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April 16, 2025

Response to: **A.18 Insulin, analogue rapid-acting – diabetes mellitus**

Dear WHO Essential Medicines List team,

I am writing this letter in my personal capacity as someone living with type 1 diabetes for more than 30 years who works as a midwife specialising in pregnancies affected by diabetes. I have personal and clinical experience using various insulins, including regular human, NPH insulin, insulin glargine, insulin detemir and now use an insulin pump with insulin lispro only. I strongly support T1International's application to add analogue rapid-acting insulins to treat diabetes mellitus to the WHO Essential Medicines List (EML) for the following reasons.

1) **The significant reduction of hypoglycaemic events** is seen when taking rapid-acting insulin analogues compared to human insulin. Hypoglycaemic events are life-threatening, highly disruptive and impede the ability of people living with diabetes to work and perform everyday tasks. Access to technologies to measure blood glucose levels is greatly reduced in low- and middle-income countries, compared to high-income countries, further strengthening the need to reduce the frequency and severity of hypoglycaemic reactions. Reducing hypoglycaemic reactions is a primary reason to support the inclusion of analogue rapid-acting insulins, not a fringe benefit.

Studies supporting reductions in hypoglycaemia include:

Melo KFS, Bahia LR, Pasinato B, Porfirio GJM, Martimbianco AL, Riera R, Calliari LEP, Minicucci WJ, Turatti LAA, Pedrosa HC, Schaan BD. Short-acting insulin analogues versus regular human insulin on postprandial glucose and hypoglycemia in type 1 diabetes mellitus: a systematic review and meta-analysis. Diabetol Metab Syndr. 2019 Jan 3;11:2. doi: 10.1186/s13098-018-0397-3. PMID: 30622653; PMCID: PMC6317184.

Pedersen-Bjergaard U, Kristensen PL, Beck-Nielsen H, Nørgaard K, Perrild H, Christiansen JS, Jensen T, Hougaard P, Parving HH, Thorsteinsson B, Tarnow L. Effect of insulin analogues on risk of severe hypoglycaemia in patients with type 1 diabetes prone to recurrent severe hypoglycaemia (HypoAna trial): a prospective, randomised, open-label, blinded-endpoint crossover trial. Lancet Diabetes Endocrinol. 2014 Jul;2(7):553-61. doi: 10.1016/S2213-8587(14)70073-7. Epub 2014 May 2. PMID: 24794703.

2) **There has been an over-emphasis on HbA1c in prior analysis of this question at the expense of other outcomes**. HbA1c is used as a marker of mean blood glucose levels over a prior 90-day period. However, as a marker of mean, frequent hypoglycaemic reactions will pull down an HbA1c. A patient with 6 hypoglycaemic reactions a week

vs 1 hypoglycaemic reaction a week may have similar HbA1c but I can assure you the one with 1 hypoglycaemic reaction will have a greatly improved quality of life. In some high-income countries, the importance placed on HbA1c is being reduced in favour of time in range and other measures of glycaemia. In addition, the flexibility offered by short-acting insulin analogues is underappreciated by an HbA1c-centric view. Human insulin requires administration up to 45 minutes before eating. Short-acting insulin analogues can be taken immediately before eating. This increases the quality of life for people with diabetes.

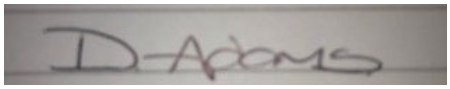
3) **Equity.** When a newly diagnosed type one diabetic person in Western Europe presents with diabetic ketoacidosis, they are immediately prescribed insulin analogues. The superiority of analogues is well understood in high-income countries and has been for decades. Insulin analogues are the mainstay of type 1 diabetes management. This recent publication eloquently summarises their benefits:

JA Elliott, S Ajmal, MTU Barone. 2025. PLOS Global Health Blog Speaking of Medicine and Health. Analogue vs Human Insulin in Low-Income Country Settings: the Debate is Over *https://speakingofmedicine.plos.org/2025/03/14/comment-analogue-vs-human-insulin-in-low-income-country-settings-the-debate-is-over/*

The Brazilian example above demonstrates that healthcare systems can acquire rapid-acting insulin analogues at a lower price by leveraging purchasing power. The high acquisition price of these agents should not be a reason for keeping off the EML. Indeed, the WHO should redouble efforts to assist Member States in acquiring all forms of diabetes treatment needed to fulfil the global diabetes coverage targets, which include 100% of people with type 1 diabetes having access to affordable insulin and blood glucose self-monitoring.

Where type 1 diabetes treatment is concerned, the WHO should advocate for and help convene stakeholders for basal/bolus regimes utilising the best insulins available, not just the least expensive or most convenient to acquire from the private sector.

Yours sincerely,



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