HEALTH ACTION INTERNATIONAL

20 May 2021

The Secretary
Expert Committee on the Selection and Use of Essential Medicines
Medicines Selection, IP and Affordability (MIA)
Department of Health Products Policy and Standards (HPS)
20 Avenue Appia
CH-1211 Geneva 27

Dear Secretary,

RE: Application to add (ultra-) long-acting insulin analogues to the WHO Model List of Essential Medicines

According to the World Health Organization (WHO), essential medicines are selected based on public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness, and are intended to be available at a price that is affordable. Health Action International's (HAI) Addressing the Challenge and Constraints of Insulin Sources and Supply (ACCISS) Study is opposed to the inclusion of long-acting analogue insulins (glargine, detemir, degludec) on the WHO Model List of Essential Medicines (EML) because the application (1) does not provide new evidence on the effectiveness of long-acting analogue insulins over NPH human insulin; (2) does not address the high price differentials between long-acting analogues and human insulin, which impacts affordability for both governments and individuals; and (3) does not recognise the recommendations from the 2019 Expert Committee meeting and the opportunity that they be addressed within the Global Diabetes Compact.

Since the last application was considered in 2019, three systematic reviews on the use of long-acting analogues have been publish and are referenced in the application—a network meta-analysis by Tricco et al.[1] and two Cochrane Reviews by Hemmingsen et al.[2] and Semlitsch et al.[3]

The current application states that these reviews support the use of long-acting analogues for people living with type 1 and type 2 diabetes, which is incorrect. The Tricco study, which is used to argue for the inclusion of analogue insulins for children and adults with type 1 and type 2 diabetes, only included subjects above the age of 16 living with type 1 diabetes. The main findings from the Cochrane reviews were that there was no clear differences between glargine with NPH insulin for all main therapeutic outcomes. While it was noted that severe hypoglycaemic episodes were reduced with detemir, the results were found to be inconsistent and, if another study was performed, there may be no clear difference between detemir and NPH insulin. Further,

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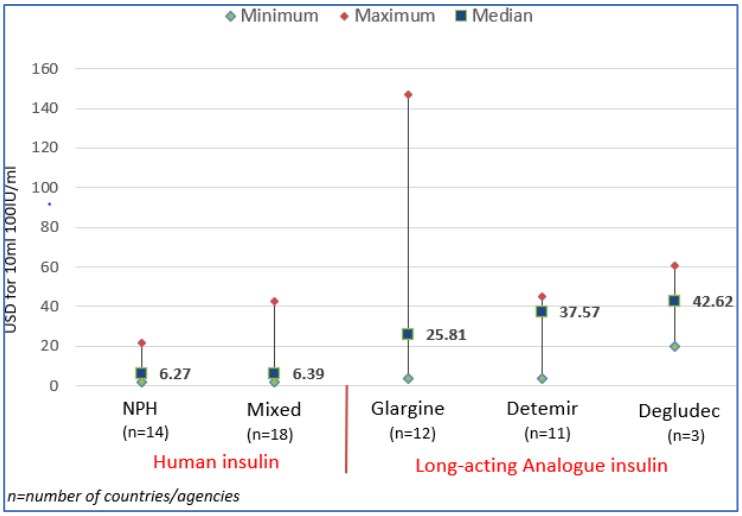
Hemmingsen suggests there was no clear difference in long-acting analogues and NPH regarding the risk of severe nocturnal hypoglycaemia. In the conclusion of the Semlitsch review it states that most trials under review did not report patient-relevant outcomes, and it cannot therefore be considered an endorsement of the use of long-acting analogues for type 2 diabetes.

Regarding prices, governments continue to pay higher prices for long-acting analogues than human insulin, as seen from data recently collected by the ACCISS Study from 19 countries and two United Nations agencies. The median procurement price, in USD for 10ml 100IU/ml, for NPH and mixed human insulin was $6.27 and $6.39 respectively, as shown in Figure 1. Median prices of long-acting analogues were up to six times higher at $25.81 (glargine), $37.57 (detemir) and $42.62 (degludec). If countries were persuaded to switch from buying human insulin to analogues, pharmaceutical budgets would have to increase to compensate for the higher prices. Without this, fewer people will receive insulin treatment.

Figure 1. Procurement prices, in USD for 10ml 100IU/ml, human and long-acting analogue insulins



The claim is made in the application that there is likely to be greater interest in analogues from biosimilar manufacturers due to greater prospects of revenues, and this will result in greater number of biosimilar competitors entering the market and lower prices. We know of over a dozen companies who currently market biosimilar long-acting analogues, including two of the three large multi-nationals who control over 90% of the global insulin market.
However, the market penetration of these biosimilar companies remains extremely low, due primarily to the domination of the market by the three multi-national companies. Coupled with the high cost of investment, it is likely that very few new manufacturers will enter the market as a consequence of adding long-acting analogues to the WHO Model EML.

It is also claimed in the application that it is reasonable to expect that with listing in the WHO Model EML, the price of long-acting analogues will reduce significantly in the near-to-medium term (e.g., five years). Significant reductions seem unlikely due to the lack of any true market competition. Godman, in his supplementary report to the Committee on insulin prices trends in selected high-, middle- and low-income countries[4] concluded that acquisition prices of long-acting analogues are falling but provides scant evidence of this. However, he makes it clear that the affordability of these insulins is problematic, particularly in Africa, Asia and South America, where access to insulin remains life-threateningly poor.

Moreover, Godman states the first priority should be to ensure NPH insulin and glucose monitoring devices are readily available and accessible nationally, for all people in need, before considering more expensive long-acting analogues. We support this view. ACCISS Study surveys have shown that human insulin remains unaffordable and out of reach of people on low wages in LMICs.[5] Buying analogues would amount to a crippling financial burden to people living with diabetes, and to governments across the globe now facing crippling debt due to the COVID-19 pandemic.

At their 2019 meeting, the WHO Expert Committee recommended a series of coordinated actions be undertaken to address insulin access and affordability.[6] The newly launched Global Diabetes Compact provides a platform to act on those original recommendations. But to improve access to insulin, additional commitments beyond the original recommendations must be made by WHO, Member States and insulin manufacturers, including:

- Ensuring human insulins remain on the market
- Addressing current regulatory barriers for biosimilar insulins
- Developing a comprehensive approach to addressing insulin prices that includes:
    - establishing a ceiling price for analogue insulin in LMICs commensurate with Novo Nordisk's ceiling price of $3 for human insulin
    - providing support for countries on pricing policies
- Implementing a global price reporting mechanism for net prices of all insulins (human and analogue) purchased by governments to assist procurers in determining reasonable prices (in line with WHA Resolution 72.8 on transparency)
- Regularly monitor 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, health professional and insulin user training and education include information about all insulins

In this centenary year of the discovery of insulin, half of all people who need insulin cannot access it. Without concrete actions taken by WHO, Member States and others, we do not see how adding long-acting analogue insulin to the WHO Model EML at this time will improve this situation.

Faithfully,

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References

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2. Hemmingsen B, Metzendorf MI, Richter B (2021) (Ultra-)long-acting insulin analogues for people with type 1 diabetes mellitus. Cochrane Database Syst Rev 3: CD013498. 10.1002/14651858.CD013498.pub2

3. Semlitsch T, Engler J, Siebenhofer A, Jeitler K, Berghold A, Horvath K (2020) (Ultra-)long-acting insulin analogues versus NPH insulin (human isophane insulin) for adults with type 2 diabetes mellitus. Cochrane Database Syst Rev 11: CD005613. 10.1002/14651858.CD005613.pub4

4. Godman B (2021) Report for the 2021 WHO Expert Committee on Selection and Use of Essential Medicines on recent insulin price trends in a sample of countries (including but not necessarily limited to low- and middle-income countries), exploring key issues and suggestions for the future to enhance utilisation and funding for long-acting insulin analogues given current concerns.

5. Ewen M, Joose H-J, Beran D, Laing R. Insulin prices, availability and affordability in 13 low-income and middle-income countries. BMJ Global Health 2019;4:e001410 doi:10.116/bmjgh-2019-001410

6. Executive summary: the selection and use of essential medicines 2019: report of the 22nd WHO Expert Committee on the selection and use of essential medicines. WHO, Geneva, 1-5 April 2019.