Weekly insulins: treatment landscape and market outlook

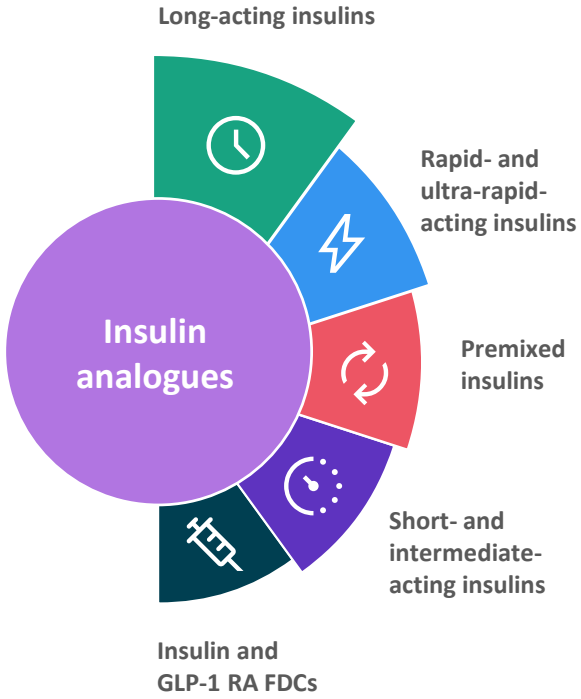
Market Trend Summary

Shambhavi Shukla | September 2024

The journey of insulin analogues

Past, present, and future in diabetes care

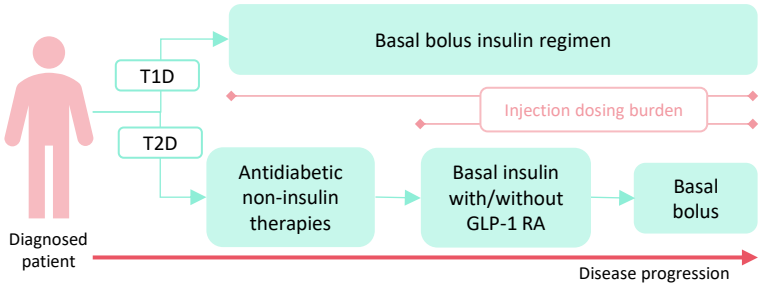
Current insulin portfolio



Position in the treatment paradigm

- Insulin analogues play a pivotal role in the management of diabetes. While they are typically prescribed as a later-line therapy to help achieve HbA1c target levels in T2D patients who are unable to manage their disease with non-insulin treatment, they are the cornerstone treatment in T1D.

Treatment journey of diabetic patients



- The insulin dosing burden is significantly higher in T1D than T2D. T1D patients typically rely on multiple daily insulin injections with a basal-bolus regimen for the majority of their lives.

- The T2D market boasts many oral therapies providing the majority of patients with an array of non-injectable treatment approaches. Only the GLP-1 RA products and insulins are available as injectable drug classes. In T2D, most GLP-1 RA products require once-weekly SC administration, while insulin treatment requires daily injections, sometimes multiple times daily.

Evolution of insulins for diabetes

- Various approaches to improve insulin treatment have been explored. Despite the non-injectable ROA, the use of MannKind's inhaled Afrezza is limited. The need for pulmonary function testing before prescription and safety concerns hold back its use.

- Ultra-rapid-acting formulations provide a faster onset of action compared with conventional rapid-acting insulins. However, physicians interviewed by Clarivate do not perceive significant clinical differences between rapid-acting and ultra-rapid insulins and do not view ultra-rapid formulations as a major advancement.

- Recognizing the high dosing burden from an injectable intense treatment regimen, there have been attempts to develop oral insulins. However, difficulties in regulating the bioavailability of an oral formulation have led to many failures, including Oramed's ORMD-0801.

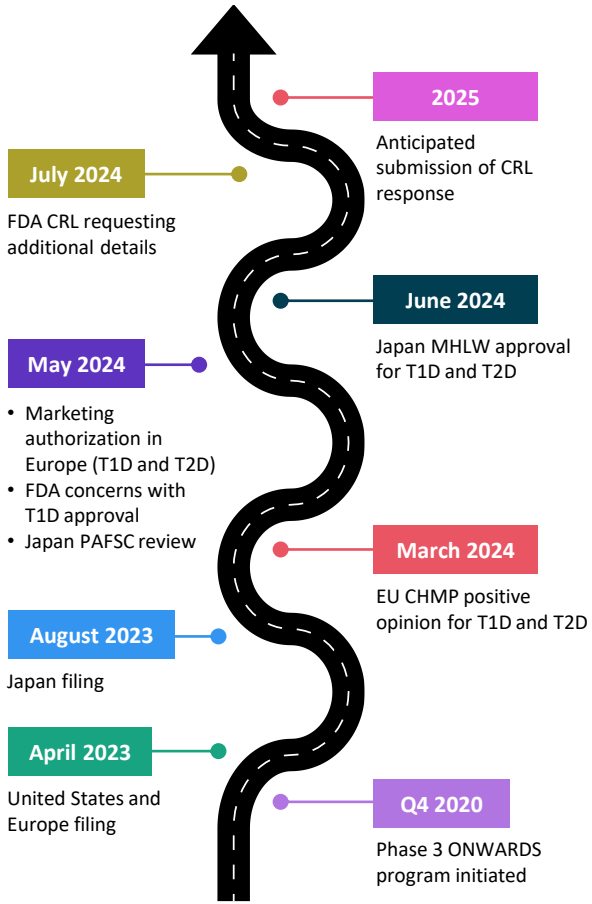
- In an alternative approach to reduce the insulin treatment burden, weekly insulin analogues are in development. Two major diabetes market players, Novo Nordisk and Eli Lilly, are pushing forward with the leading candidates in this space.

GLP-1 RA: GLP-1 receptor agonists; FDC: fixed-dose combination; T1D: type 1 diabetes; T2D: type 2 diabetes; SC: subcutaneous; ROA: route of administration

Insulin icodec (Awiqli)

Novo Nordisk

Development journey



Clinical performance

Awiqli's approval was based on results from the Phase 3 **ONWARDS** program, which included five T2D-focused studies and one T1D-focused study.

Awiqli in T1D patients:

- Awiqli demonstrated noninferiority in reducing HbA1c to insulin degludec.
- A statistically significant higher estimated rate of severe hypoglycemia was reported compared with insulin degludec.

Awiqli in T2D patients:

- Overall, Awiqli achieved noninferiority and superiority in reducing the estimated mean HbA1c and TIR compared with daily long-acting insulins.
- In insulin-naive patients, the overall observed rates of severe hypoglycemia were fewer than one event per patient-year of exposure with both Awiqli and active comparator treatment arms.

Approval journey

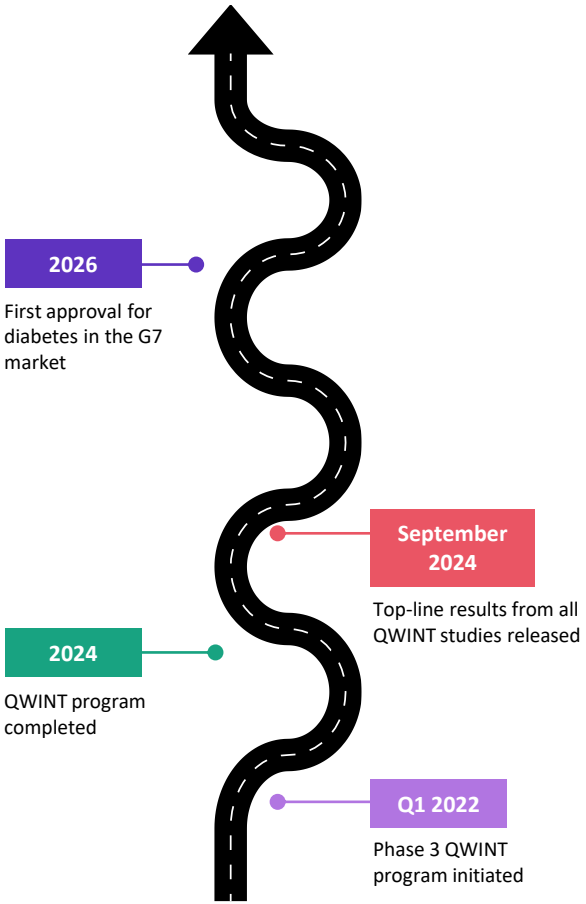
- Following the positive opinion issued by the CHMP in March 2024, Awiqli received **marketing authorization** in Europe in **May 2024** for both T1D and T2D. However, owing to the high risk of hypoglycemia, use of Awiqli among T1D patients was recommended only if the patient would benefit from once-weekly administration.
- The therapy was also **approved** in **Japan** in **June 2024** after the PAFSC review conducted in May 2024.
- Unlike Europe and Japan, Awiqli struggles in the United States for approval.
  - In **May 2024**, an independent **FDA panel** voted **against** using Awiqli for **T1D** with 7-4 votes, citing that risk for hypoglycemia outweighed minimal benefits for T1D; the panel appeared to be okay with its use for T2D. The FDA issued a **CRL** in **July 2024**, issuing requests related to the manufacturing process and the T1D indication.
  - Novo Nordisk is unlikely to fulfill the requests in 2024, likely delaying the **FDA decision** to **2025**.

T1D: type 1 diabetes; T2D: type 2 diabetes; SC: subcutaneous; TIR: Time in Range; HbA1c: glycated hemoglobin; PAFSC: Pharmaceutical Affairs and Food Sanitation Council; CRL: Complete Response Letter

Insulin efsitora alfa

Eli Lilly

Development journey



Clinical performance

Eli Lilly presented results from its Phase 3 **QWINT** program at EASD in September 2024. The program included four T2D-focused studies and one T1D-focused study.

Insulin efsitora in T1D patients:

- The QWINT-5 study successfully met its primary endpoint, demonstrating insulin efsitora's noninferiority to insulin degludec in reducing HbA1c levels.
- Overall, the rates of combined severe hypoglycemia and severe hypoglycemia incidence were higher with insulin efsitora compared with insulin degludec in the T1D population.

Insulin efsitora in T2D patients:

- Insulin efsitora demonstrated noninferiority in reducing HbA1c levels compared with daily insulin glargine and insulin degludec.
- Overall, the weekly insulin demonstrated a safety and tolerability profile similar to daily basal insulin therapies across all trials.

Next steps

- Similar to the approval hurdles faced by insulin icodec in the United States, Eli Lilly may need to provide additional data or set specific conditions for the use of insulin efsitora in T1D patients. However, just like with insulin icodec, significant concerns are not likely regarding its use in T2D patients.
- Clarivate forecasts the **first launch** of insulin efsitora in the **G7 market** for diabetes starting in **2026**.

EASD: European Association for the Study of Diabetes

Clarivate takeaways

Will weekly insulins address an unmet need in diabetes treatment?

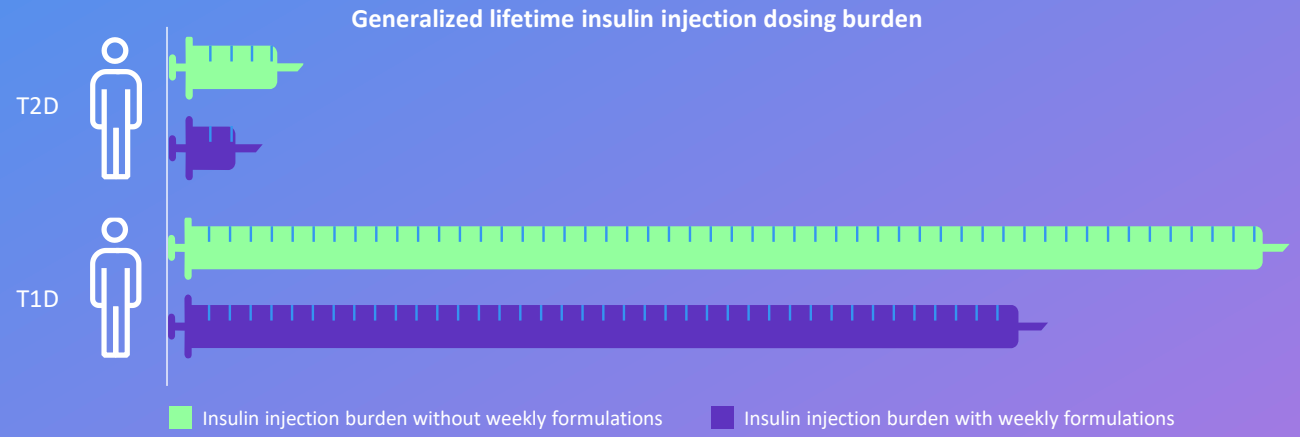
- The launch of weekly insulin represents a major advancement in diabetes treatment. The transition from daily to weekly formulations is likely to enhance the QOL for many patients by notably reducing the dosing burden associated with insulin injections.
- The weekly formulations will be beneficial for T1D patients following basal-bolus regimens, as well as for severe T2D patients managing their condition with insulins. Considering a patient's overall treatment, weekly insulins are likely to improve the injection dosing burden more significantly for individuals with T1D compared to those with T2D.

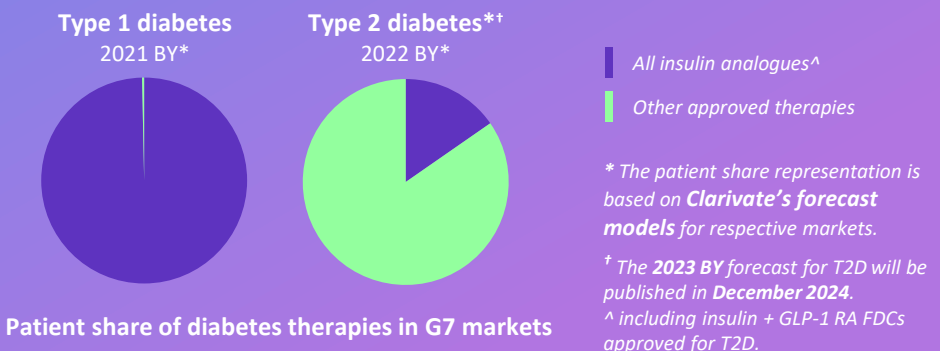
What do the physicians think of the once-weekly insulin formulation?

- Overall, physicians interviewed by Clarivate view weekly insulins as beneficial for diabetic patients.
- While fewer concerns have been raised about the use of the weekly formulation for T2D, physicians express worries about off-schedule administration, less-frequent dose adjustments, and an increased risk of hypoglycemia in T1D patients.
- Physicians also state that they need real-world performance data on weekly insulins for a few years postlaunch to be confident in their efficacy and safety, especially regarding hypoglycemia.

Will the weekly formulations lead to increased use of insulin analogues?

- Clarivate forecasts a limited overall expansion to the insulin market, as most patients who need insulin therapy will already be prescribed a daily long-acting insulin.
- We forecast a slow uptake of weekly insulins in the G7 market for diabetes. We believe physicians, caregivers, and patients will need time to familiarize themselves with the weekly dosing, dose titration, and monitoring approaches.





Patient share of diabetes therapies in G7 markets

** The patient share representation is based on **Clarivate's forecast models** for respective markets.*

*† The **2023 BY** forecast for T2D will be published in **December 2024**.*
^ including insulin + GLP-1 RA FDCs approved for T2D.

QOL: quality of life; BY: base year; 2021 BY: study period 2021–2022; 2022 BY: study period 2022-2032

About the author

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Shambhavi Shukla has authored competitive landscape and market insight reports on type 1 and type 2 diabetes, osteoporosis, and FSGS. She holds a master's degree in biotechnology from Amity University in India.

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Clarivate coverage of type 2 diabetes (T2D) and type 1 diabetes (T1D)

- Disease Landscape & Forecast | T2D (G7), providing comprehensive market intelligence insights.
- Treatment Algorithms: Claims Data Analysis | T2D (US), with details on the treatment journey and brand usage practices based on patient-level claims data.
- Epidemiology, with diagnosed incidence and prevalence data for T2D; coverage includes G7 countries.
- Current Treatment: Physician Insights | T2D (US), exploring the current prescribing trends of physicians treating T2D.
- Unmet Need | T2D (US and EU), providing a detailed, expanded analysis of the unmet needs associated with oral T2D therapies, including an Excel-based Target Product Profile Simulator.
- Access and Reimbursement | T2D (US), providing insights on the impact of payer policies on prescribing behavior in T2D.
- China In-Depth | T2D
- Disease Landscape & Forecast | T1D (G7), providing comprehensive market intelligence insights.
- Treatment Algorithms: Claims Data Analysis | T1D (US), with details on the treatment journey and brand usage practices based on patient-level claims data.
- Epidemiology, with diagnosed incidence and prevalence data for T1D; coverage includes G7 countries.

Have a question?

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