Insulin icodec explained

What is insulin icodec?

Insulin icodec is a **once-weekly basal insulin analogue** designed to cover the basal insulin requirements for a full week with a **single subcutaneous injection**. It is currently under investigation for the treatment of type 1 and 2 diabetes in the phase 3 ONWARDS programme[1–6].

The ONWARDS clinical development programme comprises six phase 3a global clinical trials, including a trial with real-world elements, involving more than 4,000 adults with type 1 or type 2 diabetes[1–6].

Once-weekly insulin icodec could significantly reduce the number of injections per year[1–6]:

x52 — vs — **x365**

The potential of once-weekly insulin icodec

Once-weekly insulin icodec has the potential to redefine insulin therapy and reinvent the insulin start experience:

- **Simple dosing and titration** could help healthcare providers to **initiate insulin icodec with confidence**[7]
- **Fewer injections could reduce treatment burden**[7,8]
- **Potential to improve adherence**, leading to **more time in range and better glycaemic control**[7,8]

Insulin icodec embodies Novo Nordisk's **commitment to sustainability** with a reduction in the number of pens (due to less frequent dosing) and aims to reduce the impact of plastic and CO_2 by 80% compared with once-daily insulin[9].

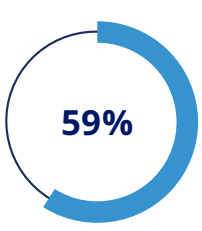
What is the current unmet need?

Insulin remains the cornerstone of diabetes treatment. However, initiation of insulin therapy in type 2 diabetes is often delayed[10], despite uncontrolled blood sugar levels, leading to increased risk of diabetes-related complications[11].

Injection burden is a major barrier to insulin initiation:

50% of people with type 2 diabetes needing insulin therapy **delay initiation** by an average of **15 months**[12].

1/3 of all people with diabetes **are not adherent to daily insulin therapy**[10,13].



of physicians identified the number of **daily injections** as a difficulty for patients[10].

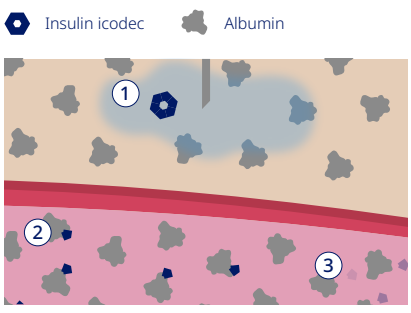
x1

Once-weekly dosing is associated with **improved patient adherence compared with once-daily dosing**[14].

How does insulin icodec work?

The insulin icodec molecule has been **engineered by modifying human insulin**, to give a **prolonged half-life of approximately 7 days**[15,16].

Three amino acid substitutions have been introduced to provide molecular stability, minimise the enzymatic breakdown of insulin icodec and reduce receptor-mediated clearance[15].



1. Once-weekly insulin icodec is injected subcutaneously
2. Although a week's worth of insulin is administered, almost all icodec binds to a protein in the blood, albumin, to form an essentially inactive depot
3. Slowly, insulin icodec is released from albumin to achieve effective glucose lowering throughout the week

Insulin icodec achieves **similar glucose-lowering effect at steady state** (after three to four weekly doses) with **considerably fewer injections** compared with once-daily insulin[17].

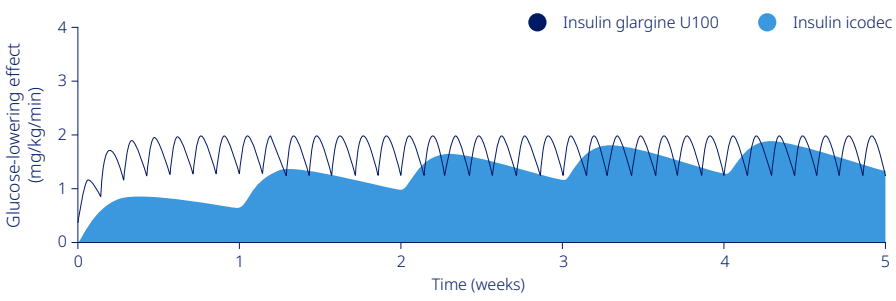


Diagram showing modelling of the increase in glucose-lowering effect over time (based on phase 1 data)

What is the formulation and dosing of insulin icodec?

Insulin icodec is **formulated as 700 units/mL** to ensure that the injection volume is similar to that of once-daily basal insulin[8]. It is designed to be injected subcutaneously once a week with an **easy-to-use pen and optional digital support** for personalised automated dose guidance.

References

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04848480 Last accessed: September 2022.
2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04880850 Last accessed: September 2022.
3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04795531 Last accessed: September 2022.
4. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04460885 Last accessed: September 2022.
5. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04770532 Last accessed: September 2022.
6. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04760626 Last accessed: September 2022.
7. Lingvay I, et al. *Diabetes Care*. 2021; 44:1–9.
8. Bajaj HS, et al. *Diabetes Care*. 2021; 44:1586–1594.
9. Corporate Environmental Strategy, Novo Nordisk, 2021.
10. Peyrot M, et al. *Diabet Med*. 2012; 29:682–689.
11. Deshpande AD, et al. *Phys Ther*. 2008; 88:1254–1264.
12. Company Investor Presentation, Novo Nordisk, 2020.
13. Okemah J, et al. *Adv Ther*. 2018; 35:1735–1745.
14. Polonsky WH, et al. *Diabetes Ther*. 2022; 13:175–187.
15. Nishimura E, et al. *Diabetes*. 2020; 69(Suppl 1):236-OR.
16. Rosenstock J, et al. *New Engl J Med*. 2020; 383:2107–2116.
17. Nishimura E, et al. *BMJ Open Diab Res Care*. 2021;9:e002301.

PromoMats ID: HQ22ICD00009 September 2022

novo nordisk®