New Drug Overview

Awiqli (insulin icodec-abae)

PDL Category: Diabetic- Insulin Penfills

Introduction

Disease Background:

- Type 2 diabetes mellitus (DM) is described as hyperglycemia because of non-autoimmune gradual loss of insulin secretion from beta-cells, frequently in the setting of insulin resistance and metabolic syndrome (*Desouza et al 2026*).
  - Worldwide, approximately 537 million people are thought to have had diabetes in 2021. In addition, it is estimated that more than 90% of those cases had type 2 DM.
- Risk factors for type 2 DM include nonmodifiable risk factors (such as age ≥ 35 years, family history, genetic factors, or high-risk race), lifestyle risk factors (such as poor diet, smoking, and not being physically active), medications, or other conditions (such as depression), among others (*Desouza et al 2026).*
- While type 2 DM can be asymptomatic and often diagnosed due to screening, adults with significant hyperglycemia may report polyuria, polydipsia, polyphagia, or blurred vision. Chronic hyperglycemia may exhibit peripheral neuropathy, frequent infections, visual impairment, kidney or bladder dysfunction, or cardiovascular dysfunction (*Desouza et al 2026).*
- Newly diagnosed patients should be a part of a comprehensive diabetes self-management education program, which could include being educated on nutrition, physical activity, optimizing metabolic control, and the prevention of complications (*Wexler 2026*).
- While metformin may be appropriate for some as initial therapy, alternative glucose-lowering agents directed by comorbidities of the patient may be appropriate, such as glucagon-like peptide 1 (GLP-1) agonist based therapy or sodium-glucose cotransporter 2 (SGLT2) inhibitor therapy that have data demonstrating cardiac and/or renal benefits. Insulin (or GLP-1 based therapy) may be appropriate as initial therapy for patients with a hemoglobin A1c (HbA1c) > 9% and a contraindication to metformin who do not have cardiorenal disease or insulin is suggested as initial therapy if symptomatic or with severe hyperglycemia (*Wexler 2026*).
- Awiqli was FDA approved in 2026.

Pharmacology/Usage

- Awiqli (insulin icodec-abae) is a long-acting human insulin analog.
  - The primary activity of insulin, including Awiqli, is regulation of glucose metabolism. Insulin and its analogs lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production.
  - Insulin also inhibits lipolysis and proteolysis, and enhances protein synthesis.
  - Awiqli binds reversibly to albumin, resulting in a depot in the circulation from which insulin icodec-abae is slowly released. The insulin receptor is activated by insulin icodec-abae leading to a stable glucose-lowering effect over the entire dosing interval of one week.
  - When insulin icodec-abae binds to the human insulin receptor it results in the same pharmacological effects as human insulin.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Awiqli (insulin icodec-abae)
• As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	✔

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(Prescribing information: Awiqli 2026)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Awiqli (insulin icodec-abae)	Solution for Injection: 700 units per ml (U-700) Available as single-patient use FlexTouch prefilled pens: -3ml (containing 2100 units) -1.5ml (containing 1050 units) -1ml (containing 700 units)	SC	Inject SC once-weekly on any day of the week on the same day each week. -Individualize and titrate the dose per patient's metabolic needs, blood glucose monitoring results, and glycemic control goal. -The weekly starting dose in insulin naïve patients is 70 units SC once weekly on the same day each week. -Refer to the PI for switching to Awiqli from daily basal insulin therapy.	• The potency of insulin analogues is expressed in units. One unit of insulin icodec-abae corresponds to 1 international unit of human insulin. • Dose adjustments may be needed with changes in renal or hepatic function or during illness to minimize the risk of hypoglycemia or hyperglycemia. As with all insulin products, glucose monitoring should be intensified and the Awiqli dosage adjusted on an individual basis with renal or hepatic impairment. • Inject SC into thigh, upper arm, or abdomen, rotating injection sites. • During changes to a patient's insulin regimen, increase the frequency of blood glucose monitoring. • Use FlexTouch pen with caution in patients with visual impairment that may rely on

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Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				audible clicks to dial their dose.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Awiqli administered once-weekly in adults with type 2 diabetes mellitus (DM), used in combination with a mealtime insulin or in combination with common oral anti-diabetic agents and/or GLP-1 receptor agonist, was assessed in 3 randomized, open-label, treat-to-target, active-controlled trials and one randomized, double-blind, treat-to-target, active-controlled trial (Trials A, B, C, and D). Blinded continuous glucose monitoring (CGM) was utilized in Trials A, C, and D. Across all 4 trials, insulin icodec-abae was titrated in 20-unit increments, and the fasting plasma glucose (FPG) glycemic target (based on the mean of the 3 most recent FPG values) was 80-130mg/dL for both treatment arms.
- Type 2 insulin naïve patients and basal-only patients treated with Awiqli achieved statistically significant improvement in glycemic control compared to insulin glargine U-100 or insulin degludec U-100. Type 2 patients with basal-bolus regimen achieved similar glycemic control with Awiqli as those achieved with insulin glargine U-100 or insulin degludec U-100.
- *Trial A* assessed the efficacy of Awiqli in a 52-week, randomized, open-label, active-controlled, parallel-group, multicenter, treat-to-target trial that included insulin naïve adult patients with type 2 DM (N = 984) inadequately controlled on ≥ 1 oral antidiabetic agents (OADs) or GLP-1 receptor agonist (RA).
  - Patients were randomized to Awiqli once-weekly or insulin glargine U-100 once-daily.
  - Pre-trial non-insulin anti-diabetic medications were continued as background therapy in both treatment arms throughout the entire trial, except for sulfonylureas and glinides, which were discontinued at randomization.
  - Included patients had a mean age of 59 years, 57% were male, and 66% were White, while having a mean duration of diabetes of 12 years.
  - Treatment with Awiqli once-weekly for 52 weeks resulted in a statistically significant reduction in HbA1c compared to once-daily insulin glargine U-100, with an estimated treatment difference of -0.18% ($p = 0.0004$ for superiority).
  - Treatment with Awiqli once-weekly for 52 weeks resulted in a statistically significantly longer Time in Range (TIR) (4.27%) compared to once-daily insulin glargine U-100 treatment during the last 4 weeks of the trial ($p < 0.001$).
  - 56.52% of the Awiqli group achieved HbA1c < 7% at the trial end versus 44.57% with insulin glargine.
- *Trial B* assessed the efficacy of Awiqli in a 26-week randomized, double-blind, active-controlled, parallel-group, multicenter, treat-to-target trial that enrolled adult insulin-naïve patients (N = 588) with type 2 DM inadequately controlled on one or more oral antidiabetic agents (OADs) or GLP-1 RA.
  - Patients were randomized to Awiqli once-weekly or insulin degludec U-100 once-daily.
  - Pre-trial non-insulin anti-diabetic medications were continued as background therapy in both treatment arms throughout the entire trial except for sulfonylureas and glinides, which were reduced at randomization by about 50% at the discretion of the investigator.
  - Included patients had a mean age of 58 years, while 63% were male, 60% were White, and the mean duration of diabetes was 11 years.
  - Treatment with Awiqli once-weekly for 26 weeks resulted in a statistically significant reduction in HbA1c compared to once-daily insulin degludec U-100, with an estimated treatment difference of -0.22% ($p = 0.0007$ for superiority).
  - 56.45% of the Awiqli group achieved HbA1c < 7% at the trial end versus 40.95% with insulin degludec.
- *Trial C* assessed the efficacy of Awiqli in a 26-week, randomized, open-label, active-controlled, parallel-group, multicenter, treat-to-target trial in adult patients with type 2 DM (N = 526) treated with once or twice daily basal insulin with or without OADs.
  - Patients were randomized to Awiqli once-weekly or insulin degludec U-100 once-daily.

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- Pre-trial non-insulin OADs/GLP-1 RAs were continued as background therapy in both treatment arms throughout the entire trial except for sulfonylureas and glinides, which were discontinued at randomization.
- Included patients had a mean age of 62 years, while 57% were male, 57% were White, and the mean duration of diabetes was 17 years.
- Treatment with Awiqli once-weekly for 26 weeks resulted in a statistically significant reduction in HbA1c compared with insulin degludec U-100 with estimated treatment difference of -0.19% (p = 0.0032 for superiority).
- Estimated Time in Range (70-180 mg/dL) during the last 4 weeks of the trial (week 22 to 26) was 62.34% for Awiqli and 59.93% for insulin degludec U-100.
- 37.53% of the Awiqli group achieved HbA1c < 7% at the trial end versus 25.35% with insulin degludec.

- *Trial D* assessed the efficacy of Awiqli in a 26-week, randomized, open-label, active-controlled, parallel-group, multicenter, treat-to-target trial in adult patients with type 2 DM (N = 582) inadequately controlled on once-daily basal insulin in combination with mealtime rapid-acting insulin with or without OADs or GLP-1 RAs.
  - Patients were randomized to Awiqli once-weekly or insulin glargine U-100 once-daily both in combination with insulin aspart before each meal.
  - Pre-trial non-insulin OADs or GLP-1 RA were continued as background therapy in both treatment arms throughout the entire trial except for sulfonylureas and glinides, which were discontinued at randomization.
  - Included patients had a mean age of 60 years, while 52% were male, 64% were White, and the mean duration of diabetes was 17 years.
  - At week 26, the difference in HbA1c reduction from baseline between Awiqli and insulin glargine U-100 was 0.02% and met the pre-specified non-inferiority margin (0.3%).
  - Estimated Time in Range (70-180 mg/dL) during the last 4 weeks of the trial (weeks 22 to 26) was 66.75% for the Awiqli arm and 66.46% for insulin glargine U-100.
  - 40.69% of the Awiqli plus insulin aspart arm achieved HbA1c < 7% at trial end compared with 45.48% in the insulin glargine plus insulin aspart arm.

Clinical guidelines

- **American Diabetes Association (ADA) Professional Practice Committee for Diabetes: Pharmacologic Approaches to glycemic treatment: Standards of Care in Diabetes-2026** (*ADA 2026*).
  - For the treatment of adults with type 2 DM:
    - The decision on which glucose-lowering treatment to use should consider individualized glycemic and weight goals, comorbidities, and the risk of hypoglycemia.
    - When starting a new treatment to lower glucose, reassess the need for and/or dose of medications with higher hypoglycemia risk to lower the risk of hypoglycemia.
    - It is recommended to consider starting insulin in adults with type 2 DM regardless of background glucose-lowering treatment or duration of disease if hyperglycemia symptoms are present or when A1c or blood glucose levels are very high (ie, A1c > 10% or blood glucose ≥ 300 mg/dL).
    - In adults with type 2 DM who do not have severe hyperglycemia or hyperglycemic crisis, GLP-1-based treatment is preferred over insulin for initial or add-on treatment to lower glucose.
    - If injectable therapy is needed for achieving glycemic goals:
      - Consider GLP-1 RA or dual GIP/GLP-1 RA in most patients before insulin.
      - If glucose is above goal, consider basal insulin, then initiation and titration of basal analog or bedtime NPH insulin.

Safety summary

- **Contraindications:**

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- During episodes of hypoglycemia.
- In patients with hypersensitivity to insulin icodec-abae or any of the excipients in Awiqli FlexTouch.

- **Box Warning:** None.

- **Warnings and precautions:**
  - Serious hypoglycemia requiring hospitalization has occurred due to accidental mix-ups between Awiqli and other insulin products or once-weekly injectable antidiabetic medications, incorrect dose selection, and dosing frequency errors. To avoid dosing errors when switching from daily basal insulin to Awiqli, follow the dosage recommendations.
    - Monitor patients for signs and symptoms of hypoglycemia, especially during the first several weeks after initiation or dose escalation of Awiqli. Ensure patients understand how to recognize and manage hypoglycemia.
  - Hypoglycemia is the most common adverse reaction associated with insulin, including Awiqli. Hypoglycemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual.
    - The long-acting effect of Awiqli may delay recovery from hypoglycemia compared to shorter-acting insulins.
  - Changes in an insulin regimen may affect glycemic control and predispose to hypoglycemia or hyperglycemia.
    - Make any changes to a patient's insulin regimen under close medical supervision with increased frequency of blood glucose monitoring.
  - Severe, life-threatening, generalized allergy can occur with insulins, including Awiqli. If hypersensitivity reactions occur, discontinue Awiqli; treat per standard of care and monitor until symptoms and signs resolve.
  - All insulins, including Awiqli, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia.
    - Monitor potassium levels in patients at risk for hypokalemia if indicated.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Awiqli) that occurred. There was no placebo data to compare with in the prescribing information.
    - The most frequently reported adverse events included injection site reactions (1.8%), peripheral edema (1.2%), and hypersensitivity (0.4%). In clinical trials after 26 to 52 weeks of treatment, patients with type 2 DM treated with Awiqli gained an average weight of 1.4 to 2.8kg. Hypoglycemia is the most commonly observed adverse reaction in patients treated with Awiqli.

- **Drug interactions:**
  - Dose reductions and increased frequency of glucose monitoring may be required when Awiqli is co-administered with drugs that may increase the risk of hypoglycemia (such as ACE inhibitors, ARBS, or MAO inhibitors, among others).
  - Dose increases and increased frequency of glucose monitoring may be required when Awiqli is co-administered with drugs that may decrease the blood glucose lowering effect of Awiqli (such as atypical antipsychotics, diuretics, estrogens, or thyroid hormones, among others).
  - Dose adjustment and increased frequency of glucose monitoring may be required when Awiqli is co-administered with drugs that may increase or decrease the blood glucose lowering effect of Awiqli (such as alcohol, beta-blockers, clonidine, and lithium salts).
  - Increased frequency of glucose monitoring may be required when Awiqli is coadministered with drugs that may blunt signs and symptoms of hypoglycemia (such as beta-blockers, clonidine, guanethidine, and reserpine).

- **Special populations:**

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- There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data with use in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy.
- The safety and efficacy of Awiqli have not been established in the pediatric population.

Conclusion

- Type 2 diabetes mellitus (DM) is described as hyperglycemia because of non-autoimmune gradual loss of insulin secretion from beta-cells, frequently in the setting of insulin resistance and metabolic syndrome (*Desouza et al 2026*).
- Awiqli is a long-acting human insulin analog indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- The dose should be individualized based on metabolic needs, blood glucose monitoring results, and glycemic control goal. Inject subcutaneously once-weekly on any day of the week on the same day each week.
- Use is contraindicated during episodes of hypoglycemia and in patients with hypersensitivity to insulin icodec-abae or any of the excipients of the product.
- The efficacy of Awiqli was assessed in three randomized, open-label, treat-to-target, active-controlled trials and one randomized, double-blind, treat-to-target, active-controlled trial.
  - Treatment with Awiqli once-weekly for 52 weeks resulted in a statistically significant reduction in HbA1c compared to once-daily insulin glargine U-100 and treatment with Awiqli once-weekly for 26 weeks resulted in a statistically significant reduction in HbA1c compared to once-daily insulin degludec U-100, both in insulin naïve adults.
  - Treatment with Awiqli once-weekly for 26 weeks resulted in a statistically significant reduction in HbA1c compared with insulin degludec U-100 in patients previously treated with basal insulin.
  - At week 26, the difference in HbA1c reduction from baseline between Awiqli and insulin glargine U-100 met the pre-specified non-inferiority margin in adults inadequately controlled on once-daily basal insulin when used in combination with insulin aspart.
- Guidelines available from the ADA discuss the use of insulin to lower glucose, including if symptoms of hyperglycemia are present or the patient has a high HbA1c or blood glucose levels.

- There is no evidence to suggest that Awiqli is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Awiqli remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.
- **PDL Placement:**

☐ Preferred
☒ Non-Preferred

References

- American Diabetes Association (AD) Professional Practice Committee for Diabetes. Pharmacologic Approaches to glycemic treatment: Standards of Care in Diabetes-2026. *Diabetes Care*. 2026; 49(Supp 1): S183-S215.
- Awiqli Package insert. Novo Nordisk; March 2026.
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- Wexler DJ. Initial management of hyperglycemia in adults with type 2 diabetes mellitus. UpToDate website. Last updated August 25, 2026. Accessed September 14, 2026. https://www.uptodate.com.

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