KIRSTY- insulin aspart-xjhz injection, solution
INSULIN DILUTING MEDIUM FOR KIRSTY- water injection, solution
Biocon Biologics Inc.

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

KIRSTY™ (insulin aspart-xjhz) injection, for subcutaneous or intravenous use
Initial U.S. Approval: 20XX

KIRSTY™ (insulin aspart-xjhz) is biosimilar* to NOVOLOG (insulin aspart)

INDICATIONS AND USAGE

- KIRSTY is rapid acting human insulin analog indicated to improve glycemic control in adults and pediatric patients with diabetes mellitus (1).

DOSAGE AND ADMINISTRATION

- See Full Prescribing Information for important preparation, administration and dosage instructions (2.1, 2.2, 2.3, 2.4, 2.5).
- *Subcutaneous injection (2.2):*
  - Inject subcutaneously within 5-10 minutes before a meal into the abdominal area, thigh, buttocks or upper arm.
  - Rotate injection sites within the same region from one injection to the next to reduce risk of lipodystrophy and localized cutaneous amyloidosis.
  - Should generally be used in regimens with an intermediate- or long-acting insulin.
- *Continuous Subcutaneous Infusion (Insulin Pump) (2.2):*
  - Refer to the insulin infusion pump user manual to see if KIRSTY or NOVOLOG can be used with the insulin pump, in which case KIRSTY can be used with the pump. Use in accordance with the insulin pump instructions for use.
  - Administer by continuous subcutaneous infusion using an insulin pump in a region recommended in the instructions from the pump manufacturer.
  - Rotate the injection sites within the same region from one injection to the next to reduce the risk of lipodystrophy and localized cutaneous amyloidosis.
  - Do not mix with other insulins or diluents in the pump.
- *Intravenous Administration (2.2):*
  - Dilute KIRSTY to concentrations from 0.05 unit/mL to 1 unit/mL insulin aspart-xjhz in infusion systems using polypropylene infusion bags.
  - KIRSTY is stable in infusion fluids such as 0.9% Sodium Chloride Injection, USP.
- Individualize and adjust the dosage of KIRSTY based on route of administration, the individual's metabolic needs, blood glucose monitoring results and glycemic control goal (2.4).
- Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness (2.4).

DOSAGE FORMS AND STRENGTHS

Injection: 100 units/mL (U-100) of insulin aspart-xjhz available as:
- 3 mL single-patient-use prefilled pen (3)
- 10 mL multiple-dose vial (3)

CONTRAINDICATIONS

- During episodes of hypoglycemia (4).
- Hypersensitivity to insulin aspart products or any of the excipients in KIRSTY.

WARNINGS AND PRECAUTIONS

- *Never share* a KIRSTY prefilled pen, needles or syringes between patients, even if the needle is

changed (5.1).
- *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 (5.2).
- *Hypoglycemia:* May be life-threatening. Increase frequency of glucose monitoring with changes to: insulin dosage, concomitantly administered glucose lowering medications, meal pattern, physical activity; and in patients with renal or hepatic impairments and hypoglycemia unawareness (5.3).
- *Medication Errors:* Accidental mix-ups between insulin products can occur. Instruct patients to check insulin labels before injection (5.4).
- *Hypersensitivity reactions*: Severe, life-threatening, generalized allergy, including anaphylaxis, may occur. Discontinue KIRSTY, treat, and monitor if indicated (5.5).
- *Hypokalemia:* May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated (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).
- *Hyperglycemia and Ketoacidosis Due to Insulin Pump Device Malfunction:* Monitor glucose and administer KIRSTY by subcutaneous injection if pump malfunction occurs (5.8).

ADVERSE REACTIONS

Adverse reactions observed with insulin aspart products include hypoglycemia, allergic reactions, local injection site reactions, lipodystrophy, rash, and pruritus (6).

To report SUSPECTED ADVERSE REACTIONS, contact Biocon Biologics at 1-833-986-1468 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), and sulfonamide antibiotics (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).

* Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of KIRSTY has been demonstrated for the condition(s) of use (e.g., indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration described in its Full Prescribing Information.

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

Revised: 7/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

KIRSTY is indicated to improve glycemic control in adults and pediatric patients with diabetes mellitus.

2 DOSAGE AND ADMINISTRATION

2.1 Important Preparation and Administration Instructions

- Always check insulin labels before administration *[see Warnings and Precautions (5.4)].*
- Inspect KIRSTY visually before use. It should appear clear and colorless. Do not use KIRSTY if particulate matter or coloration is seen.
- In patients with visual impairment who rely on audible clicks to dial their dose, use KIRSTY prefilled pen with caution.
- Do **not** mix KIRSTY with other insulins when administering using a continuous subcutaneous infusion pump.

2.2 Preparation and Administration Instructions for the Approved Routes of Administration

Subcutaneous Injection

- Inject KIRSTY subcutaneously within 5-10 minutes before a meal into the abdominal area, thigh, buttocks or upper arm.
- 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 (5.2) and Adverse Reactions (6.1, 6.3)]*.
- Dial the KIRSTY prefilled pen in 1-unit increments.
- Generally use KIRSTY (administered by subcutaneous injection) in regimens with an intermediate-or long-acting insulin.
- May dilute KIRSTY with Insulin Diluting Medium for KIRSTY for subcutaneous injection. Diluting one part KIRSTY to:
  • Nine parts diluent will yield a concentration one-tenth that of KIRSTY (equivalent to U-10).
  • One part diluent will yield a concentration one-half that of KIRSTY (equivalent to U-50). Discard any unused diluent after opening the vial of Insulin Diluting Medium for KIRSTY.

Continuous Subcutaneous Infusion (Insulin Pump)

- Can use this KIRSTY product with the continuous subcutaneous insulin infusion pumps labeled for use with KIRSTY or NOVOLOG. Refer to the insulin pump user manual to see if KIRSTY or NOVOLOG can be used with the insulin pump, in which

case KIRSTY can be used with the pump. Use KIRSTY in accordance with the insulin pump system's instructions for use.
- Train patients using continuous subcutaneous insulin fusion pump therapy to administer insulin by injection and have alternate insulin therapy available in case of pump failure.
- Administer KIRSTY by continuous subcutaneous infusion in a region recommended in the instructions from the pump manufacturer. Rotate infusion sites within the same region to reduce the risk of lipodystrophy or localized cutaneous amyloidosis [see Warnings and Precautions (5.2) and Adverse Reactions (6.1, 6.3)].
- Instruct patients to follow healthcare provider recommendations when setting basal and meal time infusion rate.

- Change the KIRSTY in the reservoir at least every 7 days or according to the pump user manual, whichever is shorter. Follow the KIRSTY-specific information for in-use time because KIRSTY-specific information may differ from general pump manual instructions.
- Change the infusion set and the infusion set insertion site according to the manufacturer's user manual.
- Do **not** dilute or mix KIRSTY when administering by continuous subcutaneous infusion.
- Do **not** expose KIRSTY in the pump reservoir to temperatures greater than 98.6°F (37°C).

Intravenous Administration
- Administer KIRSTY intravenously **only** under medical supervision with close monitoring of blood glucose and potassium levels to avoid hypoglycemia and hypokalemia *[see Warnings and Precautions (5.3, 5.6) and How Supplied/Storage and Handling (16.2)]*.
- Dilute KIRSTY to concentrations from 0.05 unit/mL to 1 unit/mL insulin aspart-xjhz in infusion systems using polypropylene infusion bags. KIRSTY is stable in infusion fluids such as 0.9% Sodium Chloride Injection, USP.

2.3 Dosage Recommendations
- Individualize the dosage of KIRSTY based on the route of administration, the patient's metabolic needs, blood glucose monitoring results and glycemic control goal.
- Dosage adjustments may be needed with changes in physical activity, changes in meal patterns (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute illness *[see Warnings and Precautions (5.2, 5.3) and Use in Specific Populations (8.6, 8.7)]*.
- When switching from another insulin to KIRSTY, a different dosage of KIRSTY may be needed *[see Warnings and Precautions (5.2)]*.
- During changes to a patient's insulin regimen, increase the frequency of blood glucose monitoring [see *Warnings and Precautions (5.2*)].

2.4 Dosage Modifications for Drug Interactions

Dosage modification may be needed when KIRSTY is used concomitantly with certain drugs *[see Drug Interactions (7)].*

2.5 Instructions for Mixing KIRSTY with Other Insulins

The table below includes instructions regarding mixing KIRSTY with other insulins.

Subcutaneous injection route	• KIRSTY may **only** be mixed with NPH insulin preparations. • If KIRSTY is mixed with NPH insulin, withdraw KIRSTY into the syringe first and inject immediately after mixing.
Continuous subcutaneous infusion route (Insulin Pump)	Do **not** mix **KIRSTY with any other insulin.**

3 DOSAGE FORMS AND STRENGTHS

Injection: 100 units/mL (U-100) is a clear and colorless solution available as:

- 10 mL multiple-dose vial
- 3 mL single-patient-use prefilled pen

4 CONTRAINDICATIONS

KIRSTY is contraindicated

- During episodes of hypoglycemia *[see Warnings and Precautions (5.3)]*
- In patients with hypersensitivity to insulin aspart products or any of the excipients in KIRSTY *[see Warnings and Precautions (5.5)]*

5 WARNINGS AND PRECAUTIONS

5.1 Never Share a KIRSTY Prefilled Pen, Needles or Syringes Between Patients

KIRSTY prefilled pens should never be shared between patients, even if the needle is changed. Patients using KIRSTY vials must never share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens.

5.2 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 (5.3)]* 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 (6.1, 6.3)].*

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. For patients with type 2 diabetes, dosage adjustments of concomitant anti-diabetic products may be

needed.

5.3 Hypoglycemia

Hypoglycemia is the most common adverse reaction of all insulins, including insulin aspart products. Severe hypoglycemia can cause seizures, may lead to unconsciousness, 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).

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.

Risk Factors for Hypoglycemia

The risk of hypoglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulins, the glucose lowering effect time course of insulin aspart products may vary in 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 *[see Clinical Pharmacology (12.2)]*. 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 concomitantly 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)].*

Risk Mitigation Strategies for Hypoglycemia

Patients and caregivers must be educated to recognize and manage hypoglycemia. Self-monitoring of blood glucose plays an essential role in the prevention and management of hypoglycemia; increased frequency of blood glucose monitoring is recommended. In patients at higher risk for hypoglycemia and patients who have reduced symptomatic awareness of hypoglycemia; increased frequency of blood glucose monitoring is recommended.

5.4 Hypoglycemia Due to Medication Errors

Accidental mix-ups between insulin products have been reported. To avoid medication errors between KIRSTY and other insulins, instruct patients to always check the insulin label before each injection.

5.5 Hypersensitivity Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulins, including insulin aspart products. If hypersensitivity reactions occur, discontinue KIRSTY; treat per standard of care and monitor until symptoms and signs resolve *[see Adverse Reactions (6)].* KIRSTY is contraindicated in patients who have had

hypersensitivity reactions to insulin aspart products or any of the excipients in KIRSTY *[see Contraindications (4)].*

5.6 Hypokalemia

All insulins, including insulin aspart products, can 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 concentration).

5.7 Fluid Retention and Heart Failure with Concomitant Use of PPAR-gamma Agonists

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 heart failure. Patients treated with insulin, including KIRSTY, and a PPAR-gamma agonist should be observed for signs and symptoms of heart failure. If 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.

5.8 Hyperglycemia and Ketoacidosis Due to Insulin Pump Device Malfunction

Malfunction of the insulin pump or insulin infusion set or insulin degradation can rapidly lead to hyperglycemia and ketoacidosis. Prompt identification and correction of the cause of hyperglycemia or ketosis is necessary. Interim subcutaneous injections with KIRSTY may be required. Patients using continuous subcutaneous insulin infusion pump therapy must be trained to administer insulin by injection and have alternate insulin therapy available in case of pump failure *[see How Supplied/Storage and Handling (16.2) and Patient Counseling Information (17)]*.

6 ADVERSE REACTIONS

The following adverse reactions are also discussed elsewhere:

- Hypoglycemia *[see Warnings and Precautions (5.3)]*
- Hypoglycemia Due to Medication Errors *[see Warnings and Precautions (5.4)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.5)]*
- Hypokalemia *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying designs, the adverse reaction rates reported in one clinical trial may not be easily compared to those rates reported in another clinical trial, and may not reflect the rates actually observed in clinical practice. The safety of insulin aspart was evaluated in two treat-to-target trials of 6 months duration, conducted in patients with type 1 diabetes or type 2 diabetes *[see Clinical Studies (14)].*

The data in Table 1 reflect the exposure of 596 patients with type 1 diabetes to insulin

aspart in one clinical trial with a mean exposure duration to insulin aspart of 24 weeks. The mean age was 39 years. Fifty-one percent were male, 94% were Caucasian, 2% were Black and 4% were other races. The mean body mass index (BMI) was 25.6 kg/m^2. The mean duration of diabetes was 15.7 years and the mean HbA_{1c} at baseline was 7.9%.

The data in Table 2 reflect the exposure of 91 patients with type 2 diabetes to insulin aspart in one clinical trial with a mean exposure duration to insulin aspart of 24 weeks. The mean age was 57 years. Sixty-three percent were male, 76% were Caucasian, 9% were Black and 15% were other races. The mean BMI was 29.7 kg/m^2. The mean duration of diabetes was 12.7 years and the mean HbA_{1c} at baseline was 8.1%.

Common adverse reactions were defined as events that occurred in ≥5%, excluding hypoglycemia, of the population studied. Common adverse events that occurred at the same rate or greater for insulin aspart-treated patients than in comparator-treated patients during clinical trials in patients with type 1 diabetes mellitus and type 2 diabetes mellitus (other than hypoglycemia) are listed in Table 1 and Table 2, respectively.

Table 1: Adverse reactions that occurred in ≥ 5% of Type 1 Diabetes Mellitus Adult Patients treated with insulin aspart and at the same rate or greater on insulin aspart than on comparator

	Insulin Aspart + NPH (%) (n= 596)	**Regular Human Insulin + NPH (%) (n= 286)**
Headache	12	10
Injury accidental	11	10
Nausea	7	5
Diarrhea	5	3

Table 2: Adverse reactions that occurred in ≥ 5% of Type 2 Diabetes Mellitus Adult Patients treated with insulin aspart and at the same rate or greater on insulin aspart than on comparator

	Insulin Aspart + NPH (%) (n= 91)	**Human Regular Insulin + NPH (%) (n= 91)**
Hyporeflexia	11	7
Onychomycosis	10	5
Sensory disturbance	9	7
Urinary tract infection	8	7
Chest pain	5	3
Headache	5	3
Skin disorder	5	2
Abdominal pain	5	1
Sinusitis	5	1

Severe Hypoglycemia

Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including insulin aspart products. 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 insulin aspart 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.

Severe hypoglycemia was defined as hypoglycemia associated with central nervous system symptoms and requiring the intervention of another person or hospitalization. The incidence of severe hypoglycemia in:

- Adult and pediatric patients with type 1 diabetes mellitus who received subcutaneous insulin aspart was 17% at 24 weeks and 6% at 24 weeks, respectively *[see Clinical Studies (14)]*.
- Adult patients with type 2 diabetes mellitus who received subcutaneous insulin aspart was 10% at 24 weeks.
- Adult and pediatric patients with type 1 diabetes mellitus, who received insulin aspart via continuous subcutaneous insulin infusion by external pump was 2% at 16 weeks and 10% at 16 weeks respectively.

No severe hypoglycemic episodes were reported in adult patients with type 2 diabetes mellitus receiving insulin aspart via continuous subcutaneous insulin infusion by external pump at 16 weeks.

Allergic Reactions

Some patients taking insulin, including insulin aspart products have experienced erythema, local edema, and pruritus at the site of injection. These conditions were usually self-limiting. Severe cases of generalized allergy (anaphylaxis) have been reported.

Adverse Reactions Associated with Insulin Initiation and Glucose Control Intensification

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.

Lipodystrophy

Administration of insulin, including insulin aspart products, subcutaneously and via subcutaneous insulin infusion by external pump, has resulted in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue) in some patients *[see Dosage and Administration (2.2)].*

Peripheral Edema

Insulins, including insulin aspart products, may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

Weight Gain

Weight gain has occurred with insulins, including insulin aspart products, and has been attributed to the anabolic effects of insulin and the decrease in glucosuria.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other insulin aspart products may be misleading.

In a 6-month study with a 6-month extension in adult subjects with type 1 diabetes, 99.8% of patients who received insulin aspart were positive for anti-insulin antibodies (AIA) at least once during the study, including 97.2% that were positive at baseline. A total of 92.1% of patients who received insulin aspart were positive for anti-drug antibodies (ADA) at least once during the study, including 64.6% that were positive at baseline.

In a phase 3 type 1 diabetes clinical trial of insulin aspart, initial increase in titers of antibodies to insulin, followed by a decrease to baseline values, was observed in regular human insulin and insulin aspart treatment groups with similar incidences. These antibodies did not cause deterioration in glycemic control or necessitate increases in insulin dose.

6.3 Post Marketing Experience

The following adverse reactions have been identified during post-approval use of insulin aspart products. Because these adverse reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Medication errors have been reported in which other insulins have been accidentally substituted for insulin aspart products.

Localized cutaneous amyloidosis at the injection site has occurred with insulin aspart products. Hyperglycemia has been reported with repeated insulin injections into areas of localized cutaneous amyloidosis; hypoglycemia has been reported with a sudden change to an unaffected injection site.

7 DRUG INTERACTIONS

The table below presents clinically significant drug interactions with KIRSTY

Drugs That May Increase the Risk of Hypoglycemia

Drugs:	Antidiabetic agents, ACE inhibitors, angiotensin II receptor blocking agents, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors, pentoxifylline, pramlintide, salicylates, somatostatin analog (e.g., octreotide), and sulfonamide antibiotics.
Intervention:	Dose adjustment and increased frequency of glucose monitoring may be required when KIRSTY is concomitantly administered with these drugs.
Drugs That May Decrease the Blood Glucose Lowering Effect of KIRSTY	
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 adjustment and increased frequency of glucose monitoring may be required when KIRSTY is concomitantly administered with these drugs.
Drugs That May Increase or Decrease the Blood Glucose Lowering Effect of KIRSTY	
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 KIRSTY is concomitantly 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 KIRSTY is concomitantly administered with these drugs.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available information from published randomized controlled trials with insulin aspart products use during the second trimester of pregnancy have not reported an association with insulin aspart products and major birth defects or adverse maternal or fetal outcomes *(see Data)*. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy *(see Clinical Considerations)*.

In animal reproduction studies, administration of subcutaneous insulin aspart to pregnant rats and rabbits during the period of organogenesis did not cause adverse developmental effects at exposures 8-times and equal to the human subcutaneous dose of 1 unit/kg/day, respectively.

Pre- and post-implantation losses and visceral/skeletal abnormalities were seen at higher exposures, which are considered secondary to maternal hypoglycemia. These effects were similar to those observed in rats administered regular human insulin *(see Data)*.

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. The estimated background risk of major birth defects is 6 to 10% in women with pre-gestational diabetes with a periconceptual HbA_{1c} >7% and has been reported to be as high as 20 to 25% in women with a periconceptual HbA_{1c} >10%. The estimated background risk of miscarriage for the indicated population is unknown.

Clinical Considerations

Disease-Associated Maternal and/or Embryo-Fetal Risk

Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, preeclampsia, spontaneous abortions, preterm delivery, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia related morbidity.

Data

Human Data

Published data from 5 randomized controlled trials of 441 pregnant women with diabetes mellitus treated with insulin aspart products during the late 2nd trimester of pregnancy did not identify an association of insulin aspart products with major birth defects or adverse maternal or fetal outcomes. However, these studies cannot definitely establish the absence of any risk because of methodological limitations, including a variable duration of treatment and small size of the majority of the trials.

Animal Data

Fertility, embryo-fetal and pre- and postnatal development studies have been performed with insulin aspart and regular human insulin in rats and rabbits. In a combined fertility and embryo-fetal development study in rats, insulin aspart was administered before mating, during mating, and throughout pregnancy. Further, in a pre- and postnatal development study insulin aspart was given throughout pregnancy and during lactation to rats. In an embryo-fetal development study insulin aspart was given to female rabbits during organogenesis. The effects of insulin aspart did not differ from those observed with subcutaneous regular human insulin. Insulin aspart, like human insulin, caused pre- and post-implantation losses and visceral/skeletal abnormalities in rats at a dose of 200 units/kg/day (approximately 32 times the human subcutaneous dose of 1 unit/kg/day, based on human exposure equivalents) and in rabbits at a dose of 10 units/kg/day (approximately three times the human subcutaneous dose of 1 unit/kg/day, based on human exposure equivalents). No significant effects were observed in rats at a dose of 50 units/kg/day and in rabbits at a dose of 3 units/kg/day. These doses are approximately 8 times the human subcutaneous dose of 1 unit/kg/day for rats and equal to the human subcutaneous dose of 1 unit/kg/day for rabbits, based on human exposure equivalents. The effects are considered secondary to maternal hypoglycemia.

8.2 Lactation

Risk Summary

There are no data on the presence of insulin aspart products in human milk, the effects on the breastfed infant, or the effect on milk production. One small published study

reported that exogenous insulin, including insulin aspart, was present in human milk. However, there is insufficient information to determine the effects of insulin aspart products on the breastfed infant. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for KIRSTY, and any potential adverse effects on the breastfed infant from KIRSTY, or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of KIRSTY to improve glycemic control have been established in pediatric patients with diabetes mellitus. Use of KIRSTY for this indication is supported by evidence from an adequate and well-controlled study of insulin aspart in 283 pediatric patients with type 1 diabetes mellitus aged 6 to 18 years and from studies in adults with diabetes mellitus *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14.1)]*.

8.5 Geriatric Use

Of the total number of patients (n=1,375) treated with insulin aspart in 3 controlled clinical studies, 2.6% (n=36) were 65 years of age or over. One-half of these patients had type 1 diabetes (18/1285) and the other half had type 2 diabetes (18/90). The HbA_{1c} response to insulin aspart, as compared to regular human insulin, did not differ by age.

8.6 Renal Impairment

Patients with renal impairment may be at increased risk of hypoglycemia and may require more frequent KIRSTY dose adjustment and more frequent blood glucose monitoring *[see Warnings and Precautions (5.3) and Clinical Pharmacology (12.3)].*

8.7 Hepatic Impairment

Patients with hepatic impairment may be at increased risk of hypoglycemia and may require more frequent KIRSTY dose adjustment and more frequent blood glucose monitoring *[see Warnings and Precautions (5.3) and Clinical Pharmacology (12.3)].*

10 OVERDOSAGE

Excess insulin administration may cause hypoglycemia and hypokalemia *[see Warnings and Precautions (5.3, 5.6)]*. Mild episodes of hypoglycemia usually can be treated with oral glucose. Adjustments in drug dosage, meal patterns, or exercise may be needed. More severe episodes with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery. Hypokalemia must be corrected appropriately.

11 DESCRIPTION

Insulin aspart-xjhz is a rapid-acting human insulin analog homologous with regular human insulin with the exception of a single substitution of the amino acid proline by aspartic acid in position B28 and is produced by recombinant DNA technology utilizing *Pichia pastoris*. Insulin aspart-xjhz has the empirical formula $C_{256}H_{381}N_{65}O_{79}S_6$ and a

molecular weight of 5825.8 Da.

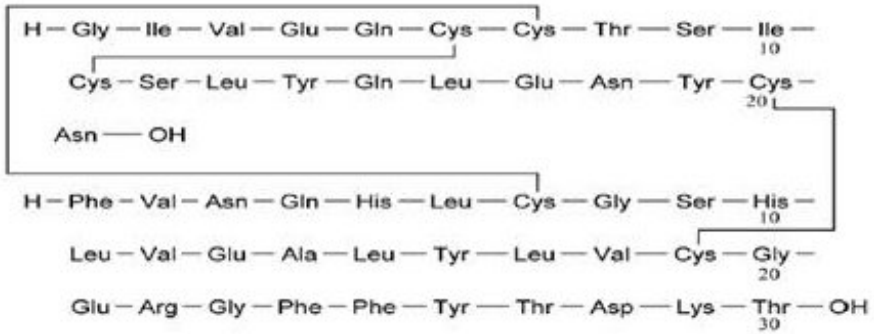


Figure 1. Structural formula of insulin aspart-xjhz.

KIRSTY (insulin aspart-xjhz) injection is a sterile, clear, and colorless solution for subcutaneous or intravenous use. Each mL contains 100 units of insulin aspart-xjhz, and the inactive ingredients dibasic sodium phosphate (0.997 mg), glycerin (16 mg), *m*-cresol (1.72 mg), phenol (1.50 mg), sodium chloride (0.58 mg), zinc (19.6 mcg), and Water for Injection, USP. KIRSTY has a pH of 7.0-7.8. Hydrochloric acid 1% and/or sodium hydroxide 1% may be added to adjust pH.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The primary activity of insulin, including insulin aspart products, is the 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 inhibits lipolysis and proteolysis, and enhances protein synthesis.

12.2 Pharmacodynamics

Pharmacodynamics of insulin aspart After Subcutaneous Administration

The pharmacodynamic profile of insulin aspart given subcutaneously in 22 patients with type 1 diabetes is shown in Figure 2. The maximum glucose-lowering effect of insulin aspart occurred between 1 and 3 hours after subcutaneous injection (0.15 units/kg). The duration of action for insulin aspart is 3 to 5 hours. The time course of action of insulin and insulin analogs such as insulin aspart products may vary considerably in different individuals or within the same individual. The parameters of insulin aspart activity (time of onset, peak time and duration) as designated in Figure 2 should be considered only as general guidelines. The rate of insulin absorption and onset of activity is affected by the site of injection, exercise, and other variables *[see Warnings and Precautions (5.3)]*.

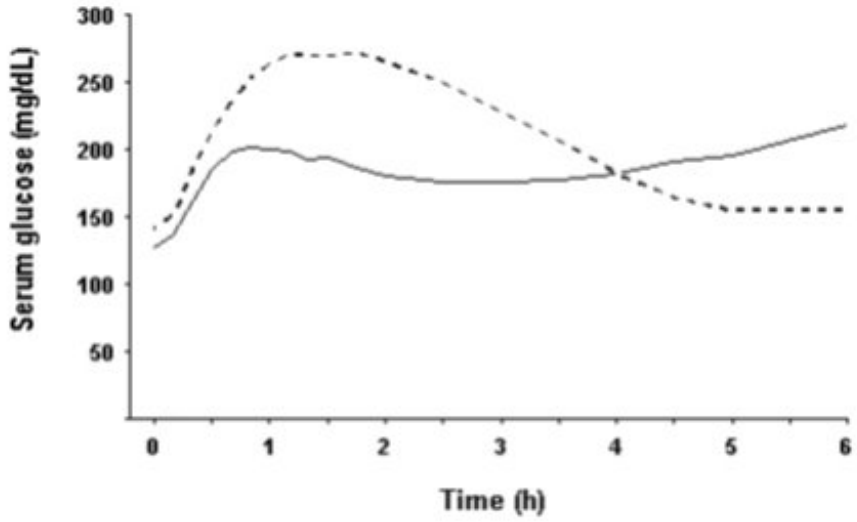


Figure 2. Serial mean serum glucose collected up to 6 hours following a single 0.15 units/kg pre-meal dose of insulin aspart (solid curve) or regular human insulin (hatched curve) injected immediately before a meal in 22 patients with type 1 diabetes.

Pharmacodynamics of insulin aspart After Intravenous Administration

A double-blind, randomized, two-way crossover study in 16 patients with type 1 diabetes demonstrated that intravenous infusion of insulin aspart resulted in a blood glucose profile that was similar to that after intravenous infusion with regular human insulin. Insulin aspart or human insulin was infused until the patient's blood glucose decreased to 36 mg/dL, or until the patient demonstrated signs of hypoglycemia (rise in heart rate and onset of sweating), defined as the time of autonomic reaction (R) (see Figure 3).

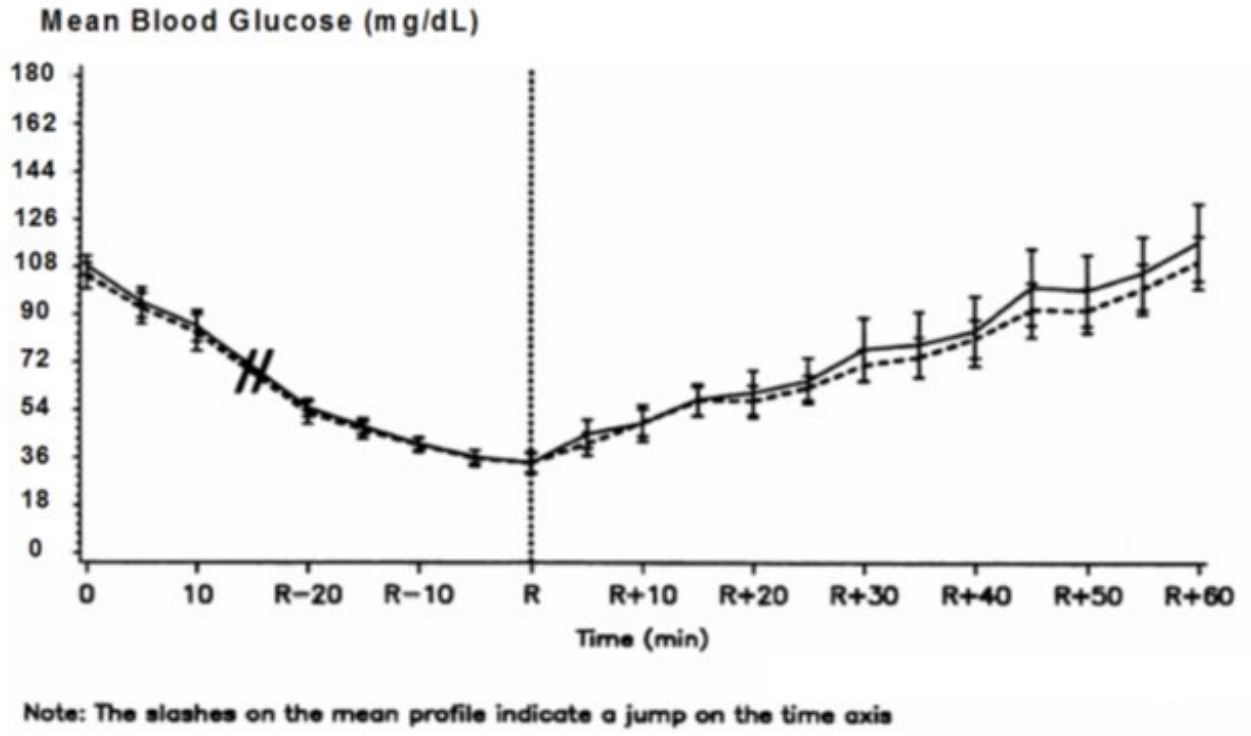


Figure 3. Mean blood glucose profiles following intravenous infusion of insulin aspart (hatched curve) and regular human insulin (solid curve) in 16 patients with type 1

diabetes. R represents the time of autonomic reaction.

12.3 Pharmacokinetics

Pharmacokinetics of subcutaneous administration of insulin aspart is presented below

Absorption and Bioavailability

In studies in healthy volunteers (total n=107) and patients with type 1 diabetes (total n=40), the median time to maximum concentration of insulin aspart in these trials was 40 to 50 minutes versus 80 to 120 minutes, for regular human insulin respectively.

The relative bioavailability of insulin aspart (0.15 units/kg) compared to regular human insulin indicates that the two insulins are absorbed to a similar extent.

In a clinical trial in patients with type 1 diabetes, insulin aspart and regular human insulin, both administered subcutaneously at a dose of 0.15 units/kg body weight, reached mean maximum concentrations of 82 and 36 mU/L, respectively.

Distribution

Insulin aspart has a low binding affinity to plasma proteins (<10%), similar to that seen with regular human insulin.

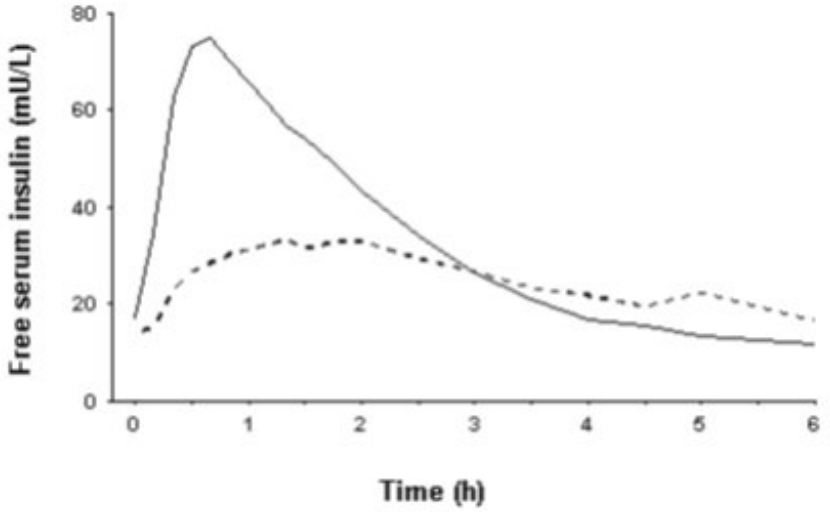


Figure 4. Serial mean serum free insulin concentration collected up to 6 hours following a single 0.15 units/kg pre-meal dose of insulin aspart (solid curve) or regular human insulin (hatched curve) injected immediately before a meal in 22 patients with type 1 diabetes.

Metabolism and Elimination

In a randomized, double-blind, crossover study 17 healthy Caucasian male subjects between 18 and 40 years of age received an intravenous infusion of either insulin aspart or regular human insulin at 1.5 mU/kg/min for 120 minutes. The mean insulin clearance was similar for the two groups with mean values of 1.2 L/h/kg for the insulin aspart group and 1.2 L/h/kg for the regular human insulin group.

After subcutaneous administration in normal male volunteers (n=24), insulin aspart was eliminated with an average apparent half-life of 81 minutes.

Specific Populations

Pediatric Patients

The pharmacokinetic and pharmacodynamic properties of insulin aspart and regular human insulin were evaluated in a single dose study in 18 pediatric patients with type 1 diabetes in 2 age groups: 6-12 years, n=9 and 13-17 years (Tanner grade ≥ 2), n=9. The relative differences in pharmacokinetics and pharmacodynamics in the pediatric patients with type 1 diabetes in both age groups between insulin aspart and regular human insulin were similar to those in healthy adult subjects and adults with type 1 diabetes.

Geriatric Patients

The pharmacokinetic and pharmacodynamic properties of insulin aspart and regular human insulin were investigated in a single dose study in 18 subjects with type 2 diabetes who were ≥ 65 years of age. The relative differences in pharmacokinetics and pharmacodynamics in geriatric patients with type 2 diabetes between insulin aspart and regular human insulin were similar to those in younger adults.

Male and Female Patients

In healthy volunteers given a single subcutaneous dose of insulin aspart 0.06 units/kg, no difference in insulin aspart levels was seen between males and females based on comparison of $AUC_{(0\text{-}10h)}$ or C_{max}.

Obese Patients

A single subcutaneous dose of 0.1 units/kg insulin aspart was administered in a study of 23 patients with type 1 diabetes and a wide range of body mass index (BMI, 22-39 kg/m^2). The pharmacokinetic parameters, AUC and C_{max}, of insulin aspart were generally unaffected by BMI in the different groups – BMI 19-23 kg/m^2 (n=4); BMI 23-27 kg/m^2 (n=7); BMI 27-32 kg/m^2 (n=6) and BMI >32 kg/m^2 (n=6). Clearance of insulin aspart was reduced by 28% in patients with BMI >32 kg/m^2 compared to patients with BMI <23 kg/m^2.

Patients with Renal Impairment

A single subcutaneous dose of 0.08 units/kg insulin aspart was administered in a study to subjects with either normal renal function (n=6) creatinine clearance (CLcr) (> 80 mL/min) or mild (n=7; CLcr = 50-80 mL/min), moderate (n=3; CLcr = 30-50 mL/min) or severe (but not requiring hemodialysis) (n=2; CLcr = <30 mL/min) renal impairment. In this study, there was no apparent effect of creatinine clearance values on AUC and C_{max} of insulin aspart.

Patients with Hepatic Impairment

A single subcutaneous dose of 0.06 units/kg insulin aspart was administered in an open-label, single-dose study of 24 subjects (n=6/group) with different degree of hepatic impairment (mild, moderate and severe) having Child-Pugh Scores ranging from 0

(healthy volunteers) to 12 (severe hepatic impairment). In this study, there was no correlation between the degree of hepatic impairment and any insulin aspart pharmacokinetic parameter.

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 aspart products. In 52-week studies, Sprague-Dawley rats were dosed subcutaneously with insulin aspart at 10, 50, and 200 units/kg/day (approximately 2, 8, and 32 times the human subcutaneous dose of 1.0 units/kg/day, based on units/body surface area, respectively). At a dose of 200 units/kg/day, insulin aspart increased the incidence of mammary gland tumors in females when compared to untreated controls. The relevance of these findings to humans is unknown.

Insulin aspart was not genotoxic in the following tests: Ames test, mouse lymphoma cell forward gene mutation test, human peripheral blood lymphocyte chromosome aberration test, *in vivo* micronucleus test in mice, and in *ex vivo* UDS test in rat liver hepatocytes.

In fertility studies in male and female rats, at subcutaneous doses up to 200 units/kg/day (approximately 32 times the human subcutaneous dose, based on units/body surface area), no direct adverse effects on male and female fertility, or general reproductive performance of animals was observed.

13.2 Animal Toxicology and/or Pharmacology

In standard biological assays in mice and rabbits, one unit of insulin aspart has the same glucose-lowering effect as one unit of regular human insulin.

14 CLINICAL STUDIES

14.1 Overview of Clinical Studies

The safety and effectiveness of subcutaneous insulin aspart were compared to regular human insulin in 596 type 1 diabetes adult, 187 pediatric type 1 diabetes, and 91 adult type 2 diabetes patients using NPH as basal insulin (see Tables 3, 4, 5). The reduction in glycated hemoglobin (HbA_{1c}) was similar to regular human insulin.

The safety and effectiveness of insulin aspart administered by continuous subcutaneous insulin infusion (CSII) by external pump were compared to buffered regular human insulin (administered by CSII), to lispro (administered by CSII) and compared to insulin aspart injections and NPH injection. Overall, the reduction in HbA_{1c} was similar to the comparator.

14.2 Clinical Studies in Adult and Pediatric Patients with Type 1 Diabetes with Subcutaneous Injections

Type 1 Diabetes - Adults (*see* Table 3)

Two 24-week, open-label, active-controlled studies were conducted to compare the safety and efficacy of insulin aspart to regular human insulin injection in adult patients with type 1 diabetes. Because the two study designs and results were similar, data are shown for only one study (see Table 3).

The mean age of the trial population was 39 years and mean duration of diabetes was 15.7 years. Fifty-one percent were male. Ninety-four percent were Caucasian, 2% were Black and 4% were Other. The mean BMI was approximately 25.6 kg/m^2.

Insulin aspart was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered by subcutaneous injection 30 minutes before meals. NPH insulin was administered as the basal insulin in either single or divided daily doses. Changes in HbA_{1c} were comparable for the two treatment regimens in this study (Table 3).

Table 3. Type 1 Diabetes Mellitus – Adult (insulin aspart plus NPH insulin vs. regular human insulin plus NPH insulin)

	Insulin Aspart + NPH (n=596)	**Regular Human Insulin + NPH (n=286)**
Baseline HbA_{1c} (%)*	7.9 ±1.1	8.0 ± 1.2
Change from Baseline HbA_{1c} (%)	-0.1 ± 0.8	0.0 ± 0.8
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	-0.2 (-0.3, -0.1)	

* Values are Mean ± SD

Type 1 Diabetes – Pediatric (*see* Table 4)

The efficacy of insulin aspart to improve glycemic control in pediatric patients with type 1 diabetes mellitus is based on an adequate and well-controlled trial of regular human insulin in pediatric patients with type 1 diabetes mellitus (Table 4). This 24-week, parallel-group study of pediatric patients with type 1 diabetes (n = 283), aged 6 to 18 years, compared two subcutaneous multiple-dose treatment regimens: insulin aspart (n=187) or regular human insulin (n=96). NPH insulin was administered as the basal insulin. Similar effects on HbA_{1c} were observed in both treatment groups (Table 4).

Subcutaneous administration of insulin aspart and regular human insulin have also been compared in pediatric patients with type 1 diabetes (n=26) aged 2 to 6 years with similar effects on HbA_{1c}.

Table 4. Pediatric Subcutaneous Administration of insulin aspart in Type 1 Diabetes (24 weeks; n=283)

	Insulin Aspart + NPH (n=187)	**Regular Human Insulin + NPH (n=96)**
Baseline HbA_{1c} (%)*	8.3 ± 1.2	8.3 ± 1.3

Change from Baseline HbA_{1c} (%)	0.1± 1.0	0.1± 1.1
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	-0.2 (-0.5, 0.1)	

* Values are Mean ± SD

14.3 Clinical Studies in Adults with Type 2 Diabetes with Subcutaneous Injections

Type 2 Diabetes - Adults (*see* Table 5)

One six-month, open-label, active-controlled study was conducted to compare the safety and efficacy of insulin aspart to regular human insulin in patients with type 2 diabetes (Table 5).

The mean age of the trial population was 56.6 years and mean duration of diabetes was 12.7 years. Sixty-three percent were male. Seventy-six percent were Caucasian, 9% were Black and 15% were Other. The mean BMI was approximately 29.7 kg/m^2.

Insulin aspart was administered by subcutaneous injection immediately prior to meals and regular human insulin was administered by subcutaneous injection 30 minutes before meals. NPH insulin was administered as the basal insulin in either single or divided daily doses. Changes in HbA_{1c} were comparable for the two treatment regimens.

Table 5. Subcutaneous insulin aspart Administration in Type 2 Diabetes (6 months; n=176)

	Insulin Aspart + NPH (n=90)	**Regular Human Insulin + NPH (n=86)**
Baseline HbA_{1c} (%)*	8.1 ± 1.2	7.8 ± 1.1
Change from Baseline HbA_{1c} (%)	-0.3 ± 1.0	-0.1 ± 0.8
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	- 0.1 (-0.4, 0.1)	

* Values are Mean ± SD

14.4 Clinical Studies in Adults and Pediatrics with Type 1 Diabetes Using Continuous Subcutaneous Insulin Infusion (CSII) by External Pump

Type 1 Diabetes – Adult (*see* Table 6)

Two open-label, parallel design studies (6 weeks [n=29] and 16 weeks [n=118]) compared insulin aspart to buffered regular human insulin (Velosulin) in adults with type 1 diabetes receiving a subcutaneous infusion with an external insulin pump.

The mean age of the trial population was 42.3 years. Thirty-nine percent were male. Ninety-eight percent were Caucasian and 2% were Black.

The two treatment regimens had comparable changes in HbA_{1c}.

Table 6. Adult Insulin Pump Study in Type 1 Diabetes (16 weeks; n=118)

	Insulin Aspart (n=59)	**Buffered human insulin (n=59)**
Baseline HbA_{1c} (%)*	7.3 ± 0.7	7.5 ± 0.8
Change from Baseline HbA_{1c} (%)	0.0 ± 0.5	0.2 ± 0.6
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	0.2 (-0.1, 0.4)	

* Values are Mean ± SD

Type 1 Diabetes – Pediatric (*see* Table 7)

A randomized, 16-week, open-label, parallel design study of pediatric patients with type 1 diabetes (n=298) aged 4-18 years compared two subcutaneous infusion regimens administered via an external insulin pump: insulin aspart (n=198) or insulin lispro (n=100). These two treatments resulted in comparable changes from baseline in HbA_{1c} (see Table 7).

Table 7. Pediatric Insulin Pump Study in Type 1 Diabetes (16 weeks; n=298)

	Insulin Aspart (n=198)	**Lispro (n=100)**
Baseline HbA_{1c} (%)*	8.0 ± 0.9	8.2 ± 0.8
Change from Baseline HbA_{1c} (%)	-0.1 ± 0.8	-0.1 ± 0.7
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	-0.1 (-0.3, 0.1)	

* Values are Mean ± SD

14.5 Clinical Studies in Adults with Type 2 Diabetes Using Continuous Subcutaneous Insulin Infusion (CSII) by External Pump

Type 2 Diabetes – Adults (*see* Table 8)

An open-label, 16-week parallel design trial compared pre-prandial insulin aspart injection in conjunction with NPH injections to insulin aspart administered by continuous subcutaneous infusion in 127 adults with type 2 diabetes.

The mean age of the trial population was 55.1 years. Sixty-four percent were male. Eighty percent were Caucasian, 12% were Black and 8% were Other. The mean BMI was approximately 32.2 kg/m^2.

The two treatment groups had similar reductions in HbA_{1c} (Table 8).

Table 8. Pump Therapy in Type 2 Diabetes (16 weeks; n=127)

	Insulin Aspart pump (n=66)	Insulin Aspart + NPH (n=61)
Baseline HbA_{1c} (%)*	8.2 ± 1.4	8.0 ± 1.1
Change from Baseline HbA_{1c} (%)	-0.6 ± 1.1	-0.5 ± 0.9
Treatment Difference in HbA_{1c}, Mean (95% confidence interval)	0.1 (-0.3, 0.4)	

* Values are Mean ± SD

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

KIRSTY (insulin aspart-xjhz) injection 100 units/mL (U-100) is available as a clear and colorless solution in:

One 10 mL multiple-dose vial per carton	83257-007-11
Five 3 mL single-patient-use prefilled pens per carton	83257-008-32

The KIRSTY prefilled pen dials in 1-unit increments.

16.2 Recommended Storage

Dispense in the original sealed carton with the enclosed Instructions for Use. Store unused KIRSTY in a refrigerator between 2°C to 8°C (36°F to 46°F). Do not freeze KIRSTY and do not use KIRSTY if it has been frozen. Do not expose KIRSTY to excessive heat or light. Do **not** withdraw KIRSTY into a syringe and store for later use.

Always remove and discard the needle after each injection from the KIRSTY prefilled pen and store without a needle attached.

The storage conditions are summarized in the following table:

Table 9. Storage conditions for vial and KIRSTY prefilled pen

KIRSTY presentation	**Not in-use (unopened)** Room Temperature (up to 30°C [86°F])	**Not in-use** (unopened) Refrigerated (2°C to 8°C [36°F to 46°F])	**In-use (opened)** Room Temperature (up to 30°C [86°F])
10 mL multiple-dose vial	28 days	Until expiration date	28* days (refrigerated/room temperature)
3 mL single-patient-use prefilled pen	28 days	Until expiration date	28 days (Do not refrigerate)

*__For insulin pump use, the total in-use time is 19 days, including 7 days pump in-use time.__

Storage in External Insulin Pump:

Change the KIRSTY in the pump reservoir at least every 7 days or according to the pump user manual instructions for KIRSTY or NOVOLOG, whichever is shorter, or after exposure to temperatures that exceed 37°C (98.6°F).

Storage of Diluted KIRSTY

KIRSTY diluted with Insulin Diluting Medium for KIRSTY to a concentration equivalent to U-10 or equivalent to U-50 prepared as indicated under *Dosage and Administration (2.2)* may remain in patient use at temperatures up to 30°C (86°F) for 28 days. Discard any unused diluent after opening the vial of Insulin Diluting Medium for KIRSTY.

Storage of KIRSTY in Intravenous Infusion Fluids

Infusion bags prepared as indicated under *Dosage and Administration (2.2)* are stable at room temperature for 12 hours. Some insulin will be initially adsorbed to the material of the infusion.

17 PATIENT COUNSELING INFORMATION

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

Never Share a KIRSTY Prefilled Pen Device Between Patients

Advise patients that they must never share a KIRSTY prefilled pen with another person even if the needle is changed, because doing so carries a risk for transmission of blood-borne pathogens. Advise patients using KIRSTY vials not to share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens *[see Warnings and Precautions (5.1)]*.

Hyperglycemia or Hypoglycemia

Inform patients that hypoglycemia is the most common adverse reaction with insulin. Instruct patients on self-management procedures including glucose monitoring, proper injection technique, and management of hypoglycemia and hyperglycemia, especially at initiation of KIRSTY therapy. Instruct patients on handling of special situations such as intercurrent conditions (illness, stress, or emotional disturbances), an inadequate or skipped insulin dose, inadvertent administration of an increased insulin dose, inadequate food intake, and skipped meals. Instruct patients on the management of hypoglycemia *[see Warnings and Precautions (5.3)]*.

Inform patients that their ability to concentrate and react may be impaired as a result of hypoglycemia. Advise patients who have frequent hypoglycemia or reduced or absent warning signs of hypoglycemia to use caution when driving or operating machinery.

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 (5.2)]*.

Hypoglycemia with Medication Errors

Instruct patients to always check the insulin label before each injection to avoid mix-ups between insulin products *[see Warnings and Precautions (5.3)]*.

Hypersensitivity Reactions

Advise patients that hypersensitivity reactions have occurred with insulin aspart products. Inform patients of the symptoms of hypersensitivity reactions *[see Warnings and Precautions (5.4)]*.

Patients Using Continuous Subcutaneous Insulin Pumps

- Train patients in both intensive insulin therapy with multiple injections and in the function of their pump and pump accessories.
- This KIRSTY product can be used with continuous subcutaneous insulin infusion pumps labeled for use with KIRSTY or NOVOLOG -refer to the insulin pump user manual to see if KIRSTY or NOVOLOG can be used with the insulin pump, in which case KIRSTY can be used with the pump. See recommended infusion sets in the insulin pump user manual.
- Instruct patients to replace insulin in the reservoir at least every 7 days or according to the user manual, whichever is shorter; infusion sets and infusion set insertion sites should be changed according to the manufacturer's user manual. By following this schedule, patients avoid insulin degradation, infusion set occlusion, and loss of the insulin preservative.
- Instruct patients to discard insulin exposed to temperatures higher than 37°C (98.6°F).
- Instruct patients to inform physician and select a new site for infusion if infusion site becomes erythematous, pruritic, or thickened.
- Instruct patients of the risk of rapid hyperglycemia and ketosis due to pump malfunction, infusion set occlusion, leakage, disconnection or kinking, and degraded insulin. If these problems cannot be promptly corrected, instruct patients to resume therapy with subcutaneous insulin injection and contact their physician *[see Warnings and Precautions (5) and How Supplied/Storage and Handling (16.2)]*.
- Instruct patients of the risk of hypoglycemia from pump malfunction. If these problems cannot be promptly corrected, instruct patients to resume therapy with subcutaneous insulin injection and contact their physician *[see Warnings and Precautions (5) and How Supplied/Storage and Handling (16.2)]*.

Kirsty™ is a trademark of Biosimilars New Co Ltd; a Biocon Biologics Company.

Manufactured by:

Biocon Biologics Inc.

245 Main st, 2nd Floor

Cambridge, MA 02142, U.S.A.

U.S License No. 2324

Product of Malaysia

PATIENT INFORMATION

KIRSTY™ (kir-Stee)
(insulin aspart-xjhz)
injection, for subcutaneous or intravenous use

Do not share your KIRSTY prefilled pen 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.

What is KIRSTY?
KIRSTY is a man-made insulin that is used to control high blood sugar in adults and children with diabetes mellitus.

Who should not take KIRSTY? Do not take KIRSTY if you:

- are having an episode of low blood sugar (hypoglycemia).
- have an allergy to insulin aspart products or any of the ingredients in KIRSTY.

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

- pregnant, planning to become pregnant, or are breastfeeding.
- taking new prescription or over-the-counter medicines, vitamins, or herbal supplements.

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

How should I take KIRSTY?

- **Read the Instructions for Use** that come with your KIRSTY**.**
- Take KIRSTY exactly as your healthcare provider tells you to.
- **KIRSTY starts acting fast.** You should eat a meal within 5 to 10 minutes after you take your dose of KIRSTY.
- 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.
- **Check your blood sugar levels.** Ask your healthcare provider what your blood sugars should be and when you should check your blood sugar levels.
- **Do not reuse or share your needles with other people.** You may give other people a serious infection or get a serious infection from them.
- KIRSTY can be injected under the skin (subcutaneously) of your stomach area (abdomen), buttocks, upper legs (thighs), or upper arms or by continuous infusion under the skin (subcutaneously) through an insulin pump into an area of your body recommended in the instructions that come with your insulin pump.
- **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.

What should I avoid while taking KIRSTY? While taking KIRSTY do not:

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

What are the possible side effects of KIRSTY?
KIRSTY 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
- sweating
- confusion
- headache
- blurred vision
- slurred speech
- shakiness
- fast heartbeat
- anxiety, irritability or mood changes
- hunger

Your insulin dose may need to change because of:

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

Other common side effects of KIRSTY may include:

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

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

What are the ingredients in KIRSTY?
Active ingredient: insulin aspart-xjhz
Inactive Ingredients: dibasic sodium phosphate , glycerin, *m*-cresol, phenol, sodium chloride, zinc, and Water for Injection, USP. Hydrochloric acid 1% and/or sodium hydroxide 1% may be added to adjust pH.
Manufactured by: Biocon Biologics Inc. 245 Main st, 2nd Floor, Cambridge, MA

02142, U.S.A.
U.S License No. 2324**,** Product of Malaysia

This Patient Information has been approved by the U.S. Food and Drug Administration. Approved: 07/2025

INSTRUCTIONS FOR USE

KIRSTY™ (kir-Stee)
(insulin aspart-xjhz)

injection, for subcutaneous use
10 mL multiple-dose vial: 100 units/mL (U-100)

Read this Instructions for Use before you start taking KIRSTY and each time you get a refill.

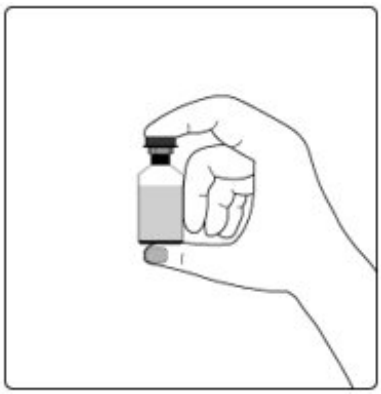
There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

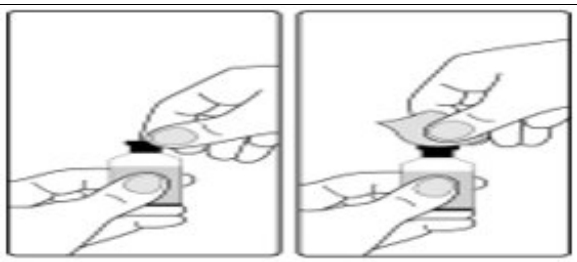
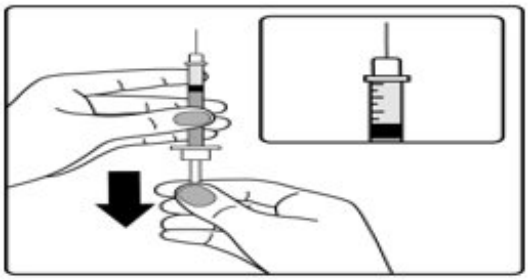
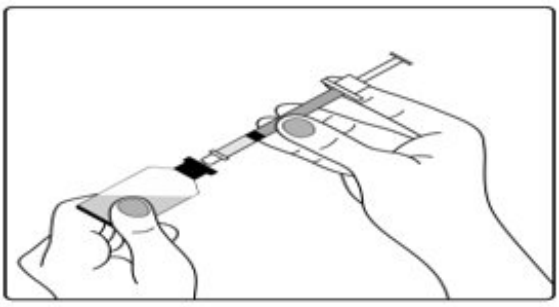
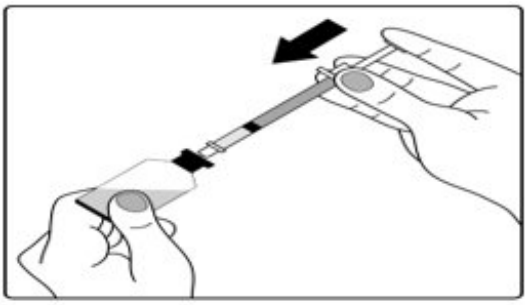
Supplies you will need to give your KIRSTY injection:

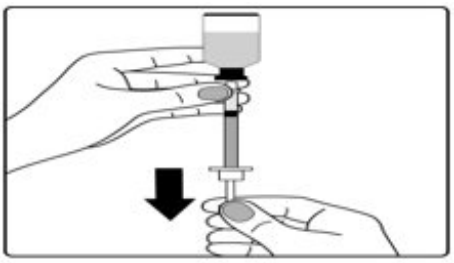
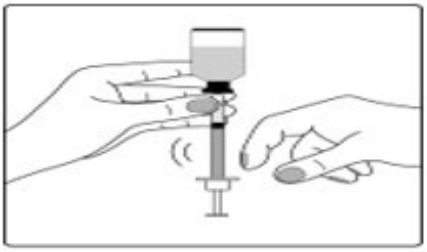
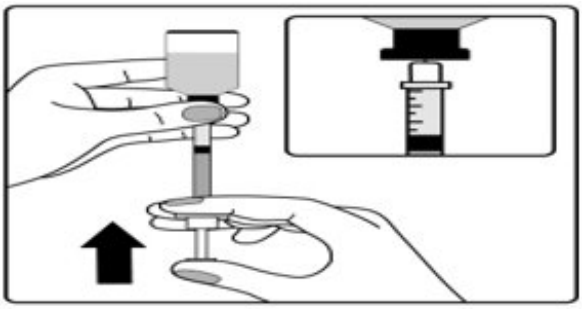
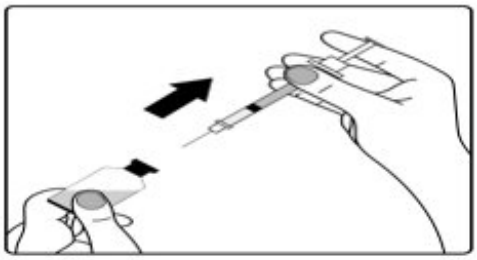
- 10 mL KIRSTY vial
- insulin syringe and needle
- alcohol swabs

Preparing your KIRSTY dose:

- Wash your hands with soap and water.
- Before you start to prepare your injection, check the KIRSTY label to make sure that you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- KIRSTY should look clear and colorless. **Do not** use KIRSTY if it is thick, cloudy, or is colored.
- **Do not** use KIRSTY past the expiration date printed on the label.



Step 1: Pull off the tamper resistant cap (See Figure A). **Step 2:** Wipe the rubber stopper with an alcohol swab (See Figure B).	 (Figure A Figure B)
Step 3: Hold the syringe with the needle pointing up. Pull down on the plunger until the black tip reaches the line for the number of units for your prescribed dose (See Figure C).	 (Figure C)
Step 4: Push the needle through the rubber stopper of the KIRSTY vial (See Figure D).	 (Figure D)
Step 5: Push the plunger all the way in. This puts air into the KIRSTY vial (See Figure E).	 (Figure E)

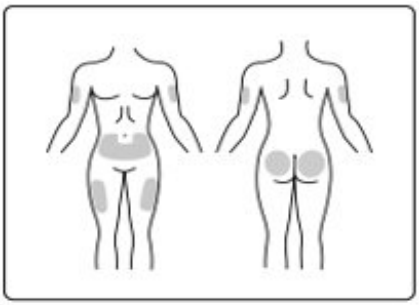
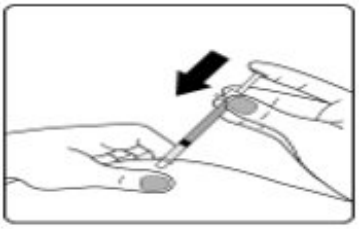
Step 6: Turn the KIRSTY vial and syringe upside down and slowly pull the plunger down until the black tip is a few units past the line for your dose (See Figure F). • If there are air bubbles, tap the syringe gently a few times to let any air bubbles rise to the top (See Figure G).	 **(Figure F)**  **(Figure G)**
Step 7: Slowly push the plunger up until the black tip reaches the line for your KIRSTY dose (See Figure H).	 **(Figure H)**
Step 8: Check the syringe to make sure you have the right dose of KIRSTY.	
Step 9: Pull the syringe out of the vial's rubber stopper (See Figure I).	 **(Figure I)**

Giving your injection:

- Inject your KIRSTY exactly as your healthcare provider has shown you. Your healthcare provider should tell you if you need to pinch the skin before injecting.
- KIRSTY can be injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs or upper arms, infused in an insulin pump (continuous subcutaneous infusion into an area of your body recommended in the instructions that come with your insulin pump), or given through a needle in your arm (intravenously) by your healthcare provider.
- If you inject KIRSTY, change (rotate) your injection sites within the area you choose for 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 same injection site 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

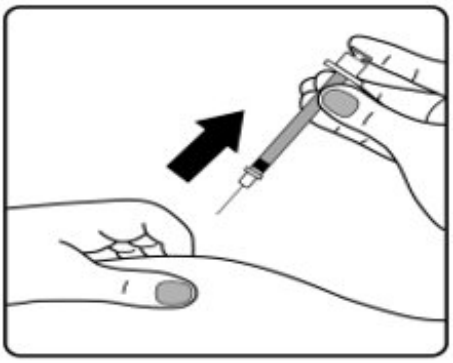
or hard, or into scars or damaged skin.

- If you use KIRSTY in an insulin pump, you should change your infusion set and insertion site according to the manufacturer's user manual. KIRSTY can be used with the continuous subcutaneous insulin infusion pumps labeled for use with KIRSTY or NOVOLOG. Read the insulin pump user manual to see if KIRSTY or NOVOLOG can be used. KIRSTY should be given into an area of your body recommended in the instructions that come with your insulin pump. Change (rotate) your insertion sites within the area you choose for each insertion to reduce your risk of getting lipodystrophy (pits in skin or thickened skin) and localized cutaneous amyloidosis (skin with lumps) at the insertion sites. Do not insert into the exact same spot for each insertion. Do not insert where the skin has pits, is thickened, or has lumps. Do not insert where the skin is tender, bruised, scaly or hard, or into scars or damaged skin. The insulin in the reservoir should be changed at least every 7 days or according to the pump user manual, whichever is shorter, even if you have not used all of the insulin.
- If you use KIRSTY in an insulin pump, see your insulin pump manual for instructions or talk to your healthcare provider.
- NPH insulin is the only type of insulin that can be mixed with KIRSTY. **Do not** mix KIRSTY with any other type of insulin.
- KIRSTY should **only** be mixed with NPH insulin if it is going to be injected right away under your skin (subcutaneously).
- KIRSTY should be drawn up into the syringe **before** you draw up your NPH insulin.
- Talk to your healthcare provider if you are not sure about the right way to mix KIRSTY and NPH insulin.

Step 10: Choose your injection site (stomach area, buttocks, upper legs or upper arms) and wipe the skin with an alcohol swab. Let the injection site dry before you inject your dose (See Figure J).	 **(Figure J)**
Step 11: Insert the needle into your skin. Push down on the plunger to inject your dose (See Figure K). **The needle should remain in the skin for at least 6 seconds to make sure you have injected all the insulin.**	 **(Figure K)**

Step 12: Pull the needle out of your skin. After that, you may see a drop of KIRSTY at the needle tip. This is normal and does not affect the dose you just received (See Figure L).

- If you see blood after you take the needle out of your skin, press the injection site lightly with a piece of gauze or an alcohol swab. **Do not** rub the area.



(Figure L)

After your injection:

- **Do not** recap the needle. Recapping the needle can lead to a needle stick injury.
- Put the empty insulin vials, used needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes 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,
  - can 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 state or local laws about how you should throw away used needles and syringes. 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.

How should I store KIRSTY?

- **Do not** freeze KIRSTY. **Do not** use KIRSTY if it has been frozen.
- Keep KIRSTY away from heat or light.
- **All unopened vials:**
  - Store unopened KIRSTY vials in the refrigerator at 36°F to 46°F (2°C to 8°C).
  - Unopened vials may be used until the expiration date printed on the label, if they have been stored in the refrigerator.
  - Unopened vials should be thrown away after 28 days, if they are stored at room temperature up to 86°F (30°C).
- **After vials have been opened:**
  - Opened KIRSTY vials can be stored in the refrigerator at 36°F to 46°F (2°C to 8°C)

or at room temperature up to 86°F (30°C).
- Throw away all opened KIRSTY vials after 28 days, even if they still have insulin left in them.
- If using KIRSTY in a pump, throw away all opened KIRSTY vials after 19 days.

General information about the safe and effective use of KIRSTY

- Always use a new syringe and needle for each injection.
- Do not share syringes or needles.
- Keep KIRSTY vials, syringes, and needles out of the reach of children.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

KIRSTY™ is a trademark of Biosimilars New Co Ltd; a Biocon Biologics Company.

Manufactured by:
Biocon Biologics Inc.
245 Main st, 2nd Floor
Cambridge, MA 02142, U.S.A.
U.S. License No. 2324

Product of Malaysia

Approved: 07/2025

INSTRUCTIONS FOR USE

KIRSTY (kir-Stee)
(insulin aspart-xjhz) injection, for subcutaneous use
Prefilled Pen

Introduction

Please read the following instructions carefully before using your KIRSTY Prefilled Pen.

Do not share your KIRSTY Prefilled Pen 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.

KIRSTY Prefilled Pen is a disposable, single-patient-use, dial-a-dose insulin pen.

You can select doses from 1 to 80 units in increments of 1 unit.

Only use needles that are compatible for use with KIRSTY Prefilled Pen which are sold separately, including needles from Embecta (such as Embecta UltraFine),

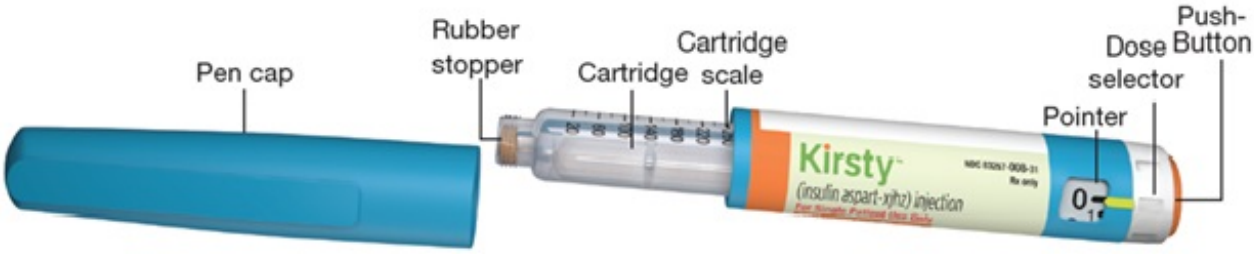
People who are blind or have vision problems should not use this Pen without help from a person trained to use the Pen.

Getting ready

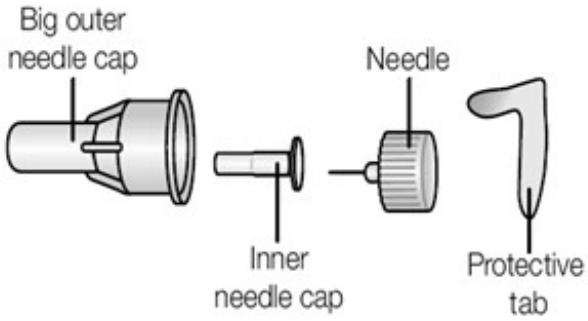
Make sure you have the following items:
- KIRSTY Prefilled Pen
- a new sterile needle (see **Step B**)

- Alcohol swabs

KIRSTY Prefilled Pen



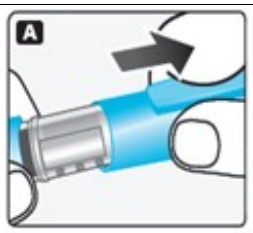
Needle (example)



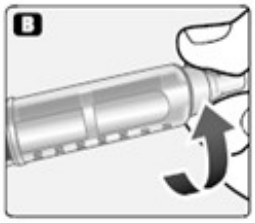
Preparing your KIRSTY Prefilled Pen

- Wash your hands with soap and water.
- Before you start to prepare your injection, check the label to make sure that you are taking the right type of insulin. This is especially important if you take more than 1 type of insulin.
- KIRSTY should look clear and colorless. Do not use your KIRSTY Prefilled Pen if the liquid contains particles or is colored.

A. Pull off the pen cap (see diagram A).
Wipe the rubber stopper with an alcohol swab.



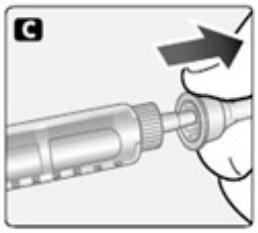
B. **Attaching the needle**
Remove the protective tab from a disposable needle.
Screw the needle tightly onto your Prefilled Pen. It is important that the needle is put on straight (see diagram B).



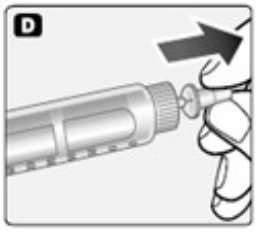
Never place a disposable needle on your KIRSTY Prefilled Pen until you are ready to take your

injection.

C. Pull off the big outer needle cap (see diagram C).



D. Pull off the inner needle cap and throw it away (dispose of it) (see diagram D).



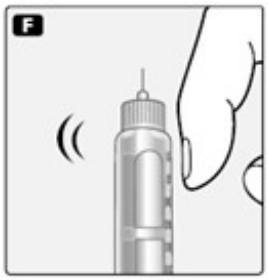
! Always use a new needle for each injection to make sure the needle is free of germs (sterile) and to prevent blocked needles. Do not reuse or share your needles with other people. You may give other people a serious infection, or get a serious infection from them.
! Be careful not to bend or damage the needle before use.
! To reduce the risk of unexpected needle sticks, **never put the inner needle cap back on the needle**.

Giving the airshot before each injection
Before each injection small amounts of air may collect in the cartridge during normal use. To avoid injecting air and to ensure proper dosing:

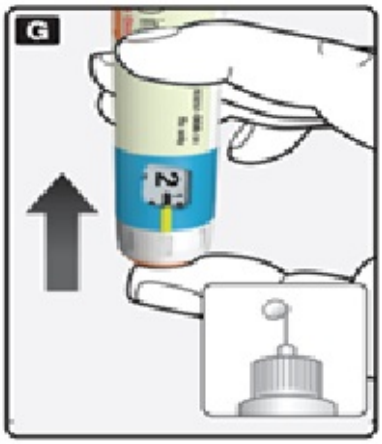
E. Turn the dose selector to select 2 units (see diagram E).

F. Hold your KIRSTY Prefilled Pen with the needle pointing up.

Tap the cartridge gently with your finger a few times to make any air bubbles collect at the top of the cartridge (see diagram F).



G. Keep the needle pointing upwards, press the push-button all the way in (see diagram G). The dose selector returns to 0.



A drop of insulin should appear at the needle tip. If not, change the needle and repeat the procedure no more than 6 times.

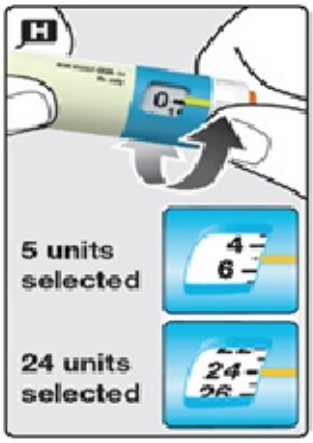
If you do not see a drop of insulin after 6 times, do not use the KIRSTY Prefilled Pen and contact Biocon Biologics Inc. at 1-833-986-1468.

A small air bubble may remain at the needle tip, but it will not be injected.

Selecting your dose

Check and make sure that the dose selector is set at 0.

H. Turn the dose selector to the number of units you need to inject.
The pointer should line up with your dose.



The dose can be corrected either up or down by turning the dose selector in either direction until the correct dose lines up with the pointer (see diagram H). When turning the dose selector, be careful not to press the push-button as insulin will come out.

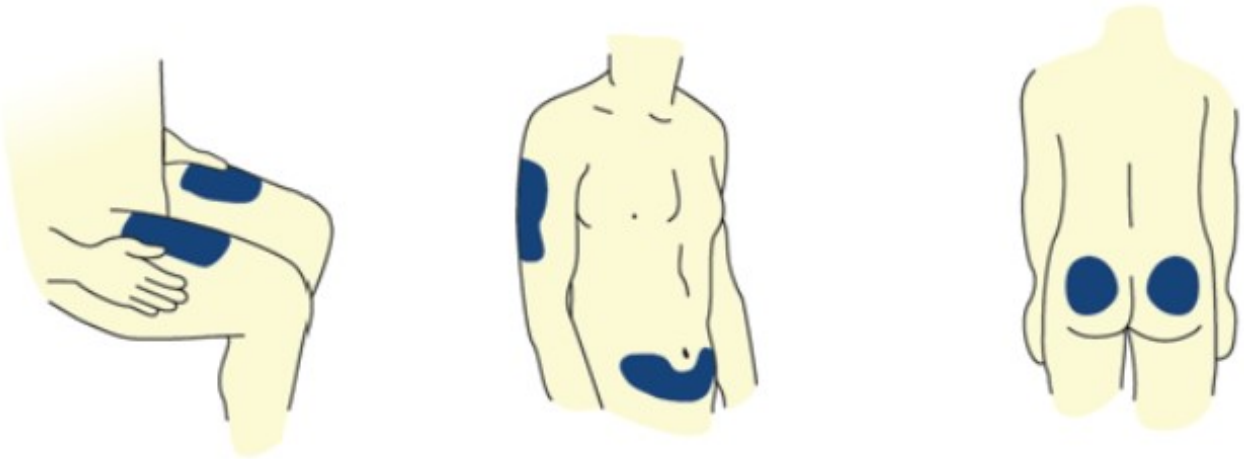
You cannot select a dose larger than the number of units left in the cartridge.

You will hear a click for every single unit dialed. Do not set the dose by counting the number of clicks you hear because you may get an incorrect dose.

! Do not use the cartridge scale printed on the cartridge to measure your dose of insulin.

Giving the injection

Do the injection exactly as shown to you by your healthcare provider. Your healthcare provider should tell you if you need to pinch the skin before injecting. Wipe the skin with an alcohol swab and let the area dry.
KIRSTY can be injected under the skin (subcutaneously) of your stomach area, buttocks, upper legs (thighs), or upper arms.



Change (rotate) your injection sites within the area you choose for 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 same injection site 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.

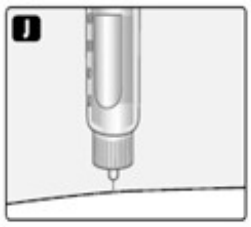
I. Insert the needle into your skin.

   Inject the dose by pressing the push-button all the way in until the 0 lines up with the pointer (see diagram I). Be careful only to push the button when injecting.

   Turning the dose selector will not inject insulin.

J. Keep the needle in the skin for at least 6 seconds, and keep the push-button pressed all the way in until the needle has been pulled out from the skin (see diagram J). This will make sure that the full dose has been given.

   You may see a drop of insulin at the needle tip. This is normal and has no effect on the dose you just received. If blood appears after you take the needle out of your skin, press the injection site lightly with an alcohol swab.



! **Do not rub the area.**

After the injection

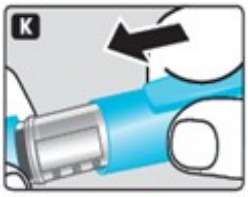
Do not recap the needle. Recapping can lead to a needle stick injury. Remove the needle from the KIRSTY Prefilled Pen after each injection and dispose of it. This helps to prevent infection, leakage of insulin, and will help to make sure you inject the right dose of insulin.

If you do not have a sharps container, carefully slip the needle into the outer needle cap. Safely remove the needle and throw it away as soon as you can.

- Put your used needles in an FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles in your household trash.
- If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:
    - made of a heavy-duty plastic,
    - can 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 state or local laws about how you should throw away used needles and syringes. 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.
- When there is not enough medicine left in your KIRSTY Prefilled Pen for your prescribed dose, the KIRSTY Prefilled Pen may be thrown away in your household trash after you have removed the needle.

The KIRSTY Prefilled Pen prevents the cartridge from being completely emptied. It is designed to deliver 300 units.

K. Put the pen cap on the KIRSTY Prefilled Pen and store the KIRSTY Prefilled Pen without the needle attached (see diagram K). Storing without the needle attached helps prevent leaking, blocking of the needle, and air from entering the Pen.



How should I store KIRSTY Prefilled Pen?

- **Do not** freeze KIRSTY. **Do not** use KIRSTY if it has been frozen.
- Keep KIRSTY away from heat or light.
- Store the KIRSTY Prefilled Pen without the needle attached.

Until first use:

- Store unused KIRSTY Prefilled Pen in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Unused KIRSTY Prefilled Pen may be used until the expiration date printed on the label, if kept in the refrigerator.
- Unused KIRSTY Prefilled Pen stored at room temperature up to 86°F (30°C) should be thrown away after 28 days.

In-use:

- Store the KIRSTY Prefilled Pen you are currently using out of the refrigerator at room temperature up to 86°F (30°C) for up to 28 days.
- The KIRSTY Prefilled Pen you are using should be thrown away after 28 days, even if it still has insulin left in it.

Maintenance

For the safe and proper use of your Prefilled Pen be sure to handle it with care. Avoid dropping your Prefilled Pen as it may damage it. If you are concerned that your Prefilled Pen is damaged, use a new one. You can clean the outside of your Prefilled Pen by wiping it with a damp cloth. Do not soak or wash your Prefilled Pen as it may damage it. Do not refill your Prefilled Pen.

! Remove the needle from the KIRSTY Prefilled Pen after each injection. This helps to ensure sterility, prevent leakage of insulin, and will help to make sure you inject the right dose of insulin for future injections.
! Be careful when handling used needles to avoid needle sticks and transfer of infectious diseases.
! Keep your KIRSTY Prefilled Pen and needles out of the reach of children.
! Use KIRSTY Prefilled Pen as directed to treat your diabetes.
! **Do not** share your KIRSTY Prefilled Pen or needles with other people.
! You may give other people a serious infection, or get a serious infection from them.
! Always use a new needle for each injection.
! Biocon Biologics Inc. is not responsible for harm due to using this insulin pen with products not recommended by Biocon Biologics Inc.
! As a precautionary measure, always carry a spare insulin delivery device in case your KIRSTY Prefilled Pen is lost or damaged.
! Remember to keep the disposable KIRSTY Prefilled Pen with you. **Do not** leave it in a car or other location where it can get too hot or too cold.

BD is a registered trademark of Becton, Dickinson and Company.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

KIRSTY™ is a trademark of Biosimilars New Co. Ltd.; a Biocon Biologics Company.

Manufactured by:
Biocon Biologics Inc.
245 Main st, 2nd Floor
Cambridge, MA 02142, U.S.A.
U.S. License No. 2324

Product of Malaysia

Approved: 07/2025

PRINCIPAL DISPLAY PANEL 10mL

NDC 83257-007-11

Kirsty™
(insulin aspart-xjhz)
injection
100 units/mL (U-100)

For intravenous or subcutaneous use
Use only with a U-100 syringe.

Rx only

One 10 mL
Multiple-Dose Vial.

Store refrigerated at 2°C to 8°C (36°F to 46°F) until first use then store either refrigerated or at room temperature (up to 30°C [86°F]) and discard after 28 days. Avoid freezing. Protect from light.

Warning: Any change of insulin should be made cautiously and only under medical supervision (see package insert).

Dosage: see Prescribing Information.

Discard unused portion of the vial 28 days after first opening.

Date of first opening: __/__/__.

Each mL contains 100 units of insulin aspart-xjhz, and the inactive ingredients dibasic sodium phosphate (0.997 mg), glycerin (16 mg), m-cresol (1.72 mg), phenol (1.50 mg), sodium chloride (0.58 mg), zinc (19.6 mcg), and Water for Injection, USP. The pH is 7.0 to 7.8. Hydrochloric acid and sodium hydroxide may be added to adjust pH.

Manufactured by:

Biocon Biologics Inc.

245 Main St, 2nd Floor Cambridge, MA 02142, U.S.A.

U.S. License No. 2324

Product of Malaysia

PRINCIPAL DISPLAY PANEL 3mL

NDC 83257-008-32

Kirsty™
(insulin aspart-xjhz) injection
For Single Patient Use Only
100 units/mL (U-100)

For Subcutaneous Use.

Dispense in this sealed carton.

***Needles not included.**

Five 3 mL Prefilled Pens

Rx only
Store refrigerated at 36° to 46°F (2° to 8°C) until first use. Avoid freezing. Protect from light. After first use of a Kirsty pen, store the pen at room temperature (up to 30°C [86°F]) for up to 28 days.

Warning

Any changes of insulin should be made cautiously and only under medical supervision.

Kirsty™ Prefilled Pen is for single patient use only.

Dosage: see Prescribing Information.

***Needles not included.**

For Subcutaneous Use.

Each mL contains 100 units of insulin aspart-xjhz, and the inactive ingredients dibasic sodium phosphate (0.997 mg), glycerin (16 mg), m-cresol (1.72 mg), phenol (1.50 mg), sodium chloride (0.58 mg), zinc (19.6 mcg), and Water for Injection, USP. The pH is 7.0 to 7.8.

Hydrochloric acid and sodium hydroxide may be added to adjust pH.

Store refrigerated at 2°C to 8°C (36°F to 46°F) until first use. Avoid freezing.

Protect from light. After first use of a Kirsty pen, store the pen at room temperature (up to 30°C [86°F]) for up to 28 days.

Discard unused portion of the pen 28 days after first opening.

Date of first opening:

Pen 1: _____ / _____ / _____.

Pen 2: _____ / _____ / _____.

Pen 3: _____ / _____ / _____.

Pen 4: _____ / _____ / _____.

Pen 5: _____ / _____ / _____.

***Embecta Ultra-fine needles are compatible with Kirsty™. These are sold separately and manufactured by Embecta.**

Manufactured by:

Biocon Biologics Inc.

245 Main St, 2nd Floor, Cambridge, MA 02142, U.S.A.

U.S. License No. 2324 Product of Malaysia

PRINCIPAL DISPLAY PANEL 10mL - Diluting Medium

NDC 83257-006-11

Insulin Diluting Medium for Kirsty™

Use only with Kirsty
This product does not contain insulin.

10 mL

Single-dose vial

Discard unused portion.

Each mL of Diluting Medium contains dibasic sodium phosphate (0.997 mg), glycerin (16 mg), m-cresol (1.5 mg), phenol (0.65 mg), and Water for Injection. Hydrochloric acid and sodium hydroxide may be added to adjust pH.

CAUTION: For use by health professionals only to dilute Kirsty or Insulin Aspart (insulin apsart-xjhz) Injection products.

Dilutions should be performed under aseptic conditions. Store unused vials at 2°C to 8°C (36°F to 46°F) and protect from light and heat – do not freeze.

Do not use the diluting medium if it does not appear water-clear and colorless or if the cap is loose or missing. The diluted insulin preparation should not be mixed with other insulin preparations in the same syringe. Do not use the diluting medium in insulin pumps. **Never use diluting medium after the expiration date printed on the box or vial label.**

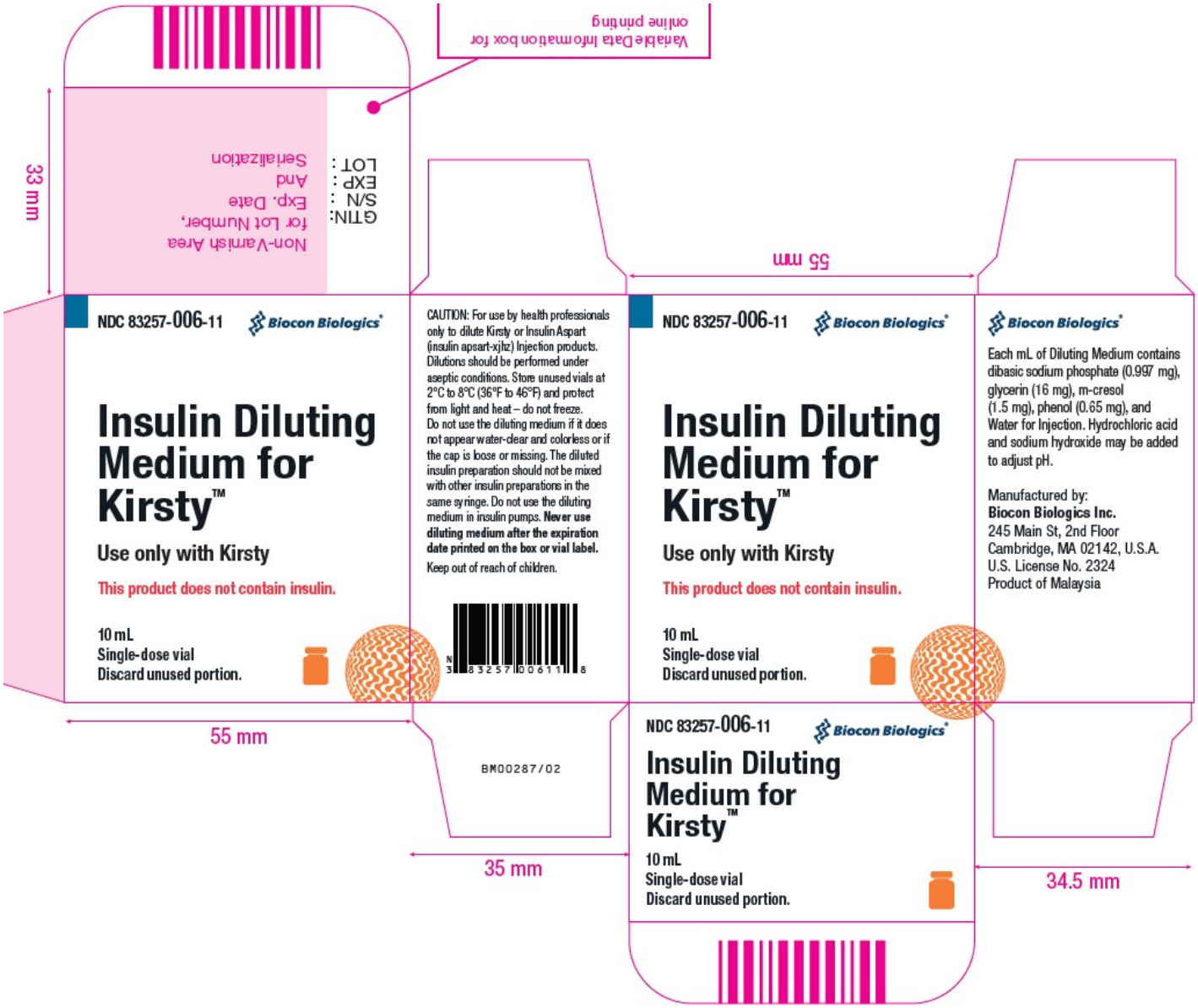
Keep out of reach of children.

Manufactured by:

Biocon Biologics Inc.

245 Main St, 2nd Floor Cambridge, MA 02142, U.S.A.

U.S. License No. 2324 Product of Malaysia



KIRSTY

insulin aspart-xjhz injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:83257-007
Route of Administration	INTRAVENOUS, SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
INSULIN ASPART (UNII: D933668QVX) (INSULIN ASPART - UNII:D933668QVX)	INSULIN ASPART	100 [iU] in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
GLYCERIN (UNII: PDC6A3C0OX)	16 mg in 1 mL

PHENOL (UNII: 339NCG44TV)	1.5 mg in 1 mL
METACRESOL (UNII: GGO4Y809LO)	1.72 mg in 1 mL
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	1.25 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.58 mg in 1 mL
WATER (UNII: 059QF0KO0R)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:83257-007-11	1 in 1 CARTON	07/15/2025	
1		10 mL in 1 VIAL, MULTI-DOSE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761188	07/15/2025	

KIRSTY

insulin aspart-xjhz injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:83257-008
Route of Administration	INTRAVENOUS, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
INSULIN ASPART (UNII: D933668QVX) (INSULIN ASPART - UNII:D933668QVX)	INSULIN ASPART	100 [iU] in 1 mL

Inactive Ingredients

Ingredient Name	Strength
GLYCERIN (UNII: PDC6A3C0OX)	16 mg in 1 mL
PHENOL (UNII: 339NCG44TV)	1.5 mg in 1 mL
METACRESOL (UNII: GGO4Y809LO)	1.72 mg in 1 mL
ZINC (UNII: J41CSQ7QDS)	19.6 ug in 1 mL
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	1.25 mg in 1 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	0.58 mg in 1 mL
WATER (UNII: 059QF0KO0R)	

HYDROCHLORIC ACID (UNII: QTT17582CB)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:83257-008-32	5 in 1 CARTON	07/15/2025	
1	NDC:83257-008-31	3 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761188	07/15/2025	

INSULIN DILUTING MEDIUM FOR KIRSTY

water injection, solution

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:83257-006
Route of Administration	INTRAVENOUS, SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
WATER (UNII: 059QF0KO0R) (WATER - UNII:059QF0KO0R)	WATER	1 mL in 1 mL

Inactive Ingredients

Ingredient Name	Strength
GLYCERIN (UNII: PDC6A3C0OX)	
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	
METACRESOL (UNII: GGO4Y809LO)	
PHENOL (UNII: 339NCG44TV)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:83257-006-11	1 in 1 CARTON	07/15/2025	
		10 mL in 1 VIAL, MULTI-DOSE; Type 2: Prefilled Drug Delivery		

1		10 mL in 1 VIAL, MULTI-DOSE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761188	07/15/2025	

Labeler - Biocon Biologics Inc. (117609395)

Establishment

Name	Address	ID/FEI	Business Operations
BIOCON SDN.BHD.		865785591	analysis(83257-007, 83257-006, 83257-008) , manufacture(83257-007, 83257-006, 83257-008) , pack(83257-007, 83257-006, 83257-008)

Revised: 1/2025 Biocon Biologics Inc.