CLOSER LOOK

MEMORANDUM

Novo Nordisk's Awiqli (once-weekly insulin icodec) receives FDA approval for adults with T2D – March 26, 2026

FDA approval of the first once-weekly insulin based on the phase 3 ONWARDS program; Novo Nordisk plans nationwide launch for 2H26

Novo Nordisk announced today the approval of its once-weekly basal insulin, Awiqli (insulin icodec), for adults with T2D in the US. Awiqli is the first once-weekly insulin to receive FDA approval and is expected to launch nationwide in 2H26.

As background, Novo Nordisk resubmitted Awiqli to the FDA in September 2025 after the administration issued a Complete Response Letter (CRL) in July 2024, requesting information about manufacturing processes as well as further information for a T1D indication. Novo Nordisk did not pursue an indication for T1D in its resubmission.

Table of Contents

Approval based on findings from the phase 3 ONWARDS program

The ONWARDS program includes six phase 3a trials evaluating once-weekly insulin icodec compared to once-daily basal insulin (glargine) across insulin-naïve, basal-experienced, and basal-bolus T2D and T1D. See table below in the appendix.

- The ONWARDS-1 trial (n=984) investigated insulin icodec in insulin-naïve adults with T2D. At Week 52, icodec use was associated with a greater reduction in A1c and an A1c <7%. Hypoglycemia rates were low and relatively similar, though slightly higher in the insulin icodec group.
- The ONWARDS-2 trial (n=526) studied insulin icodec in adults with T2D inadequately controlled on once- or twice-daily basal insulin. At Week 26, icodec conferred noninferior and statistically superior A1c reductions to once-daily insulins. Hypoglycemia rates were low but numerically higher (no statistical significance) with insulin icodec.
- The ONWARDS-3 trial (n=588) evaluated insulin icodec in adults with T2D on non-insulin glucose-lowering therapies (insulin-naïve). At Week 26, icodec use demonstrated superior A1c reductions. Hypoglycemia rates were low but ~60% greater (no statistical significance) with insulin icodec.
- The ONWARDS-4 trial (n=582) investigated insulin icodec in adults with long-standing T2D with basal-bolus insulin regimens. At Week 26, icodec conferred non-inferior A1c reductions to glargine. Icodec use was associated with lower total weekly basal insulin volume, plus reduced bolus requirements, at the end of treatment. Hypoglycemia rates were similar across icodec and glargine groups.
- The ONWARDS-5 trial (n=1,085) studied insulin icodec in adults with insulin-naïve T2D, with a more real-

world-like design including digital titration support. At Week 52, icodec and digital support use showed superior A1c reduction to glargine, along with improved patient-reported satisfaction and preference for once-weekly dosing. Hypoglycemia was similar across arms.

- The ONWARDS-6 trial (n=582) evaluated insulin icodec in adults with T1D on basal-bolus therapy. At Week 26, icodec conferred non-inferior A1c reductions to glargine. Hypoglycemia rates were higher with icodec (roughly double events per patient-year).

In its press release, Novo Nordisk cited ONWARDS 1-4 as supporting today's FDA approval.

Awiqli was first approved OUS in March 2024; Currently launched in the EU and 12 other countries

In March 2024, Awiqli was approved in its first country, Canada, for T1D and T2D. They were soon followed by the EU and the UK, which approved Awiqli for T1D and T2D in May 2024. As of today, Awiqli is now approved in the US, EU, and 13 other countries.

Though FDA labeling has not yet been released, dosing, titration, and practical use considerations will likely be similar to the EMA's. Currently, Awiqli is available in the EU and UK in prefilled, FlexTouch pens. Depending on volume, pens can contain 700, 1,050, or 2,100 units, depending on volume – though dose is specified directly by the patient in insulin units.

For insulin-naïve T2D, the recommended starting dose of Awiqli is 70 units after an initial 110-unit "loading dose." Adjustments are specified based on fasting plasma glucose levels. When switching from daily basal to Awiqli, EMA labeling recommends an initial dose of 7x the individual's daily basal insulin dose. For faster glycemic control in both T1D and T2D, the EMA also recommends a one-time "loading dose," wherein patients increase this 7x figure by 50% for their first dose. Subsequent weekly doses should reflect the 7x daily dose number.

Resubmission and approval follow the EMDAC meeting in May 2024 and Complete Response Letter in July 2024

Novo Nordisk first submitted Awiqli to the FDA in April 2023. Subsequently, the FDA held an EMDAC meeting in May 2024, which ended in a 4:7 vote against Awiqli's benefit-to-risk profile. Nevertheless, panelists agreed that some patients would benefit from a once-weekly insulin. Still, they cited concerns related to higher rates of severe hypoglycemia observed in the ONWARDS 6 trial, which compared Awiqli and daily insulin degludec in T1D. Panelists also emphasized a need to further understand: (i) who may benefit most from this therapy; (ii) how this therapy could confer benefits in the real world; and (iii) to what degree strategies, such as CGM use and bolus adjustments, can mitigate hypoglycemia risk without offsetting those benefits. While all of these could have been addressed post-approval, the CRL prompted months of delays for Novo Nordisk.

Later that year, in July 2024, the FDA issued a CRL including requests related to the manufacturing process and questions around the risk-to-benefit ratio of a T1D indication. Upon the receipt of the CRL, Novo Nordisk had said that it would address the requests after 2024.

Lilly's once-weekly insulin efsitora alfa demonstrated similarly promising results for T2D in phase 3 QWINT trials

Separately, Lilly's once-weekly insulin efsitora alfa also demonstrated noninferior efficacy in A1c reduction across its phase 3 QWINT program, which compared insulin efsitora alfa to insulin glargine and insulin degludec in people with T2D (QWINT-1, QWINT-2, QWINT-3, and QWINT-4), and T1D (QWINT-5).

Rates of severe or clinically significant hypoglycemia were not statistically different between participants taking insulin efsitora alfa compared to insulin glargine or degludec, except in the QWINT-1 trial, in which hypoglycemia rates were 40% lower in participants taking insulin efsitora alfa. However, in QWINT-5, insulin efsitora alfa was associated with higher rates of severe hypoglycemia than insulin degludec in T1D, inspiring uncertainty around the pursuit of this indication in the US and what the company might hear from the FDA – particularly after Novo Nordisk's experience.

Lilly submitted for regulatory approval for T2D in the EU in 2Q25. In 1Q25, Lilly also shared plans to file for approval in the US and Japan for T2D. Management did not provide clear plans for the T1D indication or what the next steps in the US might look like for once-weekly insulin's role in T1D.

Once-weekly insulin can significantly lower the burden of diabetes management

At ATTD 2026, experts highlighted the benefits of once-weekly insulin in managing T2D. Once-weekly insulin can lower the injection burden from once-daily to once-weekly and reduce the barrier to initiating insulin treatment without compromising glycemic benefits or introducing hypoglycemia risks.

Provider and patient education would be important for the uptake of once-weekly insulin. For example, Dr. Athena Philis-Tsimikas (Scripps Health) clarified that a missed or doubled dose of once-weekly insulin had minimal effects on Time in Range. GLP-1 RA use did not affect the safety or efficacy of insulin icodec either. Finally, in perioperative settings, once-weekly insulins should be discontinued weeks ahead of the operation (four weeks for insulin icodec; eight weeks for efsitora alfa).

KOL Commentary: Awiqli may offer access benefits for broader populations

Dr. Zachary Bloomgarden (Mount Sinai Hospital): An important implication is that, as long as CGM is only available to people using insulin, [Awiqli] would allow us to even more easily offer to many people the option to use low-dose weekly insulin – when appropriate – in conjunction with starting to use sensors. I see low dose weekly insulin with GLP-1 RAs and CGM as a major opportunity to easily get people with diabetes to a sub 7.0% A1c goal!

Close Concerns' Questions

1. Does Novo Nordisk plan to pursue a T1D indication for Awiqli?
2. Will FDA guidance for Awiqli in T2D differ from the EMA's?
3. How might this approval of Awiqli impact Standards of Care for those with T2D on basal insulin?
4. How does Novo Nordisk plan to promote education and raise awareness about once-weekly insulin?
5. How should once-weekly insulin be used in children, pregnant or lactating women, individuals with hypoglycemia unawareness, or those newly diagnosed with T1D?
6. How does Novo Nordisk envision the role of CGMs to be for people taking once-weekly insulin? Could this mitigate concerns patients may have about the high weekly dosage?

-- by Elizabeth Rose, Kat Moon, Nour Khachemoune, and Kelly Close

Appendix: Results from the ONWARDS program across six phase 3 trials in type 1 and type 2 diabetes

	Enrollment	Comparator/ Design	Timeline	Primary outcome (* = statistically significant)
ONWARDS 1	984	vs. glargine U100; insulin naïve patients with T2D; 78 weeks	Topline results announced June 2022; Completed November 2022	A1c change*: -1.55% vs. -1.35% from 8.5% baseline
ONWARDS 2	526	vs. degludec; patients on basal insulin with T2D; 26 weeks	Topline results announced April 28, 2022; Completed March 2022	A1c change*: -0.93% vs. -0.71% from 8% baseline
ONWARDS 3	574	vs. degludec; insulin	Topline results	A1c change*: -1.57%

		naïve patients with T2D; 26 weeks; injected as pen	announced July 2022; Completed June 2022	vs. 1.36% from 8.5% baseline
ONWARDS 4	578	vs. glargine; patients on basal and bolus insulin with T2D; 26 weeks	Topline results announced July 2022; Completed June 2022	A1c change: -1.16% vs. -1.18% from 8.3% baseline
ONWARDS 5	1,085	vs. glargine U100, glargine U300, and degludec; insulin naïve patients with T2D with an app providing dosing recommendations; 52 weeks	Topline results announced in October 2022; Completed August 2022	A1c change*: -1.68% vs. -1.31% from 8.9% baseline
ONWARDS 6	580	vs. degludec; patients on basal and bolus insulin with T1D; 26 weeks	Topline results announced June 2022; Completed December 2022	A1c change: -0.47% vs. -0.51% from 7.6% baseline Icodec had significantly greater severe hypoglycemia (20 vs. 10 events/ patient-year)