

Health Action International/ACCISS Study Statement to the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines.

Application to list long-acting analogue insulins (glargine, detemir and degludec) in the WHO Model List of Essential Medicines.

At the last meeting of the Expert Committee, it was concluded that while long-acting analogue insulins are an effective treatment for type 1 diabetes, the available evidence showed that efficacy and safety advantages of analogues compared to NPH human insulin were insufficiently large enough to justify the price differential. The Committee recommended that World Health Organization (WHO) take a comprehensive approach to address access to insulin and gave specific recommendations.

On the issue of the effectiveness of long-acting analogues over NPH human insulin, since 2019, three systematic reviews on the use of long-acting analogues have been published and are referenced in the current application. Two are Cochrane reviews (by Hemmingsen et al. and Semlitsch et al.) and the third is a network meta-analysis by Tricco et al. The application states that these three reviews are an “endorsement” of the use of long-acting analogues, but this conclusion is not supported by the review findings.

The application uses the Tricco study to argue for the inclusion of analogues for children and adults, and for both type 1 and type 2 diabetes, but this study only included those over 16 years with type 1 diabetes. The Cochrane review by Semlitsch found that most trials did not report patient-relevant outcomes, therefore it cannot be considered an endorsement for analogue use in type 2 diabetes. The Cochrane review by Hemmingsen concluded that both glargine and detemir showed no benefits compared to NPH insulin for severe nocturnal hypoglycaemia or any other of the main outcomes. Therefore, the application fails to provide any new evidence that would justify listing long-acting analogues in the Model List of Essential Medicines (EML).

On the issue of the price differential, the application does not provide any new price data. As part of the ACCISS Study, we collected recent government procurement prices. Long-acting analogues were up to six times the price of NPH insulin, which is what was found in earlier surveys. These higher prices impact treatment affordability for both governments and individuals.

Of concern is the impact that listing these analogues in the EML will have in resource-constrained countries. It will pressure governments to add them to their national EMLs and procure them. Unless there are significant increases in pharmaceutical budgets, less insulin can be purchased, which will result in fewer people receiving insulin.

The application claims that there is likely to be greater interest in analogues from biosimilar manufacturers due to greater prospects of revenues, resulting in more biosimilar competitors entering the market and lower prices. Over a dozen companies currently market biosimilar long-acting analogues, but their market penetration is extremely low, due primarily to the domination of the three large multi-national companies. Because of this, and the high cost of investment, very few new manufacturers are likely to enter the market because of listing analogues in the Model

List. The application also claims it is reasonable to expect that with EML inclusion, analogue prices will drop significantly in the next five years. This seems unlikely due to the lack of true market competition.

In lower-income countries, and some wealthy nations, access to insulin remains life-threateningly poor. However, there is a way forward. Last month's World Health Assembly resolution on diabetes and the Global Diabetes Compact provide platforms to act both on the Expert Committee's original recommendations and additional commitments needed by WHO, countries, and insulin manufacturers, including:

- Ensuring more affordable human insulins remain on the market
- Developing a comprehensive approach to addressing high insulin prices that includes establishing a ceiling price for both analogue and human insulin in low- and middle-income countries, and providing support to countries on procurement and pricing policies
- Implementing a global reporting mechanism of net prices of all insulins purchased by governments
- Regularly monitoring the availability, patient price and affordability of all insulins
- Including insulin and diabetes-related supplies in Universal Health Coverage
- Strengthening health systems and policy frameworks to ensure clinical guidelines, and health professional and insulin-user training and education

The Compact and the Resolution provide the foundations to finally address what is needed to guarantee access to insulin for all. Until the fundamental issues are addressed, adding long-acting analogues to the EML may create even more problems.