HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Awiqli® safely and effectively. See full prescribing information for Awiqli.

Awiqli (insulin icodec-abae) injection, for subcutaneous use
Initial U.S. Approval: 2026

----------RECENT MAJOR CHANGES----------
Indications and Usage (1) 10/2026

----------INDICATIONS AND USAGE----------
Awiqli is a long-acting human insulin analog indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients 10 years of age and older with type 2 diabetes mellitus (1)

----------DOSAGE AND ADMINISTRATION----------
- Individualize dose based on type of diabetes, metabolic needs, blood glucose monitoring results and glycemic control goals. (2.1)
- See Full Prescribing Information for important administration instructions (2.2)
- Inject Awiqli subcutaneously into the thigh, upper arm, or abdomen. (2.2)
- Rotate injection sites to reduce risk of lipodystrophy and localized cutaneous amyloidosis. (2.2)
- See Full Prescribing Information for the recommended starting dosage in insulin naïve patients (2.3) and recommendations for switching patients from daily basal insulin. (2.4)
- Closely monitor glucose when switching to Awiqli. (2.4)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 700 units/mL (U-700) available as a clear and colorless solution:
- 3 mL single-patient-use FlexTouch prefilled pen (containing 2,100 units) (3)
- 1.5 mL single-patient-use FlexTouch prefilled pen (containing 1,050 units) (3)
- 1 mL single-patient-use FlexTouch prefilled pen (containing 700 units) (3)

----------CONTRAINDICATIONS----------
- During episodes of hypoglycemia (4)
- Hypersensitivity to insulin icodec-abae or any of the excipients in Awiqli (4)

----------WARNINGS AND PRECAUTIONS----------
- *Hypoglycemia Due to Medication Errors and Accidental Overdose:* Accidental mix-ups between insulin products can occur. Advise patients to always check the product label before each injection to confirm they are using Awiqli and not another insulin or injectable antidiabetic medicine. DO NOT transfer Awiqli from the Awiqli FlexTouch pen into a syringe for administration as overdosage and severe hypoglycemia can result. (5.1)
- *Hypoglycemia:* May be life-threatening. Increase monitoring with changes to: insulin dosage, co-administered glucose lowering medications, meal pattern, physical activity, and in patients with renal impairment, hepatic impairment or hypoglycemia unawareness. (5.2)
- *Hyperglycemia or Hypoglycemia with Changes in Insulin Regimen:* Make changes to a patient's insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) under close medical supervision with increased frequency of blood glucose monitoring. (5.3)
- *Hypersensitivity Reactions:* Severe, life-threatening, generalized allergy, including anaphylaxis, can occur. Discontinue Awiqli, monitor and treat if indicated. (5.4)
- *Hypokalemia:* May be life-threatening. Monitor potassium levels in patients at risk for hypokalemia and treat if indicated. (5.5)
- *Never share* an Awiqli FlexTouch pen between patients, even if the needle is changed. (5.6)
- *Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs):* Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation if heart failure occurs. (5.7)

----------ADVERSE REACTIONS----------
Adverse reactions commonly associated with Awiqli are:
- hypoglycemia, hypersensitivity reactions (e.g., urticaria, swelling face and lips), injection site reactions, lipodystrophy, pruritus, rash, edema, and weight gain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk at 1-844-668-6463 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- *Drugs that may increase the risk of hypoglycemia:* antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, salicylates, somatostatin analog (e.g., octreotide), sulfonamide antibiotics, GLP-1 receptor agonists, DPP-4 inhibitors, and SGLT-2 inhibitors. (7)
- *Drugs that may decrease the blood glucose lowering effect:* atypical antipsychotics, corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens (e.g., in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline), and thyroid hormones. (7)
- *Drugs that may increase or decrease the blood glucose lowering effect:* Alcohol, beta-blockers, clonidine, lithium salts, and pentamidine. (7)
- *Drugs that may blunt the signs and symptoms of hypoglycemia*: beta-blockers, clonidine, guanethidine, and reserpine. (7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Awiqli is indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients 10 years of age and older with type 2 diabetes mellitus.

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Instructions

Awiqli FlexTouch is available as a single-patient-use FlexTouch pen.

- Inject Awiqli subcutaneously once weekly on any day of the week on the same day each week.
- The Awiqli FlexTouch pen delivers doses in 10-unit increments and can deliver up to 700 units in a single injection.
- Individualize and titrate the dose of Awiqli based on the patient's metabolic needs, blood glucose monitoring results, and glycemic control goal.
- The potency of insulin analogues, including insulin icodec-abae is expressed in units. One (1) 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. Due to the long half-life of Awiqli, adjustment of dose is not advised during acute illness nor if patients make short-term changes in their physical activity level or usual diet. In these situations, consider other applicable adjustments, e.g. glucose intake or changes to other glucose lowering medication *[see Warnings and Precautions (5.2, 5.3)]*.

2.2 Important Administration Instructions

- Always check the product label before administration *[see Warnings and Precautions (5.1)]*.
- Inspect visually for particulate matter and discoloration. Only use Awiqli if the solution appears clear and colorless.
- Inject Awiqli subcutaneously into the thigh, upper arm, or abdomen.
- Rotate injection sites within the same region from one injection to the next to reduce the risk of lipodystrophy and localized cutaneous amyloidosis. Do not inject into areas of lipodystrophy or localized cutaneous amyloidosis *[see Warnings and Precautions (5.3), Adverse Reactions (6.1)]*.
- During changes to a patient's insulin regimen, increase the frequency of blood glucose monitoring *[see Warnings and Precautions (5.2, 5.3)]*.
- Use Awiqli FlexTouch pen with caution in patients with visual impairment that may rely on audible clicks to dial their dose.
- DO NOT administer Awiqli intramuscularly, intravenously or in an insulin infusion pump.
- DO NOT dilute or mix Awiqli with any other insulin or solution.
- DO NOT transfer Awiqli from the Awiqli FlexTouch pen into a syringe for administration *[see Warnings and Precautions (5.1)]*.

2.3 Recommended Dosage in Insulin Naïve Patients

The recommended starting dosage of Awiqli in insulin naïve patients is 70 units administered subcutaneously once weekly on the same day each week.

2.4 Switching to Awiqli from Daily Basal Insulin Therapy

- Administer the first dose of Awiqli on the day after the last dose of daily basal insulin.
- Week 1 dosage: The recommended one-time starting dosage of Awiqli FlexTouch is 1.5 times the total daily basal dosage multiplied by 7 rounded to the nearest 10 units.

- Week 2 dosage: The recommended dosage is the previous total daily basal insulin dose multiplied by 7 and then rounded to the nearest 10 units.
- See **Table 1** for examples of Awiqli dosage for Week 1 and 2, when switching from daily basal insulin therapy.
- Week 3 dosage and beyond: The recommended dosage of Awiqli can be titrated from the previous dosage based on the patient's metabolic needs, blood glucose monitoring results, and glycemic control goal.
- When switching from daily basal insulin to once-weekly Awiqli close glucose monitoring is recommended. Doses and timing of concurrent rapid-acting or short-acting insulin products or other concomitant antidiabetic treatment may need to be adjusted *[see Warnings and Precautions (5.1)]*.

Table 1. Example Awiqli Weekly Dosages When Switching from Daily Basal Insulin Therapy

Previous Total Daily Dosage of Basal Insulin (units)	Week 1 Dosage of Awiqli (units)[a]	Week 2 Dosage of Awiqli (units)[b]
10	110	70
11	120	80
12	130	80
13	140	90
14	150	100
15	160	110
16	170	110
17	180	120
18	190	130
19	200	130
20	210	140
21	220	150
22	230	150
23	240	160
24	250	170
25	260	180
26	270	180
27	280	190
28	290	200
29	300	200
30	320	210
31	330	220
32	340	220
33	350	230
34	360	240
35	370	250

Previous Total Daily Dosage of Basal Insulin (units)	Week 1 Dosage of Awiqli (units)[a]	Week 2 Dosage of Awiqli (units)[b]
36	380	250
37	390	260
38	400	270
39	410	270
40	420	280
41	430	290
42	440	290
43	450	300
44	460	310
45	470	320
46	480	320
47	490	330
48	500	340
49	510	340
50	530	350
100	1,050[c]	700

[a] Week 1 dose only: Multiply the previous total daily basal insulin dosage by 7, then multiply by 1.5, and round to the nearest 10 units.
[b] Week 2 dose: Previous total daily basal insulin dosage multiplied by 7, then rounded to the nearest 10 units.
[c] When the required dose is larger than 700 units, split the dose into two injections (e.g., a 1,050-unit dose could be administered as a 700-unit injection followed by a 350-unit injection).

2.5 Recommendations Regarding Missed Doses

- If a dose is missed, administer the missed dose as soon as possible within 4 days. Resume the once-weekly dosing schedule, one week from the day the missed dose was administered.
- If more than 4 days have passed, skip the missed dose and administer the next dose on the regularly scheduled day.
- Increase blood glucose monitoring with missed doses.

3 DOSAGE FORMS AND STRENGTHS

Injection: 700 units per mL (U-700) available as a clear and colorless solution:

- 3 mL single-patient-use FlexTouch prefilled pen (containing 2,100 units)
- 1.5 mL single-patient-use FlexTouch prefilled pen (containing 1,050 units)
- 1 mL single-patient-use FlexTouch prefilled pen (containing 700 units)

4 CONTRAINDICATIONS

Awiqli is contraindicated:

- During episodes of hypoglycemia *[see Warnings and Precautions (5.2)]*.
- In patients with hypersensitivity to insulin icodec-abae or any of the excipients in Awiqli FlexTouch. Serious hypersensitivity reactions have included anaphylaxis *[see Warnings and Precautions (5.4)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypoglycemia Due to Medication Errors and Accidental Overdose

Serious hypoglycemia requiring hospitalization has occurred due to accidental mix-ups between Awiqli and other insulin products or once-weekly injectable antidiabetic medicines, incorrect dose selection, and dosing frequency errors.

To avoid dosing errors when switching from daily basal insulin to Awiqli, follow the dosage recommendations in the *Dosage and Administration Section (2.2)*. Administer Awiqli once weekly only.

Advise patients to always check the product label before each injection to confirm they are using Awiqli and not another insulin or injectable antidiabetic medicine. Prior to initiation, train patients and their caregiver(s) on how to select their weekly Awiqli dosage. Advise patients using other injectable medications for glycemic control that the dosage selection of Awiqli differs *[see Dosage and Administration (2.2, 2.3, 2.4), Instructions for Use].* Instruct patients to visually verify the dialed units on the dose counter of the Awiqli FlexTouch prefilled pen before each injection to avoid dosing errors. Do not dial the maximum single dose (700 units) of Awiqli unless this is the prescribed dose *[see Dosage and Administration (2.4)]*. Do not use a syringe to remove Awiqli from the Awiqli FlexTouch disposable insulin prefilled pen.

Monitor patients for signs and symptoms of hypoglycemia, particularly during the first several weeks after initiation or dose escalation of Awiqli. Ensure patients understand how to recognize and manage hypoglycemia *[see Warnings and Precautions (5.2)].*

5.2 Hypoglycemia

Hypoglycemia is the most common adverse reaction associated with insulin, including Awiqli *[see Adverse Reactions (6.1)].* Severe hypoglycemia can cause seizures, may be life-threatening or cause death. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery). Awiqli, or any insulin, should not be used during episodes of hypoglycemia *[see Contraindications (4)].*

Hypoglycemia can happen suddenly and symptoms may differ in each individual and change over time in the same individual. Symptomatic awareness of hypoglycemia may be less pronounced in patients with longstanding diabetes, in patients with diabetic nerve disease, in patients using medications that block the sympathetic nervous system (e.g., beta-blockers) *[see Drug Interactions (7)],* or in patients who experience recurrent hypoglycemia.

The long-acting effect of Awiqli may delay recovery from hypoglycemia compared to shorter-acting insulins.

<u>Risk Factors for Hypoglycemia</u>
The risk of hypoglycemia generally increases with intensity of glycemic control. The risk of hypoglycemia after an injection is related to the duration of action of the insulin *[see Clinical Pharmacology (12.2)]* and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulins, the glucose lowering effect over time of Awiqli may vary among different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature.

Other factors which may increase the risk of hypoglycemia include changes in meal pattern (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to co-administered medication *[see Drug Interactions (7)]*. Patients with renal or hepatic impairment may be at higher risk of hypoglycemia *[see Use in Specific Populations (8.6, 8.7)]*.

<u>Risk Mitigation Strategies for Hypoglycemia</u>
Educate patients and caregivers to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia, increased frequency of blood glucose monitoring is recommended.

5.3 Hyperglycemia or Hypoglycemia with Changes in Insulin Regimen

Changes in an insulin regimen (e.g., insulin strength, manufacturer, type, injection site or method of administration) may affect glycemic control and predispose to hypoglycemia *[see Warnings and Precautions (5.2)]* or hyperglycemia. Repeated insulin injections into areas of lipodystrophy or localized cutaneous amyloidosis have been reported to result in hyperglycemia; and a sudden change in the injection site (to an unaffected area) has been reported to result in hypoglycemia *[see Adverse Reactions (6)]*.

Make any changes to a patient's insulin regimen under close medical supervision with increased frequency of blood glucose monitoring. Advise patients who have repeatedly injected into areas of lipodystrophy or localized cutaneous amyloidosis to change the injection site to unaffected areas and closely monitor for hypoglycemia. Adjustments in concomitant anti-diabetic treatment may be needed *[see Dosage and Administration (2.4)]*.

5.4 Hypersensitivity Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulins, including Awiqli. If hypersensitivity reactions occur, discontinue Awiqli; treat per standard of care and monitor until symptoms and signs resolve. Awiqli is contraindicated in patients who have had hypersensitivity reactions to insulin icodec-abae or any of the excipients *[see Contraindications (4)]*.

5.5 Hypokalemia

All insulins, including Awiqli, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death. Monitor potassium levels in patients at risk for hypokalemia if indicated (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentrations).

5.6 Never Share an Awiqli FlexTouch Pen or Needle Between Patients

Awiqli FlexTouch disposable prefilled pens should never be shared between patients, even if the needle is changed. Sharing poses a risk for transmission of blood-borne pathogens.

5.7 Fluid Retention and Congestive Heart Failure with Concomitant Use of a PPAR Gamma Agonist

Thiazolidinediones (TZDs), which are peroxisome proliferator-activated receptor (PPAR)-gamma agonists can cause dose related fluid retention, particularly when used in combination with insulin. Fluid retention may lead to or exacerbate congestive heart failure. Patients treated with insulin, including Awiqli and a PPAR-gamma agonist should be observed for signs and symptoms of congestive heart failure. If congestive heart failure develops, it should be managed according to current standards of care and discontinuation or dose reduction of the PPAR-gamma agonist must be considered.

6 ADVERSE REACTIONS

The following adverse reactions are also discussed elsewhere:

- Hypoglycemia Due to Medication Errors and Accidental Overdose *[see Warnings and Precautions (5.1)]*
- Hypoglycemia *[see Warnings and Precautions (5.2)]*
- Hypersensitivity reactions *[see Warnings and Precautions (5.4)]*
- Hypokalemia *[see Warnings and Precautions (5.5)]*

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of Awiqli in patients with type 2 diabetes was evaluated in five clinical trials involving 1,880 adults with type 2 diabetes exposed to Awiqli, with a mean exposure duration of 26 to 52 weeks across the five trials *[see Clinical Studies (14)]*. The type 2 diabetes population had the following characteristics: mean age was 59 years and 5% were older than 75 years, 59% were male, 71% were White, 3.6% were Black or African American, and 13% were Hispanic or Latino ethnicity. The mean BMI was 30.7 kg/m^2. The mean duration of

diabetes was 13 years and the mean HbA_{1c} at baseline was 8.6%. At baseline, the mean eGFR was 86.1 mL/min/1.73 m^2 and 11% of patients had an eGFR less than 60 mL/min/1.73 m^2.

Common Adverse Reactions

Hypoglycemia

Hypoglycemia is the most commonly observed adverse reaction in patients treated with Awiqli *[see Warnings and Precautions (5.2)]*. The rates of reported hypoglycemia depend on the definition of hypoglycemia used, diabetes type, insulin dose, intensity of glucose control, background therapies, and other intrinsic and extrinsic patient factors. For these reasons, comparing rates of hypoglycemia in clinical trials for Awiqli with the incidence of hypoglycemia for other products may be misleading and also, may not be representative of hypoglycemia rates that will occur in clinical practice.

In clinical trials *[see Clinical Studies (14)]*, events of severe hypoglycemia (level 3) were defined as an episode associated with severe cognitive impairment requiring external assistance for recovery. Hypoglycemia episodes with a glucose level below 54 mg/dL with or without associated symptoms (level 2 hypoglycemia) were also assessed in patients with type 2 diabetes.

In the clinical trials of patients with type 2 diabetes, percentages of adults randomized to Awiqli who experienced at least one episode of severe or clinically significant (level 2) hypoglycemia in clinical trials are shown in **Table 2**.

Table 2: Proportion (%) of Patients with Type 2 Diabetes Experiencing at Least One Episode of Severe (Level 3) or Clinically Significant (Level 2) Hypoglycemia in Clinical Trials

	Type 2 Diabetes				
	Trial A	**Trial B**	**Trial C**	**Trial D**	**Trial E[c]**
	Awiqli + Anti-Diabetic Drugs[d] Insulin Naïve 52 Weeks (N=492)	**Awiqli + Anti-Diabetic Drugs[e] Insulin Naïve 26 Weeks (N=293)**	**Awiqli + Anti-Diabetic Drugs[d] 26 Weeks (N=262)**	**Awiqli ± Anti-Diabetic Drugs[d] + Insulin Aspart 26 Weeks (N=291)**	**Awiqli + Anti-Diabetic Drugs[d] Insulin Naïve 52 Weeks (N=542)**
Level 3 Hypoglycemia[a]	0.2	0	0	1.4	0
Level 2 Hypoglycemia[b]	9.8	8.9	14.1	50.9	11.8

[a] Level 3 hypoglycemia is an episode associated with severe cognitive impairment requiring external assistance for recovery.
[b] Level 2 hypoglycemia is hypoglycemia episode with a self-measured blood glucose level below 54 mg/dL with or without associated symptoms.
[c] In Trial E, Awiqli arm titration was performed via a digital titration app.
[d] Excludes sulfonylureas and glinides.
[e] Sulfonylurea and glinide dosage decreased by 50% at the discretion of the investigator.

Insulin Initiation and Intensification of Glucose Control

Intensification or rapid improvement in glucose control has been associated with a transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy, and acute painful peripheral neuropathy. However, long-term glycemic control decreases the risk of diabetic retinopathy and neuropathy.

Allergic Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, generalized skin reactions, angioedema, bronchospasm, hypotension, and shock may occur with any insulin, including Awiqli. Hypersensitivity (manifested with urticaria, swelling of face and lips swelling) were reported in 0.4% of patients treated with Awiqli.

In the three clinical trials in type 2 patients with antibody samples collected (Trial B, C, and D), hypersensitivity reactions occurred in 0.6% of Awiqli-treated patients with anti-insulin icodec-abae antibodies and in 0.4% of Awiqli-treated patients who did not develop anti-insulin icodec-abae antibodies *[see Clinical Pharmacology (12.6)]*.

Lipodystrophy
Long-term use of insulin, including Awiqli, can cause lipodystrophy at the site of repeated insulin injections. Lipodystrophy includes lipohypertrophy (thickening of adipose tissue) and lipoatrophy (thinning of adipose tissue) and may affect insulin absorption *[see Dosage and Administration (2.2)]*. In clinical trials, lipodystrophy, lipohypertrophy, or lipoatrophy was reported in 0.0% of patients treated with Awiqli.

Injection Site Reactions
Patients taking Awiqli may experience injection site reactions, including pruritus, bruising, erythema, pain, injection site hypersensitivity, swelling, urticaria and injection site mass. In the clinical trials, injection site reactions occurred in 1.8% of patients treated with Awiqli.

In the three clinical trials in type 2 patients with antibody samples collected (Trial B, C, and D), injection site reactions occurred in 2.3% of Awiqli-treated patients with anti-insulin icodec-abae antibodies and in 2.4% of Awiqli-treated patients who did not develop anti-insulin icodec-abae antibodies *[see Clinical Pharmacology (12.6)]*.

Weight Gain
Weight gain can occur with insulin therapy, including Awiqli, and has been attributed to the anabolic effects of insulin. In the clinical trials after 26 to 52 weeks of treatment, patients with type 2 diabetes treated with Awiqli gained an average weight of 1.4 to 2.8 kg.

Peripheral Edema
Awiqli may cause sodium retention and edema. In the clinical trials, peripheral edema occurred in 1.2% of patients with type 2 diabetes mellitus treated with Awiqli.

7 DRUG INTERACTIONS

Table 3 includes clinically significant drug interactions with Awiqli.

Table 3: Clinically Significant Drug Interactions with Awiqli

Drugs That May Increase the Risk of Hypoglycemia	
Drugs:	Antidiabetic agents, angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, salicylates, somatostatin analogs (e.g., octreotide), and sulfonamide antibiotics, glucagon-like peptide-1 (GLP-1) receptor agonists, dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium-glucose co-transporter 2 (SGLT-2) inhibitors.
Intervention:	Dose reductions and increased frequency of glucose monitoring may be required when Awiqli is co-administered with these drugs.
Drugs That May Decrease the Blood Glucose Lowering Effect of Awiqli	
Drugs:	Atypical antipsychotics (e.g., olanzapine and clozapine), corticosteroids, danazol, diuretics, estrogens, glucagon, isoniazid, niacin, oral contraceptives, phenothiazines, progestogens (e.g., in oral contraceptives), protease inhibitors, somatropin, sympathomimetic agents (e.g., albuterol, epinephrine, terbutaline), and thyroid hormones.
Intervention:	Dose increases and increased frequency of glucose monitoring may be required when Awiqli is co-administered with these drugs.

Drugs That May Increase or Decrease the Blood Glucose Lowering Effect of Awiqli	
Drugs:	Alcohol, beta-blockers, clonidine, and lithium salts. Pentamidine may cause hypoglycemia, which may sometimes be followed by hyperglycemia.
Intervention:	Dose adjustment and increased frequency of glucose monitoring may be required when Awiqli is co-administered with these drugs.
Drugs That May Blunt Signs and Symptoms of Hypoglycemia	
Drugs:	Beta-blockers, clonidine, guanethidine, and reserpine.
Intervention:	Increased frequency of glucose monitoring may be required when Awiqli is co-administered with these drugs.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data with Awiqli 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 (see *Clinical Considerations*).

Rats and rabbits were exposed to insulin icodec-abae in animal reproduction studies during organogenesis. No adverse developmental effects were observed in rats or rabbits at exposures approximately equal to human exposure at a dose of 230 U/week (see *Data*).

The estimated background risk of major birth defects is 6 to 10% in women with pre-gestational diabetes with an HbA_{1c} >7 and has been reported to be as high as 20 to 25% in women with an HbA_{1c} >10. The estimated background risk of miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Clinical Considerations

Disease-associated Maternal and/or Embryo/fetal Risk

Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, pre-eclampsia, spontaneous abortions, pre-term delivery, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, still birth, and macrosomia related morbidity.

Data

Animal Data

Insulin icodec-abae was investigated in studies covering the periods of embryo-fetal development and pre- and post-natal development in rats and the period of embryo-fetal development in rabbits. In these studies, insulin icodec-abae did not cause adverse effects on embryo-fetal development when given subcutaneously at up to 10 U/kg/day in rats and 3 U/kg/day in rabbits, resulting in exposures comparable to human exposure (AUC) at a human subcutaneous dose of 230 U/week. Maternal deaths and abortions were observed in rabbits at human exposures secondary to maternal hypoglycemia.

In a pre- and postnatal developmental study in rats where insulin icodec-abae was given by the subcutaneous route at doses up to 8.3 U/kg/day (from Gestation Day 6 through Lactation Day 20), maternal and pup mortality occurred during the lactation period at exposures approximately equal to human exposures, which were secondary to maternal hypoglycemia.

8.2 Lactation

Risk Summary

There are no data on the presence of insulin icodec-abae in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered

along with the mother's clinical need for Awiqli and any potential adverse effects on the breastfed infant from Awiqli or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of Awiqli to improve glycemic control in pediatric patients 10 years of age and older with type 2 diabetes mellitus have been established. Use of Awiqli for this indication is supported by evidence from adequate and well-controlled studies in adults with type 2 diabetes mellitus and a pharmacokinetic study in pediatric patients 10 years of age and older with type 2 diabetes *[*see *Clinical Pharmacology (12.3)].*

The safety and effectiveness of Awiqli has not been established in pediatric patients with type 2 diabetes younger than 10 years of age.

8.5 Geriatric Use

In controlled clinical trials *[see Clinical Studies (14)]* a total of 646 (34.4%) of the 1,880 Awiqli-treated patients with type 2 diabetes were 65 years of age or older and 97 (5.2%) were 75 years of age or older. No overall differences in safety or effectiveness of Awiqli have been observed between patients 65 years of age and older and younger adult patients.

Greater caution should be exercised when Awiqli is administered to geriatric patients since greater sensitivity of some older individuals to the effects of Awiqli cannot be ruled out. The initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemia. Hypoglycemia may be more difficult to recognize in the elderly. More frequent glucose monitoring is recommended and the insulin dose is to be adjusted on an individual basis.

8.6 Renal Impairment

No clinically relevant difference in the pharmacokinetics of Awiqli was identified in a study comparing healthy subjects and subjects with renal impairment including subjects with end stage renal disease. Additional dose adjustment should not be necessary for patients with renal impairment *[see Dosage and Administration (2.3, 2.4), Clinical Pharmacology (12.3)]*. However, as with all insulin products, glucose monitoring should be intensified and the Awiqli dosage adjusted on an individual basis in patients with renal impairment.

8.7 Hepatic Impairment

No difference in the pharmacokinetics of Awiqli was identified in a study comparing healthy subjects and subjects with hepatic impairment (mild, moderate, and severe hepatic impairment) *[see Clinical Pharmacology (12.3)]*. Additional dose adjustment should not be necessary for patients with hepatic impairment *[see Dosage and Administration (2.3, 2.4), Clinical Pharmacology (12.3)].* However, as with all insulin products, glucose monitoring should be intensified and the Awiqli dosage adjusted on an individual basis in patients with hepatic impairment.

10 OVERDOSAGE

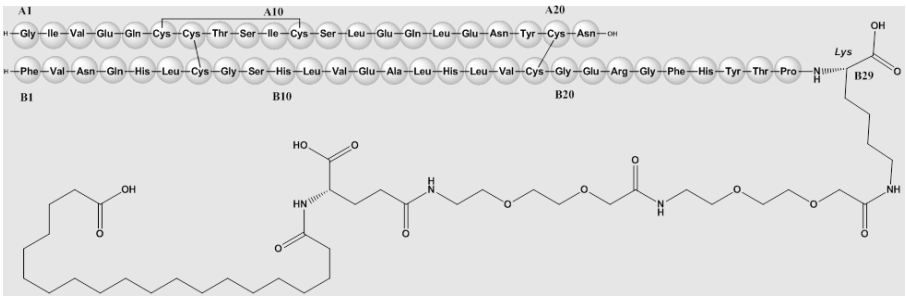
An excess of insulin relative to food intake, energy expenditure, or both may lead to severe and sometimes prolonged and life-threatening hypoglycemia and hypokalemia *[see Warnings and Precautions (5.2, 5.5)]*. Mild episodes of hypoglycemia usually can be treated with oral glucose. Lowering the dosage of Awiqli, adjustments in meal patterns, or physical activity may be needed. More severe episodes of hypoglycemia with coma, seizure, or neurologic impairment may be treated with a glucagon product for emergency use or concentrated intravenous glucose. After apparent clinical recovery from hypoglycemia, continued observation and additional carbohydrate intake may be necessary to avoid reoccurrence of hypoglycemia. Hypokalemia must be corrected appropriately. Overdosing has been investigated in a clinical pharmacology trial *[see Clinical Pharmacology (12.2)]*.

11 DESCRIPTION

Insulin icodec-abae is a once-weekly basal human insulin analog for subcutaneous injection produced by a process that includes expression of recombinant DNA in *Saccharomyces cerevisiae* followed by chemical modification. Insulin icodec-abae differs from human insulin in that the amino acid threonine in position B30

has been omitted, Tyr(A14) has been substituted with Glu and Tyr(B16) and Phe(B25) have been substituted with His. The side chain is connected to the peptide backbone via the amino group in the side chain at Lys(B29). Insulin icodec-abae has a molecular formula of $C_{280}H_{435}N_{71}O_{87}S_6$ and a molecular weight of 6380.26 Da. It has the following structure:

Figure 1: Structural Formula of Insulin Icodec-abae



Awiqli (insulin icodec-abae) injection is a sterile, clear and colorless solution available as 700 units/mL (U-700) for subcutaneous use.

Each mL contains 700 units of insulin icodec-abae and glycerin (15 mg), metacresol (1.08 mg), phenol (5.65 mg), sodium chloride (1.17 mg), zinc acetate (101 mcg), and water for injection.

Awiqli has a pH of approximately 7.4. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

12 CLINICAL PHARMACOLOGY

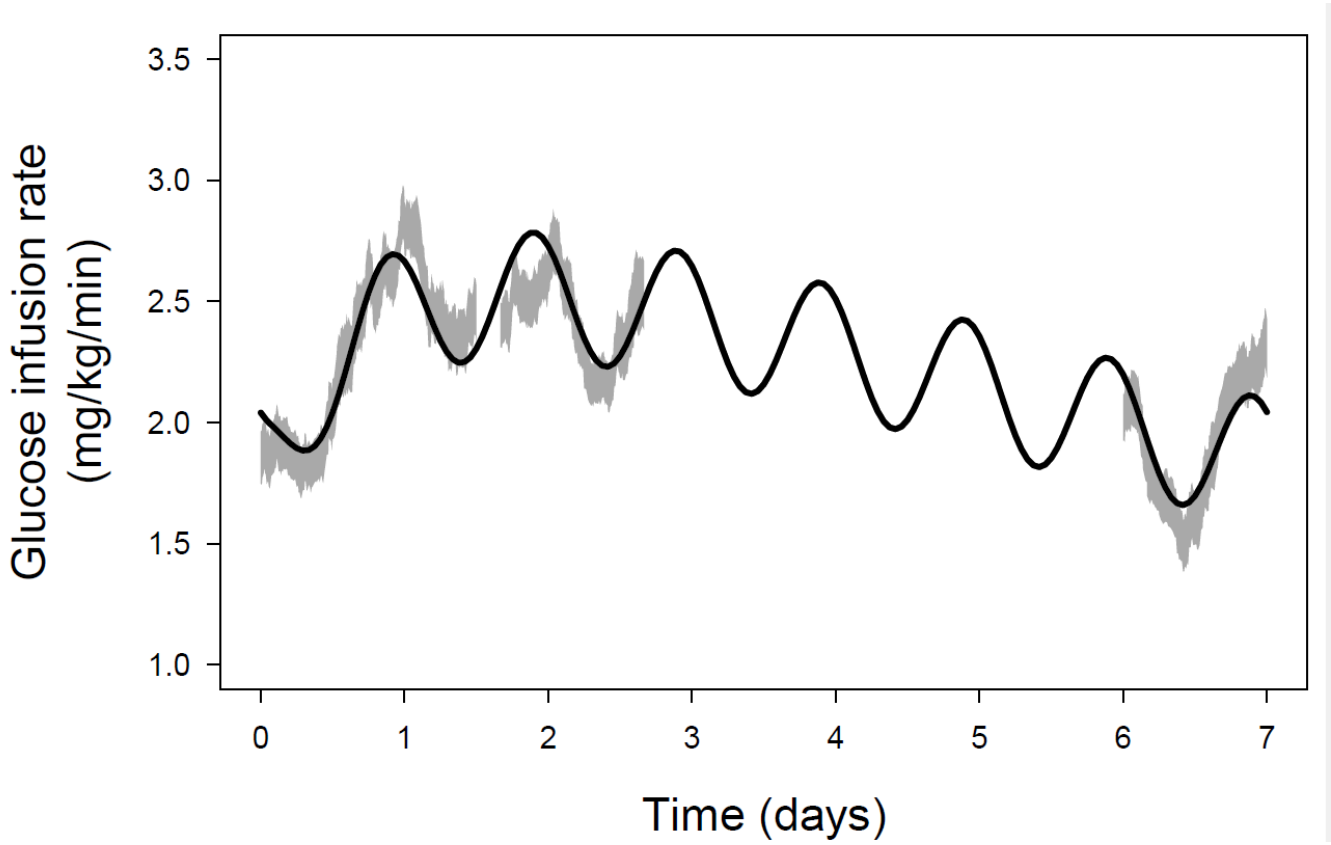
12.1 Mechanism of Action

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 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.

12.2 Pharmacodynamics

Euglycemic clamps were performed at steady state in a single-center, open-label, one-period, multiple-dose study in 46 patients with Type 2 diabetes from 0 to 36 hours, 40 to 64 hours, and 144 to 168 hours post dose. Individualized insulin icodec-abae doses were used to obtain pre-breakfast self-monitored plasma glucose within 80-126 mg/dL, the mean dose at steady state was 2.9 U/kg/week (range: 1.5-5.6 U/kg/week). Glucose infusion rate profiles for all three clamps are shown together with the model-derived data suggesting the duration of the glucose-lowering effect to cover a full week (**Figure 2**).

Figure 2: Full-week Glucose Infusion Rate Profile of Insulin Icodec-abae at Steady-state in Type 2 Diabetes



12.3 Pharmacokinetics

Absorption

Dose proportionality in total exposure is observed after subcutaneous administration of Awiqli within the therapeutic dose range.

Insulin icodec-abae concentration reached steady state levels after 2 to 3 weeks of Awiqli administration with a one-time 50% additional dose for the first dose *[see Dosage and Administration (2.4)]* and after 3 to 4 weeks when initiating Awiqli without a one-time additional dose *[see Dosage and Administration (2.4)]*. In patients with type 2 diabetes, after 8 weekly doses with 2.9 U/kg of Awiqli maximum insulin icodec-abae concentrations of 283 nmol/L were attained at a median of 15 hours (t_{max}) post-dose.

Distribution

The affinity of Awiqli to serum albumin corresponds to a plasma protein binding of >99% in human plasma.

The results of the in vitro protein binding studies demonstrate that there is no clinically relevant interaction between Awiqli and fatty acids or other protein-bound drugs.

Elimination

The half-life after subcutaneous administration is approximately one week independent of dose. Degradation of insulin icodec-abae is similar to that of human insulin; all metabolites formed are inactive.

Specific Populations

Age, Sex, Race, Ethnicity, and Body Weight

The effect of covariates on the pharmacokinetics of Awiqli was examined in a population PK analysis of several exploratory and confirmatory trials. Age (18 to 86 years), sex, race (68% white, 4% Black, and 25% Asian) and ethnicity (86% not of Hispanic or Latino origin, 13% Hispanic or Latino) did not meaningfully affect the pharmacokinetics and pharmacodynamics of Awiqli.

Body weight had a clear effect on Awiqli exposure which decreased with increasing body weight (40 to 160 kg).

Pediatrics

A single dose (5.6 U/kg) study investigating pharmacokinetic properties of Awiqli in 18 pediatric patients 10 years of age and older with type 2 diabetes was conducted. The results show these pediatric patients have faster absorption (approximately 44% higher C_{max}) after administration of the first dose compared to adults with type 2 diabetes, however, similar C_{max} and AUC are achieved at steady state.

Renal Impairment

The pharmacokinetics of insulin icodec-abae were studied in 58 subjects with normal or impaired renal function/end-stage renal disease following administration of single subcutaneous dose (1.5 U/kg) of Awiqli. Renal function was defined using measured iohexol clearance as follows: ≥90 mL/min (normal), 60-89 mL/min (mild), 30-59 mL/min (moderate) and <30 mL/min (severe). Subjects requiring hemodialysis were classified as having end-stage renal disease (ESRD). In this study, there was no apparent effect of renal function or dialysis on the pharmacokinetics of insulin icodec-abae.

Hepatic Impairment

A single subcutaneous dose of 1.5 U/kg Awiqli was administered in an open-label, single-dose study of 25 subjects with normal or different degree of hepatic impairment (mild, moderate and severe) classified based on Child-Pugh Scores ranging from 0 (healthy volunteers) to 12 (severe hepatic impairment). In this study, there was no apparent impact of the degree of hepatic impairment on the pharmacokinetic parameters of insulin icodec-abae.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies (ADA) is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of ADAs in the studies described below with the incidence of ADAs in other studies, including those of Awiqli.

During the 26-week treatment periods with ADA sampling conducted up to 31 weeks in three clinical trials in adults with Type 2 diabetes mellitus *[see Clinical Studies (14)]*, 4/243 (1.6%) (insulin naïve) and 131/548 (23.9%) (insulin experienced) of Awiqli-treated patients were positive for anti-insulin icodec-abae antibodies at baseline.192/243 (79.0%) (insulin naïve) and 389/550 (70.7%) (insulin experienced) were positive for anti-insulin icodec-abae antibodies at least once during the trials. In these trials, 188/243 (77.4%) (insulin naïve) and 370/550 (67.3%) (insulin experienced) of patients were positive for anti-insulin icodec-abae antibodies cross-reacting with human insulin at least once during the trial.

In vitro neutralizing activity of anti-insulin icodec-abae antibodies on insulin receptor action was tested in follow-up (Week 31) samples from one trial in insulin-naïve Type 2 patients. A total of 178 anti-insulin icodec-abae antibody positive samples were tested and in vitro neutralizing activity was detected in 23/178 (12.9%) of the anti-insulin icodec-abae antibody positive follow-up samples.

The patients with anti-insulin icodec-abae antibodies had increased insulin icodec-abae concentrations (increase in geometric mean ratio up to 1.2 compared to patients who did not develop anti-insulin icodec-abae antibodies). There was no identified clinically significant effect of anti-insulin icodec-abae antibodies on safety or effectiveness of Awiqli over the treatment duration of 26 weeks.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Standard 2-year carcinogenicity studies in animals have not been performed to evaluate the carcinogenic potential of insulin icodec-abae. In a 52-week study including human insulin (NPH insulin) as comparator, Sprague-Dawley rats were dosed subcutaneously with insulin icodec-abae at 3.3, 5 (female only), 6.7 and 10 (male only) U/kg/day, resulting in 4 times (males) and 2 times (females) the human exposure (AUC) when compared to a human subcutaneous dose of 230 U/week. Human insulin was dosed at 6.7 U/kg/day. No

treatment-related increases in benign or malignant tumors were recorded in female mammary glands from rats dosed with insulin icodec-abae. Further, no treatment related changes in the occurrence of hyperplastic or neoplastic lesions were seen in other tissues in animals dosed with insulin icodec-abae when compared to vehicle or human insulin.

Genotoxicity testing of insulin icodec-abae was not performed.

In a combined fertility and embryo-fetal study in male and female rats, treatment with insulin icodec-abae up to 17 U/kg/day in males and 10 U/kg/day in females (4 times and comparable to human exposure (AUC) at 230 U/week, respectively) prior to mating and in female rats during gestation had no effect on mating performance and fertility.

14 CLINICAL STUDIES

14.1 Overview of Clinical Trials

The efficacy of Awiqli administered once-weekly in adult patients with type 2 diabetes, used in combination with a mealtime insulin or in combination with common oral anti-diabetic agents and/or GLP-1 receptor agonist, was evaluated in three 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 four 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 to 130 mg/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.

14.2 Insulin Naïve Adults with Type 2 Diabetes Mellitus

The efficacy of Awiqli was evaluated in a 52-week randomized, open label, active-controlled, parallel-group, multicenter, multinational, treat-to-target trial that enrolled 984 insulin naïve adult patients with type 2 diabetes mellitus inadequately controlled on one or more oral antidiabetic agents (OADs) or GLP-1 receptor agonist [Trial A (NCT04460885)]. Patients were randomized to Awiqli once-weekly or insulin glargine U-100 once-daily according to the approved labeling. 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.

The trial population had the following characteristics: mean age was 59 years; mean duration of diabetes was 12 years; 57% were male, 66% were White, 28% were Asian, 3% were Black or African American, and 11% were Hispanic or Latino ethnicity; and 11% of patients had eGFR <60 mL/min/1.73m^2. The mean BMI was approximately 30.1 kg/m^2.

Treatment with Awiqli once weekly for 52 weeks resulted in a statistically significant reduction in HbA_{1c} compared to once daily insulin glargine U-100 with an estimated treatment difference of -0.18% $[-0.29\%; -0.08\%]_{95\%CI}$ (see **Table 4**).

Treatment with Awiqli once-weekly for 52 weeks also resulted in a statistically significantly longer Time in Range (TIR) (4.27% $[1.92; 6.62]_{95CI}$, ~ 1 hour per day) compared to once daily insulin glargine U-100 treatment during the last 4 weeks of the trial (Weeks 48 to 52) (see **Table 4**).

Table 4: Results at Week 52 in Trial A Comparing Awiqli to Insulin Glargine U-100 in Insulin Naïve Adult Patients with Type 2 Diabetes Mellitus on OAD(s) or GLP-1 Receptor Agonist

	Awiqli + OAD(s)/GLP-1 Receptor Agonist	**Insulin Glargine + OAD(s)/GLP-1 Receptor Agonist**
N	492	492
HbA_{1c} (%)		

Baseline	8.5	8.44
End of trial (LSMean)[a, b]	6.96	7.15
Change from baseline (LSMean)[a,b]	-1.51	-1.33
Estimated treatment difference[a,b] [95%CI] Awiqli – insulin glargine U-100	-0.18 [-0.29; -0.08][c]	
Proportion Achieving HbA_{1c} < 7% at Trial End (LSMean)[d]	56.52%	44.57%
FPG (mg/dL)		
Baseline	185.31	185.71
End of trial (LSMean)[a,b]	125.19	125.43
Change from baseline (LSMean)[a,b]	-60.32	-60.08
TIR (70-180 mg/dL) (%)		
Week 48 to 52 (LSMean)[e]	71.27	67
Estimated treatment difference[e] [95%CI] Awiqli – insulin glargine U-100	4.27 [1.92; 6.62][f]	
Weekly Basal Insulin Dose (Units)		
End of trial (LSMean)[e,g]	214.23	222.39

[a] Estimated using an ANCOVA with treatment, and region as fixed factors and baseline response as covariate.
[b] Missing values were imputed by the baseline value adding a random term, using multiple imputation.
There were 2.6% of patients in the Awiqli arm and 2.6% in the glargine arm for whom HbA_{1c} data was missing at Week 52.
[c] p=0.0004 (two-sided) for superiority, adjusted for multiplicity.
[d] Estimated using logistic regression with treatment, and region as fixed factors and baseline HbA_{1c} as covariate.
[e] Estimated using an ANOVA with treatment, and region as fixed factors. Missing values were imputed using multiple imputation based on patients in the insulin glargine arm who completed their randomized treatment.
[f] p<0.001 (two-sided) for superiority, adjusted for multiplicity.
[g] Dose was log-transformed before analysis.

The efficacy of Awiqli was evaluated in a 26-week randomized, double blinded, active-controlled, parallel-group, multicenter, multinational, treat-to-target trial that enrolled 588 adult insulin-naïve patients with type 2 diabetes mellitus inadequately controlled on one or more oral antidiabetic agents (OADs) or GLP-1 receptor agonist [Trial B (NCT04795531)]. Patients were randomized to Awiqli once weekly or insulin degludec U-100 once daily according to the approved labeling. 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 approximately 50% at the discretion of the investigator.

The trial population had the following characteristics: mean age was 58 years; mean duration of diabetes was 11 years; 63% were male; 60% were White, 28% were Asian, 3% were Black or African American, and 28% were Hispanic or Latino ethnicity; and 8% of patients had eGFR <60 mL/min/1.73m^2. The mean BMI was approximately 29.6 kg/m^2.

Treatment with Awiqli once-weekly for 26 weeks resulted in a statistically significant reduction in HbA_{1c} compared to once-daily insulin degludec U-100 with an estimated treatment difference of -0.22 $[-0.35; -0.09]_{95\%CI}$ (see **Table 5**).

Table 5: Results at Week 26 in Trial B Comparing Awiqli to Insulin Degludec U-100 in Insulin Naïve Adult Patients with Type 2 Diabetes Mellitus on OAD(s) or GLP-1 Receptor Agonist

	Awiqli + OAD(s)/GLP-1 RA	**Insulin Degludec + OAD(s)/GLP-1 Receptor Agonist**
N	294	294
HbA_{1c} (%)		
Baseline	8.55	8.48
End of trial (LSMean)[a,b*]	6.96	7.18
Change from baseline (LSMean)[a, b]	-1.56	-1.34
Estimated treatment difference[a,b] [95%CI] Awiqli – insulin degludec U-100	-0.22 [-0.35; -0.09][c]	
Proportion Achieving HbA_{1c} < 7% at Trial End (LSMean)[d]	56.45%	40.95%
FPG (mg/dL)		
Baseline	186.78	176.20
End of trial (LSMean)[a,b]	127.16	127.53
Change from baseline (LSMean)[a,b]	-54.28	-53.9
Weekly Basal Insulin Dose (Units)		
End of trial (LSMean)[e]	204.28	186.52

[a] Estimated using an ANCOVA with treatment, SU or glinide use (yes/no), and region as fixed factors and baseline response as covariate.
[b] Missing values were imputed by the baseline value adding a random term, using multiple imputation.
There were 3.7% of patients in the Awiqli arm and 3.1% in the degludec arm for whom HbA_{1c} data was missing at Week 26.
[c] p=0.0007 (two-sided) for superiority, adjusted for multiplicity.
[d] Estimated using logistic regression with treatment, SU or glinides use (yes/no) and region as fixed factors and baseline HbA_{1c} as covariate.
[e] Estimated using an ANOVA with treatment, SU or glinide use (yes/no), and region as fixed factors. Dose was log-transformed before analysis. Missing values were imputed using multiple imputation based on patients in the insulin glargine arm who completed their randomized treatment.

14.3 Adults with Type 2 Diabetes Mellitus Previously Treated with Basal Insulin

The efficacy of Awiqli was evaluated in a 26-week randomized, open label, active-controlled, parallel-group, multicenter, multinational, treat-to-target trial in 526 adult patients with type 2 diabetes mellitus treated with once or twice daily basal insulin with or without OADs [Trial C (NCT04770532)]. Patients were randomized to Awiqli once-weekly or insulin degludec U-100 once daily according to the approved labeling. Pre-trial non-insulin OADs/GLP-1 receptor agonist were continued as background therapy in both treatment arms throughout the entire trial except for sulfonylureas and glinides, which were discontinued at randomization.

The trial population had the following characteristics: mean age was 62 years; mean duration of diabetes was 17 years; 57% were male, 57% were White, 4% were Black or African American, 37% were Asian, and 6% were Hispanic or Latino ethnicity; and 15% of patients had eGFR <60 mL/min/1.73m^2. The mean BMI was approximately 29.6 kg/m^2.

Treatment with Awiqli once-weekly for 26 weeks resulted in a statistically significant reduction in HbA_{1c} compared with insulin degludec U-100 with estimated treatment difference of -0.19[-0.32; -0.06]$_{95\%CI}$ (see **Table 6**).

Estimated time in Range (70 to 180 mg/dL) during the last 4 weeks of the trial (Weeks 22 to 26) was 62.34% for Awiqli and 59.93% for insulin degludec U-100.

Table 6: Results at Week 26 in Trial C Comparing Awiqli to Insulin Degludec U-100 in Adult Patients with Type 2 Diabetes Mellitus Previously Treated with Basal Insulin

	Awiqli ± OAD(s)/GLP-1 Receptor Agonist	**Insulin Degludec ± OAD(s)/GLP-1 Receptor Agonist**
N	263	263
HbA_{1c} (%)		
Baseline	8.17	8.1
End of trial (LSMean)[a,b]	7.23	7.43
Change from baseline (LSMean)[a,b]	-0.90	-0.71
Estimated treatment difference[a,b] [95%CI] Awiqli – insulin degludec U-100	-0.19 [-0.32; -0.06][c]	
Proportion (%) Achieving HbA_{1c} < 7% at Trial End (LSMean)[d]	37.53	25.35
FPG (mg/dL)		
Baseline	152.24	150.7
End of trial (LSMean)[a,b]	123.01	122.3
Change from baseline (LSMean)[a,b]	-28.47	-29.18
Weekly Basal Insulin Dose (Units)		
End of trial (LSMean)[e]	247.99	262.69

[a] Estimated using an ANCOVA with treatment, personal CGM device use (yes/no) and region as fixed factors and baseline response as covariate.
[b] Missing values were imputed by the baseline value adding a random term, using multiple imputation.
There were 2.7% of patients in the Awiqli arm and 3.8% in the degludec arm for whom HbA_{1c} data was missing at Week 26.
[c] p=0.0032 (two-sided) for superiority, adjusted for multiplicity.
[d] Estimated using logistic regression with treatment, personal CGM use (yes/no) and region as fixed factors and baseline HbA_{1c} as covariate.
[e] Estimated using an ANOVA with treatment, personal CGM device use (yes/no), and region as fixed factors. Dose was log-transformed before analysis. Missing values were imputed using multiple imputation based on patients in the degludec arm who completed their randomized treatment.

The efficacy of Awiqli was evaluated in a 26-week randomized, open-label, active-controlled, parallel-group, multicenter, multinational, treat-to-target trial in 582 adult patients with type 2 diabetes mellitus inadequately controlled on once-daily basal insulin in combination with mealtime rapid-acting insulin with or without oral antidiabetic agents (OADs) or GLP-1 receptor agonist [Trial D (NCT04880850)]. Patients were randomized to Awiqli once-weekly or insulin glargine U-100 once daily according to the approved

labeling both in combination with insulin aspart before each meal. Pre-trial non-insulin OADs or GLP-1 receptor agonist were continued as background therapy in both treatment arms throughout the entire trial except for sulfonylureas and glinides, which were discontinued at randomization.

The trial population had the following characteristics: mean age was 60 years; mean duration of diabetes was 17 years; 52% were male; 64% were White, 32% were Asian, 4% Black or African American, and 18% were Hispanic; and 16% of patients had eGFR <60 mL/min/1.73m^2. The mean BMI was approximately 30.3 kg/m^2.

At Week 26, the difference in HbA_{1c} reduction from baseline between Awiqli and insulin glargine U-100 was 0.02% with a 95% confidence interval of [-0.11; 0.15] and met the pre-specified non-inferiority margin (0.3%) (see **Table 7**).

Estimated time in Range (70 to 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.

Table 7: Results at Week 26 in Trial D Comparing Awiqli to Insulin Glargine U-100 in Adult Patients with Type 2 Diabetes Mellitus Receiving Insulin Aspart at Mealtimes with or without OADs or GLP-1 Receptor Agonist

	Awiqli + Insulin Aspart ± OAD(s)/GLP-1 Receptor Agonist	**Insulin Glargine + Insulin Aspart ± OAD(s)/GLP-1 Receptor Agonist**
N	291	291
HbA_{1c} (%)		
Baseline	8.29	8.31
End of trial (LSMean)[a,b]	7.14	7.12
Change from baseline LSMean)[a,b]	-1.16	-1.18
Estimated treatment difference[a,b] [95%CI] Awiqli – insulin glargine U-100	0.02 [-0.11; 0.15]	
Proportion Achieving HbA_{1c} <7% at Trial End (LSMean)[c]	40.69	45.48
FPG (mg/dL)		
Baseline	166.59	173.05
End of trial (LSMean)[a,b]	138.28	140.76
Change from baseline LSMean)[a,b]	-31.54	-29.06
Weekly Basal Insulin Dose (Units)		
End of trial (LSMean)[d]	321.90	283.46
Weekly Bolus Insulin Dose (Units)		
End of trial (LSMean)[d]	197.54	260.61

[a] Estimated using an ANCOVA with treatment, personal CGM device use (yes/no) and region as fixed factors and baseline response as covariate.
[b] Missing values were imputed by the baseline value adding a random term, using multiple imputation.

There were 5.5% of patients in the Awiqli arm and 9.3% in the glargine arm for whom HbA_{1c} data was missing at Week 26.
[c] Estimated using logistic regression with treatment, personal CGM use (yes/no) and region as fixed factors and baseline HbA_{1c} as covariate.
[d] Estimated using an ANOVA with treatment, personal CGM device use (yes/no), and region as fixed factors. Dose was log-transformed before analysis. Missing values were imputed using multiple imputation based on patients in the glargine arm who completed their randomized treatment.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Awiqli (insulin icodec-abae) injection is a 700 units/mL (U-700) clear and colorless solution available as follows:

Table 8: Presentations of Awiqli FlexTouch

Awiqli Presentation	NDC Number	Total Units	Max Dose per Injection (units)	Dose Increment (units)	Package Size
3 mL single-patient-use FlexTouch Pen	0169-3121-13	2,100	700	10	1 pen/pack with 13 disposable needles Trade only
1.5 mL single-patient-use FlexTouch Pen	0169-3105-11	1,050	700	10	1 pen/pack with 13 disposable needles Trade only
1 mL single-patient-use FlexTouch Pen	0169-3170-97	700	700	10	1 pen/pack with 9 disposable needles Sample only

Awiqli U-700 FlexTouch pen dials in 10-unit increments.

Dispense in this sealed carton with the enclosed Instructions for Use.

Storage and Handling

Dispense in the original sealed carton with the enclosed Instructions for Use.

Do not store in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze. Do not use Awiqli if it has been frozen.

The storage conditions are summarized in **Table 9**:

Table 9: Storage Conditions for 3 mL, 1.5 mL, and 1 mL Single-Patient-Use Awiqli FlexTouch Pen

	Not in-use (unopened)		**In-use (opened)**	
	Refrigerated 36ºF to 46ºF (2ºC to 8ºC)	**Room Temperature below 86ºF (30ºC)***	**Room Temperature below 86ºF (30ºC)***	**Refrigerated 36ºF to 46ºF (2ºC to 8ºC)**
Awiqli FlexTouch	Until expiration date	12 weeks	12 weeks	12 weeks

* The total time at room temperature cannot exceed more than 12 weeks including in-use time.

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Hypoglycemia Due to Medication Errors and Accidental Overdose
Advise patients to always check the product label before each injection to confirm they are using Awiqli and not another insulin or injectable antidiabetic medicine. Advise patients using other injectable medications for glycemic control that the dosage selection of Awiqli differs. Instruct patients to visually verify the dialed units on the dose counter of the Awiqli FlexTouch prefilled pen before each injection to avoid dosing errors *[see Warnings and Precautions (5.1)]*.

Hypoglycemia
Inform patients that hypoglycemia is the most common adverse reaction with insulin. Inform patients of the symptoms of hypoglycemia (e.g., impaired ability to concentrate and react). This may present a risk in situations where these abilities are especially important, such as driving or operating other machinery. Advise patients who have frequent hypoglycemia or reduced or absent warning signs of hypoglycemia to use caution when driving or operating machinery *[see Warnings and Precautions (5.2)]*.

Hyperglycemia or Hypoglycemia with Changes in Insulin Regimen
Advise patients that changes in insulin regimen can predispose to hyperglycemia or hypoglycemia and that changes in insulin regimen should be made under close medical supervision *[see Warnings and Precautions (5.3)]*.

Hypersensitivity Reactions
Advise patients that hypersensitivity reactions have occurred with Awiqli. Inform patients on the symptoms of hypersensitivity reactions *[see Warnings and Precautions (5.4)]*.

Never Share an Awiqli FlexTouch Pen or Needle Between Patients
Awiqli FlexTouch disposable prefilled pens should never be shared between patients, even if the needle is changed. Sharing poses a risk for transmission of blood-borne pathogens *[see Warnings and Precautions (5.6)]*.

Manufactured by:
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For information about Awiqli contact:
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800 Scudders Mill Road
Plainsboro, NJ 08536
1-844-668-6463

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Patent Information: http://novonordisk-us.com/products/product-patents.html

PATIENT INFORMATION
Awiqli® FlexTouch® [Ah–wik-lee]
(insulin icodec-abae)
injection, for subcutaneous use

Do not share your Awiqli FlexTouch pen or needles with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.

Make sure you use the right type and dose of insulin. Always check the label on your insulin pen before each injection to avoid mix-ups with Awiqli and other insulin products or injectable medicines used to treat diabetes. If you use another injectable medicine to treat your diabetes, pay close attention to how you select your Awiqli dosage. The dosage of Awiqli is different from other injectable medicines used to treat diabetes.

Always make sure that you select the correct dosage of your Awiqli FlexTouch pen as prescribed by your healthcare provider, to avoid dosing errors and accidental overdose. People who are blind or have vision problems should not use this pen without help from a person trained to use the pen.

Do not dial the maximum single dosage (700 units) of your Awiqli FlexTouch Pen, unless prescribed by your healthcare provider.

Do not use a syringe to withdraw Awiqli from your pen.

Talk to your healthcare provider if you have any questions about how to correctly dose Awiqli FlexTouch.

What is Awiqli?

- Awiqli is a long-acting man-made insulin (U-700) that is used to control high blood sugar in adults and children who are 10 years of age and older with type 2 diabetes mellitus.
- It is not known if Awiqli is safe and effective in children less than 10 years of age.
- Awiqli FlexTouch is only available in one concentration (U-700):
  - The Awiqli FlexTouch pen can be injected from 10 units to 700 units in a single injection, in 10-unit increments.

Who should not take Awiqli?

Do not take Awiqli if you:

- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to Awiqli or any of the ingredients in Awiqli. See the end of this Patient Information leaflet for a complete list of ingredients in Awiqli.

Before taking Awiqli, tell your healthcare provider about all your medical conditions including, if you:

- have liver or kidney problems.
- take other medicines, especially ones called TZDs (thiazolidinediones).
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with Awiqli.
- are pregnant, planning to become pregnant, or are breastfeeding.
- are taking new prescription or over-the-counter medicines, vitamins, or herbal supplements.

Before you start taking Awiqli, talk to your healthcare provider about low blood sugar and how to manage it.

How should I take Awiqli FlexTouch?

- **Read the Instructions for Use** that come with your Awiqli FlexTouch Pen.
- **Your healthcare provider should show you how to use Awiqli FlexTouch Pen before you use it for the first time.**
- Take Awiqli exactly as your healthcare provider tells you to. **Do not do any conversion of your dose. The dose counter always shows the selected dose in units.** Awiqli FlexTouch pens are made to deliver your insulin dose in units.
- Know the type and strength of insulin you take. **Do not** change the type of insulin you take unless your healthcare provider tells you to. The amount of insulin and the best time for you to take your insulin may need to change if you take different types of insulin.
- Inject Awiqli FlexTouch 1 time each week on any day of the week on the same day each week.
- If you need to change the day of the week, you may do so if your last dose has been at least **4 days**.
- If you missed your dose, take your missed dose as soon as possible as long as it has been 4 days or less. Then continue the 1 time each week schedule 1 week from the day your missed dose was taken.
- If more than 4 days have passed, skip the missed dose and take your next Awiqli dose on your regularly scheduled day.
- **Check your blood sugar levels.** Ask your healthcare provider what your blood sugar should be and when you should check your blood sugar levels.

- **Never** inject Awiqli FlexTouch into a vein or muscle or use Awiqli in an infusion pump.
- **Never** use a syringe to remove Awiqli from the FlexTouch pen.
- **Do not** dilute or mix Awiqli with any other insulin or solution.
- Awiqli FlexTouch can be injected under the skin (subcutaneously) of your upper legs (thighs), upper arms, or stomach area (abdomen).
- **Change (rotate) your injection sites within the area you choose with each dose** to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the injection sites.
- **Do not** use the exact same spot for each injection.
- **Do not** inject where the skin has pits, is thickened, or has lumps.
- **Do not** inject where the skin is tender, bruised, scaly or hard, or into scars or damaged skin.

Keep Awiqli and all medicines out of the reach of children.

What should I avoid while taking Awiqli?

While taking Awiqli do not:

- Drive or operate heavy machinery, until you know how Awiqli affects you.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

What are the possible side effects of Awiqli?

Awiqli may cause serious side effects that can lead to death, including:

- **Low blood sugar (hypoglycemia).** Signs and symptoms that may indicate low blood sugar include:
  - dizziness or light-headedness
  - blurred vision
  - anxiety, irritability, or mood changes
  - sweating
  - slurred speech
  - hunger
  - confusion
  - shakiness
  - headache
  - fast heartbeat
- **Severe allergic reaction (whole body reaction).** Stop using Awiqli and get medical help right away, if you have any of these signs or symptoms of a severe allergic reaction:
  - a rash over your whole body, trouble breathing, a fast heartbeat, or sweating.
- **Low potassium in your blood (hypokalemia).**
- **Heart failure.** Taking certain diabetes pills called thiazolidinediones or “TZDs” with Awiqli may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure, it may get worse while you take TZDs with Awiqli. Your healthcare provider should monitor you closely while you are taking TZDs with Awiqli. Tell your healthcare provider if you have any new or worse symptoms of heart failure including shortness of breath, tiredness, swelling of your ankles or feet and sudden weight gain. Treatment with TZDs and Awiqli may need to be adjusted or stopped by your healthcare provider if you have new or worse heart failure.

Your insulin dose may need to change because of:

- change in level of physical activity or exercise
- increased stress
- change in diet
- weight gain or loss
- illness

Common side effects of Awiqli may include:

- hypoglycemia, serious allergic reactions (whole body reactions), reactions at the injection site, skin thickening or pits at the injection site (lipodystrophy), itching, rash, swelling of your hands and feet, and weight gain.

Get emergency medical help if you have:

- trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

These are not all the possible side effects of Awiqli. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of Awiqli.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about Awiqli that is written for health professionals. **Do not** use Awiqli FlexTouch for a condition for which it was not prescribed. **Do not** give Awiqli to other people, even if they have the same symptoms that you have. It may harm them.

What are the ingredients in Awiqli?

Active Ingredient: insulin icodec-abae

Inactive Ingredients: Glycerin; metacresol; phenol; sodium chloride; zinc acetate and water for injection. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

Manufactured by:

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800 Scudders Mill Road
Plainsboro, NJ 08536
U.S. License No. 1261
At: Novo Nordisk A/S
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For more information, go to www.awiqli.com or call 1-844-668-6463.
Patent Information: http://novonordisk-us.com/products/product-patents.html
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This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: 10/2026

INSTRUCTIONS FOR USE
Awiqli® [Ah–wik-lee] FlexTouch®
(insulin icodec-abae)
injection, for subcutaneous use
700 units/mL (U-700)

Read these instructions carefully, and talk to your healthcare provider about how to use the needle and inject Awiqli before you begin using your Awiqli FlexTouch Pen. Make sure that you know how to give yourself an injection with the pen before you start your treatment.

Important information before you start using your pen:

- **Do not share your Awiqli FlexTouch Pen or needles with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.**
- People who are blind or have vision problems should not use this pen without help from a person trained to use the pen.
- Make sure you use the right type and dose of insulin. Always check the label on your insulin pen before each injection to avoid mix-ups with Awiqli and other insulin products or injectable medicines used to treat diabetes.
- If you use another injectable medicine to treat your diabetes, pay close attention to how you select your Awiqli dosage. The dosage of Awiqli is different from other injectable medicines used to treat diabetes.
- Always make sure that you select the correct dosage of your Awiqli FlexTouch Pen as prescribed by your healthcare provider, to avoid taking the wrong dose or taking too much Awiqli.
- **Do not** dial the maximum single dose (700 units) of your Awiqli FlexTouch Pen, unless prescribed by your healthcare provider.
- **Do not** use a syringe to withdraw Awiqli from your pen.
- **Do not** try to refill your pen. After it is empty, it must be thrown away (disposed of).
- Needles are for single use only. **Do not** re-use your needles as it may lead to contamination, infection, and blocked needles, which may lead to you injecting the wrong dose.
- Caregivers must be careful when handling used needles to prevent accidental needle stick injuries and infection.

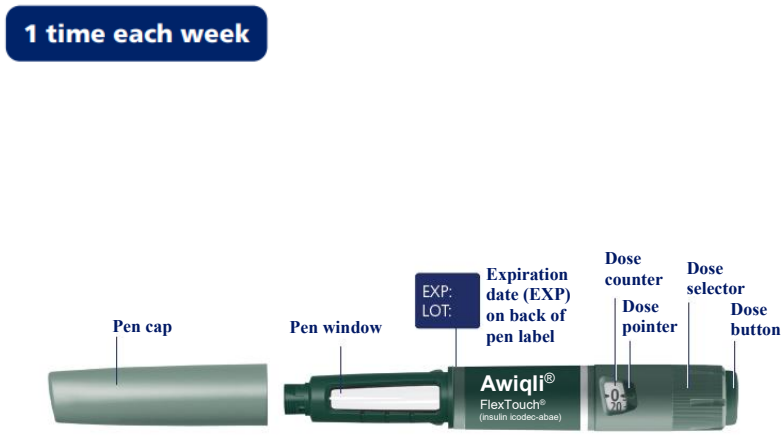
Information about your pen
Awiqli FlexTouch Pen (pen) is a prefilled disposable single-patient-use pen containing 700 units of insulin icodec-abae. You can inject from 10 to 700 units in a single injection. The units can be increased by 10 units at a time.

Supplies you will need to give your Awiqli injection:
- Awiqli FlexTouch Pen (included)
- 1 new NovoFine Plus, or NovoFine needle (included)
- 1 alcohol swab (not included)
- 1 cotton ball or gauze pad (not included)
- 1 sharps disposal container for throwing away (disposing of) used Awiqli FlexTouch Pens and needles. See "**Disposing of used Awiqli FlexTouch pens and needles**" at the end of this Instructions for Use.

Look at the pictures to get to know the different parts of your pen and needle.

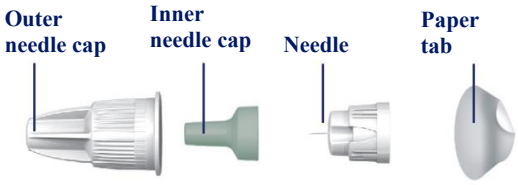
Awiqli FlexTouch Pen

Note: Your pen may differ in size from the pen shown in the pictures. These instructions apply to all Awiqli FlexTouch Pens.



Needle

About your needles:
Your pen is designed to be used with NovoFine® Plus, or NovoFine® disposable needles up to a length of 8 mm. Disposable needles are included in the pack. **Always check the flow as described in Step 2 and use a new needle for each injection.** Always throw away the needle after each use in a sharps disposal container.

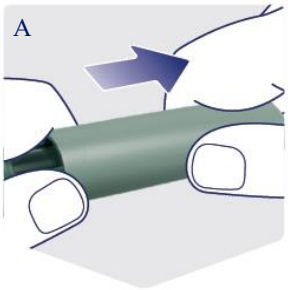
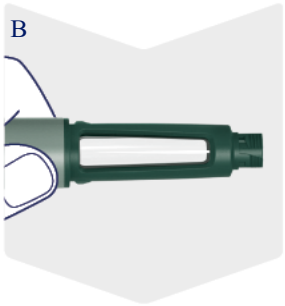
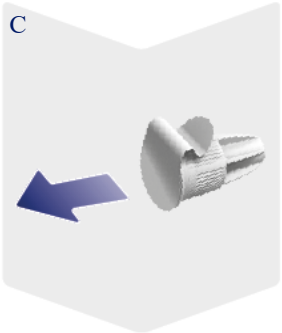
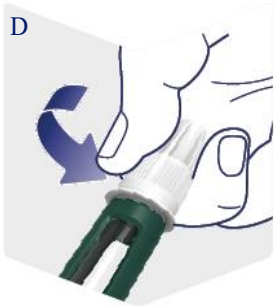


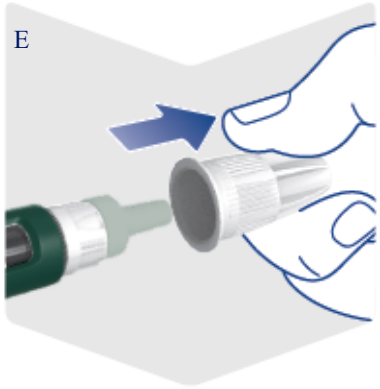
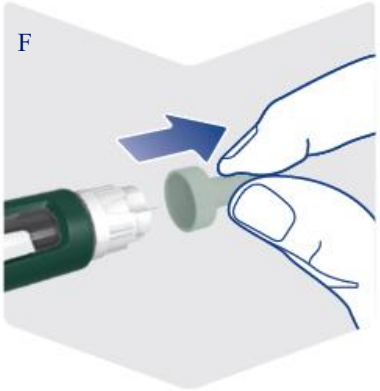
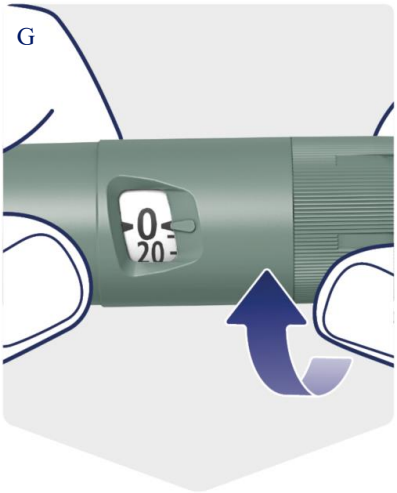
Step 1: Prepare your pen with a new needle

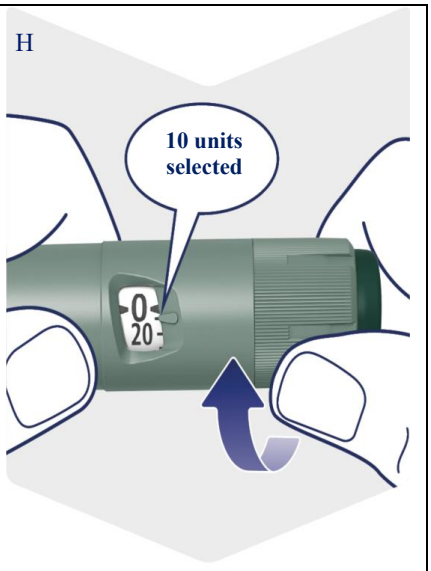
Wash your hands with soap and water.

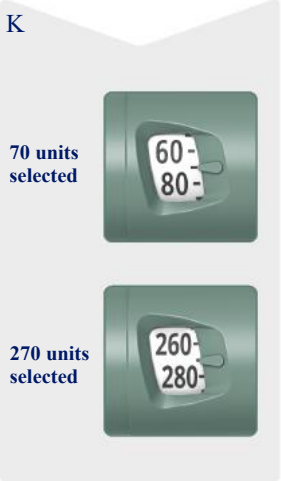
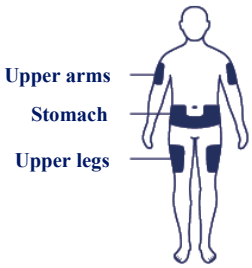
Check the name and concentration on the pen label to make sure that your pen contains Awiqli 700 units/mL.

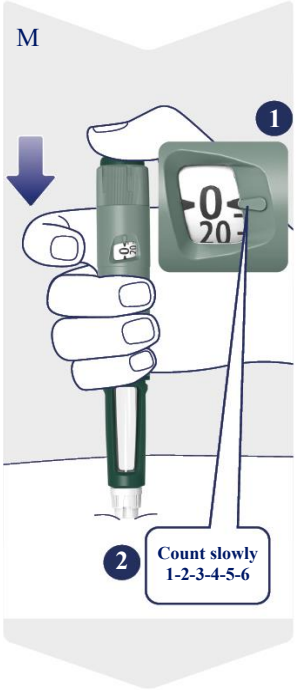
Pull off the pen cap. See **Figure A**.

	
Always check that Awiqli in your pen is clear and colorless. Look through the pen window. If Awiqli looks cloudy or contains particles, **do not** use the pen. See **Figure B**.	
Always use a new needle for each injection. Check the paper tab and the outer needle cap for damage. If you see any damage, this could mean the needle is not clean. Throw away the needle in a sharps disposal container and use a new one. **Take a needle and tear off the paper tab. Do not** attach a new needle to your pen until you are ready to give your injection. See **Figure C**.	
Push the needle straight onto the pen. Turn forward until it is on tight. See **Figure D**.	
The needle is covered by 2 caps. You must remove both caps. If you forget to remove both caps, you will not inject any **Awiqli.** Pull off the outer needle cap and keep it for later. See **Figure E**.	

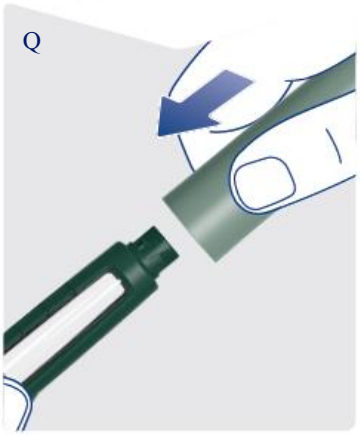
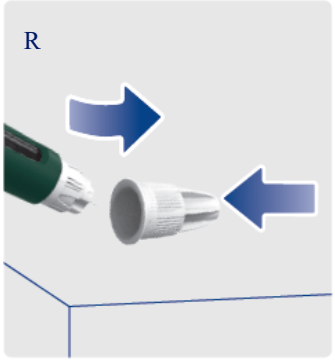
Pull off the inner needle cap and throw it away. See **Figure F**. A drop of Awiqli may appear at the needle tip. This is normal, but you must still check the Awiqli flow before each injection. See **Step 2**. **Never use a bent or damaged needle.**	 
Step 2: Check the flow before each injection	
Always check the flow before each injection. This helps you to make sure you will get your full Awiqli dose. Turn the dose selector forward until you see the 10 units mark (this is the first mark) on the dose counter. See **Figure G**.	
Make sure that the mark lines up with the dose pointer. See **Figure H**.	

	
Hold the pen with the needle pointing up. See **Figure I**. **Press and hold in the dose button until the dose counter shows 0.** The 0 must line up with the dose pointer. **A drop of Awiqli should appear at the needle tip.** This drop indicates that your pen is ready for use. See **Figure I**. **If a drop does not appear, repeat Step 2 to check the flow again.** This should only be done 3 times in total. **If there is still no drop**, you might have a blocked needle. Change the needle as described in **Step 6** and **Step 1**. Then check the flow again. **Do not use the pen** if a drop of Awiqli still does not appear. Contact Novo Nordisk at 1-844-668-6463.	

Step 3: Set your dose	
Check that the dose pointer is set at ·0·. Turn the dose selector to select the number of units you need to inject. See **Figure J**. The units shown in the dose counter will help you select your dose. The dose can be increased by 10 units at a time. You will hear a 'click' every time you turn the dose selector. **Do not** set the dose by counting the number of clicks you hear. If you select a wrong dose, you can turn the dose selector forwards or backwards to the correct dose.	J
When your dose lines up with the dose pointer, you have selected your dose. **Make sure you select the dose prescribed by your healthcare provider.** **Figure K** shows examples of how to choose your dose correctly. If the dose counter stops before you reach your prescribed dose, see "**Do you have enough Awiqli?**" section below in this Instructions for Use.	K 
Step 4: Choose your injection site	
Choose an injection site on your stomach (keep a 2-inch distance from your belly button), upper legs, or upper arms. You may inject in the same body area each week, but make sure it is not in the same spot that was used for your last injection. Clean the injection site with an alcohol swab. **Do not** touch the injection site after cleaning.	
Step 5: Inject your dose	
Fully insert the needle straight into your skin.	

Make sure you can see the dose counter. Do not cover the dose counter or touch it with your fingers. This could stop the injection. **Press and hold down** the dose button. See **Figure L**.	L
1 **Keep pressing the dose button until the dose counter shows 0.** The mark for 0 must line up with the dose pointer. See **Figure M**. **You may hear or feel a click when the dose counter returns to 0.** 2 **After the dose counter reaches 0,continue pressing the dose button with the needle in your skin and slowly count to 6**. See **Figure M**.	M 
Remove the needle from your skin by pulling straight up. See **Figure N**. You can then release the dose button.	

If you remove the needle before you counted to 6 and after the dose counter showed ·0·, you may not have received your full dose. If blood appears at the injection site, press lightly with a cotton ball or gauze pad. You may see a drop of Awiqli at the needle tip after injecting. This is normal and does not affect your dose.	
Step 6: After your injection	
Carefully remove the needle from the pen and throw it away (dispose of it) after each injection. **Never store your pen with the needle attached.** Remove the needle before storing your pen to reduce the chances of contamination, infection, and blocked needle leading to incorrect dose. See **Figure O** **Never try to put the inner needle cap back on the needle.** You may stick yourself with the needle.	
Place the needle in a sharps disposal container right away to reduce the risk of needle sticks. See **Figure P**. See "**Disposing of used Awiqli FlexTouch Pens and needles**" below for more information about how to dispose of used pens and needles the right way.	

Put the pen cap on your pen after each use to protect Awiqli from light. See **Figure Q**.	
If you do not have a sharps container, carefully slip the needle into the outer needle cap. See **Figure R**. After the needle is covered, carefully push the outer needle cap completely on and unscrew the needle. For disposal, see "**Disposing of used Awiqli FlexTouch pens and needles**".	
Do you have enough Awiqli? • **Turn the dose selector forward until it stops.** The dose pointer will line up with the number of units of insulin that is left in your pen. • **If the dose counter shows less than 700**, the number shown in the dose counter is the number of units left in your pen. • **If the dose counter shows 700**, there are at least 700 units left in your pen. • **If the dose counter stops before you reach your dose**, there is not enough Awiqli left for a full dose. Use a new pen to inject your full dose.	

Disposing of used Awiqli FlexTouch pens and needles

- Put your used needles and Awiqli FlexTouch pens that are no longer usable in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) the loose needles in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,

- able to be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be local or state laws about how you should throw away used needles. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this.
- Do not recycle your used sharps disposal container.
- Safely dispose of Awiqli FlexTouch pens that are expired or no longer needed in a sharps disposal container.
- The pen cap and the empty carton can be disposed of in your household trash.

How should I store my Awiqli FlexTouch pens?

- Store your unused Awiqli FlexTouch pens in the refrigerator between 36°F to 46°F (2°C to 8°C) until the expiration date printed on the carton.
- Store the pen you are currently using for up to 12 weeks at room temperature below 86°F (30°C) or in a refrigerator between 36°F to 46°F (2°C to 8°C).
- Unused Awiqli FlexTouch pen stored at room temperature below 86°F (30°C) should be thrown away after 12 weeks.
- When stored in the refrigerator, **do not** store Awiqli FlexTouch pens directly next to the cooling element.
- **Do not freeze Awiqli. Do not use Awiqli if it has been frozen.** Throw it away in a sharps disposal container if it has been frozen.
- **Avoid exposing Awiqli to direct sunlight.**
- Keep Awiqli away from heat, microwaves and out of the light.
- **Keep the pen cap on when the pen is not in use.**
- **Keep the Awiqli FlexTouch pen and all medicines out of the reach of children**

Caring for your pen

- **Treat your pen with care**. Rough handling or misuse may cause incorrect dosing, which can lead to too high or too low blood sugar levels.
- **Do not drop your pen** or knock it against hard surfaces.
- **Do not try to repair your pen** or pull it apart.
- **Do not expose your pen to dust, dirt, or liquid.**
- **Do not wash, soak, or lubricate your pen.** It may be cleaned with a mild detergent on a moistened cloth.
- After you have taken your first injection, your pen should be thrown away (disposed of) after 12 weeks, even if it still has Awiqli left in it. Write the disposal date on your calendar.
- Unused Awiqli FlexTouch pens may be used until the expiration date ('EXP') printed on the label, if kept in the refrigerator.

This Instructions for Use has been approved by the U.S. Food and Drug Administration Issued: 03/2026

Back of leaflet:

Manufactured by:
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Plainsboro, NJ 08536
U.S. License No. 1261

At: Novo Nordisk A/S
Novo Allé
2880 Bagsvaerd
Denmark

For information about Awiqli, contact:
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800 Scudders Mill Road
Plainsboro, NJ 08536
1-844-668-6463

Novo Nordisk®, Awiqli®, FlexTouch®, NovoFine® and NovoFine® Plus are registered trademarks of Novo Nordisk A/S.

Patent Information: http://novonordisk-us.com/products/product-patents.html

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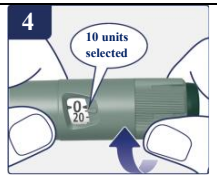
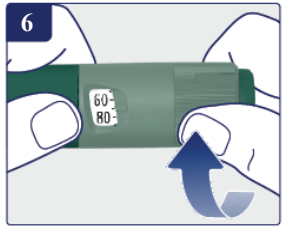
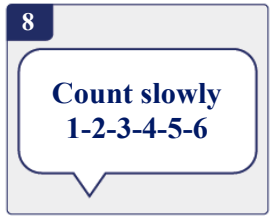
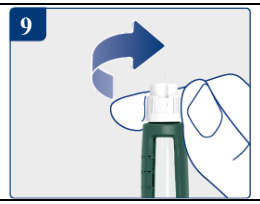
<u>Front of leaflet</u>

Instructions for Use and Patient Information

Awiqli®
FlexTouch®
(insulin icodec-abae) injection
700 units/mL (U-700)

Pen delivers between 10 and 700 units.
Use once weekly

This is a Quick Guide. **Read the Instructions for Use for important information before you begin using your pen.**	For more information go to www.awiqli.com
Check your Awiqli® FlexTouch® pen **Check the pen label** to make sure that your pen contains insulin icodec 700 units/mL. Make sure that the insulin icodec in your pen window is clear, colorless and does not contain particles.	
Attach a new needle **Take a new needle**. Tear off the paper tab on the needle. Push and turn the needle until tight. The needle is covered by two caps, **remove both caps.**	
Check the flow before each injection Turn the dose selector until you see the 10 units (first mark) on the dose counter. Hold the pen with the needle pointing up. Press and hold in the dose button. Make sure a drop appears.	
Set your dose Turn the dose selector to select the number of units you need to inject. In the figure, 70 units is shown as an example.	

Inject your dose Insert the needle straight into the stomach, upper legs, or upper arms. Press and hold down the dose button. **After the dose counter reaches** ·0·, slowly count to 6 while keeping the needle in your skin. Remove the needle from your skin.	 
After your injection **Carefully remove the needle** and place it in a sharps disposal container. Put the pen cap back on the pen.