence certainty. Is there evidence of efficacy in diverse settings (e.g. low-resource settings) and/or populations (e.g. children, the elderly, pregnant patients)? Some of the studies conducted in LMIC, yet it sponsored by the pharma; only one cost-effectiveness study conducted in LMIC (Brazil) and did not show as cost-effective. No specific high-quality evidence is presented on children or pregnant women
Does the application provide adequate evidence of the safety and adverse effects associated with the medicine?	☒ Yes ☐ No ☐ Not applicable Comments: The safety and adverse effects show small or no difference compare to human insulin
Are there any adverse effects of concern, or that may require special monitoring?	☐ Yes ☒ No ☐ Not applicable Comments:
Briefly summarize your assessment of the overall benefit to risk ratio of the medicine (e.g. favourable, uncertain, etc.)	Small benefit of the LA insulin analogues over human insulin in term of prevention of hypoglicemia and reduction of A1c

Briefly summarize your assessment of the overall quality of the evidence for the medicine(s) (e.g. high, moderate, low etc.)	The overall quality of evidence is low
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: Its use as well as other facets of treatment involved, such as diagnostic tests, specialized treatment facilities, administration requirements, monitoring requirements and skill levels of health care providers, are identical to those needed for human insulin, except for the possible need for a pen device that accepts replaceable cartridges.
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: Approved in US, EMA, Japan, Canada, Australia Registered in 45 countries
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: Guidelines on second- and third-line medicines and type of insulin for the control of blood glucose levels in nonpregnant adults with diabetes mellitus (WHO, 2018) “Consider long-acting insulin analogues to manage blood glucose in adults with type 1 or type 2 diabetes who have frequent severe hypoglycaemia with human insulin” (weak recommendation,* moderate-quality evidence for severe hypoglycaemia).

Briefly summarize your assessment of any issues regarding access, cost and affordability of the medicine in different settings.	The challenge of access to insulin persists for many populations globally due to two main factors affordability and availability. For LMIC access to the cheaper human insulin is yet to be improve. However, in several Asian countries, the price of LA insulin analogue is not highly different with the human insulin. Therefore, some advocation and policy actions to reduce the price must be put forward.
Any additional comments	In giving insulin therapy we must also consider patient's value. The LA insulin analogue which was given once a day is surely preferable for the patients. The mode of delivery is also a factor to consider. The use of pens which is more convenient for patients could also improve adherence.
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.	Its small difference in effectiveness and safety compare to human insulin with its current high price might lower its cost-effectiveness, especially in limited setting. However, efforts through advocacy and policy action (some already on their way) should be continuously pursued to improve its affordability and access. Moreover, patients' value is also highly matter. Hence, we recommend to include in the EML.
References (if required)	International Diabetes Federation. IDF Diabetes Atlas: Ninth edition 2019 [Internet]. Available from: https://diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9efinal-web.pdf World Health Organization. Guidelines on second-and third-line medicines and type of insulin for the control of blood glucose levels in non-pregnant adults with diabetes mellitus [Internet]. 2018 [cited 2021 Feb 14]. Available from: https://apps.who.int/iris/bitstream/handle/10665/272433/9789241550284-eng.pdf