# Insulin Overview

<table>
<thead>
<tr>
<th>Type</th>
<th>Brand Name</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
<th>Role in glucose management</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid-Acting</strong></td>
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<tr>
<td>lispro</td>
<td>Humalog</td>
<td>15-30 min</td>
<td>30-90 min</td>
<td>3-5 hrs</td>
<td>Rapid acting insulin covers insulin needs for meals eaten at the same time as the injection.</td>
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<tr>
<td>aspart</td>
<td>NovoLog</td>
<td>10-20 min</td>
<td>40-50 min</td>
<td>3-5 hrs</td>
<td></td>
</tr>
<tr>
<td>glulisine</td>
<td>Apidra</td>
<td>20-30 min</td>
<td>30-90 min</td>
<td>1-2 ½ hrs</td>
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<tr>
<td><strong>Short-Acting</strong></td>
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<tr>
<td>Regular insulin</td>
<td>Humulin R</td>
<td>30 min – 1 hr</td>
<td>2-5 hrs</td>
<td>5-8 hrs</td>
<td>Short acting insulin covers meals that are eaten within 30-60 minutes after the injection.</td>
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<tr>
<td></td>
<td>Novolin R</td>
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<tr>
<td><strong>Intermediate-Acting</strong></td>
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<tr>
<td>NPH insulin</td>
<td>Humulin N</td>
<td>1-2 hrs</td>
<td>4-12 hrs</td>
<td>18-24 hrs</td>
<td>Intermediate acting insulin covers insulin needs for half the day or overnight. It is often used in combination with rapid or short acting insulin.</td>
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<tr>
<td></td>
<td>Novolin N</td>
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<tr>
<td><strong>Long-Acting</strong></td>
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<tr>
<td>glargine</td>
<td>Lantus</td>
<td>1-1 ½ hrs</td>
<td>No peak; insulin is delivered at a steady level</td>
<td>20-24 hrs 24 hrs</td>
<td>Long-acting insulin covers insulin needs for a full day. It is often combined with rapid or short acting insulin when needed.</td>
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<tr>
<td>detemir</td>
<td>Toujeo</td>
<td>6 hrs</td>
<td></td>
<td>Up to 24 hrs</td>
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<tr>
<td></td>
<td>Levemir</td>
<td>1-2 hrs</td>
<td></td>
<td>Up to 24 hrs</td>
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<tr>
<td><strong>Ultra-Long-Acting</strong></td>
<td></td>
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<tr>
<td>degludec</td>
<td>Tresiba</td>
<td>1 hr</td>
<td>No peak; insulin is delivered at a steady level</td>
<td>42 hrs</td>
<td>Ultra-long-acting insulin can cover insulin needs beyond 24 hours. It is often combined with rapid or short acting insulin when needed.</td>
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<tr>
<td><strong>Pre-Mixed or Combination</strong></td>
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<tr>
<td></td>
<td>Humulin 70/30</td>
<td>30 min</td>
<td>2-4 hrs</td>
<td>14-24 hrs</td>
<td>These products are a combination of intermediate and short-acting insulin in one bottle or pen (The numbers following the brand name indicate the percentage of each type of insulin). They are usually taken 2 or 3 times a day before meals.</td>
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<tr>
<td></td>
<td>Novolin 70/30</td>
<td>30 min</td>
<td>2 12 hrs</td>
<td>Up to 24 hrs</td>
<td></td>
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<tr>
<td></td>
<td>Humulin 50/50</td>
<td>30 min</td>
<td>2-5 hrs</td>
<td>18-24 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Humalog 75/25</td>
<td>15 min</td>
<td>30 min – 2 ½ hrs</td>
<td>16-20 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NovoLog 70/30</td>
<td>10-20 min</td>
<td>1-4 hrs</td>
<td>Up to 24 hrs</td>
<td></td>
</tr>
<tr>
<td>degludec + aspart</td>
<td>Ryzodeg 70/30</td>
<td>10-20 min</td>
<td>60-90 min</td>
<td>&gt;24 hrs</td>
<td>This product is a combination of an ultra-long-acting and rapid-acting insulin in one pen (The numbers following the brand name indicate the percentage of each type of insulin). This is usually taken once daily.</td>
</tr>
</tbody>
</table>
INSULIN SUMMARY

Insulin is a pancreatic hormone that is secreted by beta-cells of the islets of Langerhans and is essential for the metabolism of glucose.

Insulin regulates carbohydrate, fat and protein metabolism by several mechanisms:

- Insulin promotes the storage and inhibits the breakdown of glucose, fat and amino acids
- Insulin lowers glucose concentrations by facilitating the uptake of glucose in muscle and adipose tissue
- Insulin inhibits hepatic glucose production (glycogenolysis and gluconeogenesis)
- Insulin regulates fat metabolism by enhancing the storage of fat and inhibiting the mobilization of fat for energy in adipose tissues
- Insulin is involved in the regulation of protein metabolism by increasing protein synthesis and inhibiting proteolysis in muscle tissue

Diabetes mellitus type 1 is caused by insulin deficiency while diabetes type 2 is caused by a combination of insulin deficiency and resistance. Biosynthetic insulin can be used in patients with diabetes to temporarily restore their ability to use carbohydrates, fats and proteins and to convert glycogen to fat.

RAPID-ACTING INSULINS

A. HUMALOG (lispro)

Indications:

- Humalog is a rapid acting human insulin analog indicated to improve glycemic control in adults and children with type 1 or type 2 diabetes.

Pharmacology:

- Insulin lowers blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat and by inhibiting glucose production. It also works to inhibit lipolysis and proteolysis, and enhance protein synthesis. Humalog has been shown to be equipotent to human insulin on a molar basis; one unit of Humalog has the same glucose-lowering effect as one unit of regular human insulin. It is produced from a chemical modification of regular human insulin in which the amino acids at positions B28 and B29 are reversed. Humalog has an onset of activity that is 15 to 30 minutes. It reaches mean peak plasma concentration 30-90 minutes post-dose when given SC. It has a duration of action of roughly 3 to 5 hours. Concentrations are higher after abdominal administration than those following deltoid or thigh injections. Humalog should be given with 15 minutes prior to or immediately after a meal due to its rapid onset.

How Supplied:

- Humalog 100units/mL (U-100) is available as
  - 10mL vials
  - 3mL vials
  - 3mL pre-filled pen (Humalog Kwik-Pen)
  - 3mL cartridges

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**Dosage and Administration:**

- The dose of Humalog must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Administer within 15 minutes before a meal or immediately after a meal.
- Can adjust insulin dose to the amount of carbohydrates eaten.
- Can be administered subcutaneously or intravenously under medical supervision.
- When using in a pump, the Humalog in the reservoir should be changed at least every 7 days while the infusion set and infusion set insertion site should be changed at least every 3 days.

**Drug Interactions:**

- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine).
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin.

**Adverse Effects:**

- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.

**Precautions and Contraindications:**

- Do not use during episodes of hypoglycemia.
- All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death.
- Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs).
- Humalog for SC injection should not be mixed with insulins other than NPH insulin. Do not mix Humalog with any insulin for use in a continuous infusion pump.
- Pregnancy category B.
- Not studied in children with type 2 diabetes or in children with type 1 diabetes < 3 years of age.

**Key advice to patients:**

- Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
- Patient should be instructed on how to manage sick days or skipped meal.
- Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
- Store unopened product in refrigerator.
- Do not use if product has been frozen.
- Opened container can be stored for up to 28 days at room temperature.
- Patient should check for particulate matter and discoloration prior to administration.
- If mixing with NPH insulin, Humalog should be drawn up into the syringe prior to the NPH.
**B. NOVOLOG (aspart)**

**Indications:**
- NovoLog is a rapid acting human insulin analog indicated to improve glycemic control in adults and children with type 1 or type 2 diabetes.

**Pharmacology:**
- Insulin lowers blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat and by inhibiting glucose production. It also works to inhibit lipolysis and proteolysis, and enhance protein synthesis. NovoLog has been shown to be equipotent to human insulin on a molar basis; one unit of NovoLog has the same glucose-lowering effect as one unit of regular human insulin. It is produced from a chemical modification of regular human insulin; the amino acid proline at position B28 in human insulin is replaced by aspartic acid. This substitution alters the insulin molecule and increases absorption. NovoLog has an onset of activity that is 15 to 30 minutes. It reaches mean peak plasma concentration 40-50 minutes post-dose when give SC. It has a duration of action of roughly 3 to 5 hours. Concentrations are higher after abdominal administration than those following deltoid or thigh injections. NovoLog should be given with 15 minutes prior to or immediately after a meal due to its rapid onset.

**How Supplied:**
- NovoLog 100units/mL (U-100) is available as
  - 10mL vials
  - 3mL cartridges
  - 3mL NovoLog FlexPen
  - 3mL NovoLog FlexTouch

**Dosage and Administration:**
- The dose of NovoLog must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Administer within 15 minutes before a meal or immediately after a meal.
- Can adjust insulin dose to the amount of carbohydrates eaten.
- Can be administered subcutaneously or intravenously under medical supervision
- When using in a pump, the NovoLog in the reservoir should be changed at least every 6 days while the infusion set and infusion set insertion site should be changed at least every 3 days.

**Drug Interactions:**
- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin i
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
• The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:

• Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.

Precautions and Contraindications:

• Do not use during episodes of hypoglycemia.
• All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
• Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
• Like all insulins, NovoLog requirements may be reduced in patients with renal or hepatic impairment
• NovoLog for SC injection should not be mixed with insulins other than NPH insulin. Do not mix NovoLog with any insulin for use in a continuous infusion pump.
• Pregnancy category B
• Not studied in children with type 2 diabetes or in children with type 1 diabetes < 2 years of age

Key advice to patients:

• Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
• Patient should be instructed on how to manage sick days or skipped meal.
• Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
• Store unopened product in refrigerator
• Do not use if product has been frozen
• Opened container can be stored for up to 28 days at room temperature
• Patient should check for particulate matter and discoloration prior to administration.
• If mixing with NPH insulin, Humalog should be drawn up into the syringe prior to the NPH.

C. APIDRA (glulisine)

Indications:

• Apidra is a rapid acting human insulin analog indicated to improve glycemic control in adults and children with type 1 or type 2 diabetes.

Pharmacology:

• Insulin lowers blood glucose by stimulating peripheral glucose uptake by skeletal muscle and fat and by inhibiting glucose production. It also works to inhibit lipolysis and proteolysis, and enhance protein synthesis. Apidra has been shown to be equipotent to human insulin on a molar basis; one unit of Apidra has the same glucose-lowering effect as one unit of regular human
insulin. It is produced from a chemical modification of regular human insulin; the amino acid asparagine at position B3 in regular insulin is replace by lysine, and the amino acid lysine at position B29 is replaced by glutamic acid. This substitution alters the insulin molecule and increases absorption. Apidra has an onset of action of about 20 minutes. It reaches mean peak plasma concentration 30-90 minutes post-dose when give SC. It has a duration of action of roughly 1-2½ hours. Concentrations are higher after abdominal administration than those following deltoid or thigh injections. Apidra should be given with 15 minutes prior to or immediately after a meal due to its rapid onset.

How Supplied:

- Apidra 100units/mL (U-100) is available as
  - 10mL vials
  - 3mL SoloStar prefilled syringe

Dosage and Administration:

- The dose of Apidra must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Administer within 15 minutes before a meal or within 20 minutes after starting a meal.
- Can adjust insulin dose to the amount of carbohydrates eaten.
- Can be administered subcutaneously or intravenously under medical supervision
- When using in a pump, the Apidra in the reservoir should be changed at least every 48 hours while the infusion set and infusion set insertion site should be changed at least every 3 days.

Drug Interactions:

- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
- The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:

- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.

Precautions and Contraindications:

- Do not use during episodes of hypoglycemia.
- All insulins can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death.
Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
Like all insulins, NovoLog requirements may be reduced in patients with renal or hepatic impairment
Use caution in patients predisposed to hypokalemia
Apidra for SC injection should not be mixed with insulins other than NPH insulin. Do not mix Apidra with any insulin for use in a continuous infusion pump.
Pregnancy category C
Not studied in children under the age of 4

Key advice to patients:
- Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
- Patient should be instructed on how to manage sick days or skipped meal.
- Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
- Store unopened product in refrigerator
- Do not use if product has been frozen
- Opened container can be stored for up to 28 days at room temperature
- Patient should check for particulate matter and discoloration prior to administration.
- If mixing with NPH insulin, Apidra should be drawn up into the syringe prior to the NPH.

SHORT-ACTING INSULINS

A. REGULAR INSULIN - NOVOLIN R and HUMULIN R

Indications:
- Regular insulin is a short acting recombinant human insulin indicated to improve glycemic control in adults and children with type 1 or type 2 diabetes.

Pharmacology:
- Regular insulin is an unmodified soluble insulin solution which is quickly absorbed from a SC site. Regular insulin has a slower onset of action and longer duration of action compared to the rapid-acting insulin analogs due to insulin hexamers that slowly dissociate into monomers. The glucose lowering effect begins approximately 30 minutes after the dose is injected. Mean peak is seen 2 to 5 hours after the dose is given and the duration of action is between 5 and 8 hours.

How Supplied:
- Novolin R 100units/mL (U-100) is available as
  - 10mL vials
- Humulin R 100units/mL (u-100) is available as
  - 10mL vials
- Humulin R 500units/mL (U-500) is available as
  - 20mL vials
Dosage and Administration:
- The dose of regular insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Administer 30-60 minutes before a meal.
- Can be administered subcutaneously, intramuscularly or intravenously under medical supervision
- Use in pumps is not recommended due to risk of precipitation

Drug Interactions:
- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin i
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
- The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:
- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.

Precautions and Contraindications:
- Do not use during episodes of hypoglycemia.
- All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
- Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
- Like all insulins, requirements may be reduced in patients with renal or hepatic impairment
- Regular insulin should not be mixed with any insulin for intravenous use. Do not mix with insulins other than NPH insulin for subcutaneous use.

Key advice to patients:
- Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
- Patient should be instructed on how to manage sick days or skipped meal.
- Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
- Store in refrigerator
- Product is stable for 28 days after initial use (may be kept at room temperature while using)
- Do not use if product has been frozen
- Patient should check for particulate matter and discoloration prior to administration.
- If mixing with NPH insulin, regular should be drawn up into the syringe prior to the NPH.

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INTERMEDIATE-ACTING INSULINS

A. NPH INSULINS – HUMULIN N and NOVOLIN N

Indications:
- NPH insulin is an intermediate acting insulin indicated to improve glycemic control in adults and children with type 1 or type 2 diabetes.

Pharmacology:
- Neutral Protamine Hagedorn (NPH) or isophane insulin is an intermediate acting insulin that is produced by adding zinc and protamine to regular insulin causing a delay in absorption and a prolongation of the duration of action. Combination with protamine enhances the aggregation of insulin into dimers and hexamers after SC injection; a depot is formed and the insulin is released slowly. After SC injection, the onset of activity is approximately 1 to 4 hours with peak activity occurring between 4 and 14 hours (mean 5.5 hrs). The duration of activity ranges from 10-24 hours.

How Supplied:
- Novolin N 100units/mL (U-100) is available as
  - 10mL vials
- Humulin N 100units/mL (u-100) is available as
  - 10mL vials
  - 3mL vials
  - 3mL prefilled pens (Humulin N KwikPen)

Dosage and Administration:
- The dose of NPH insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Should only be administered subcutaneously

Drug Interactions:
- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin if
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
- The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

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Adverse Effects:

- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
- Injection site reactions
- Lipodystrophy
- Pruritus
- Rash
- Weight gain
- Edema

Precautions and Contraindications:

- Do not use during episodes of hypoglycemia.
- All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
- Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
- Like all insulins, requirements may be reduced in patients with renal or hepatic impairment
- Regular insulin should not be mixed with any insulin for intravenous use. Do not mix with insulins other than NPH insulin for subcutaneous use.

Key advice to patients:

- Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
- Patient should be instructed on how to manage sick days or skipped meal.
- Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
- Store in refrigerator
- Product is stable for 28 days after initial use (may be kept at room temperature while using)
- Do not use if product has been frozen
- Product should be uniformly cloudy
- If mixing with rapid or short acting insulin, the rapid or short acting insulin should be drawn up into the syringe prior to the NPH.

LONG-ACTING (BASAL) INSULINS

A. LANTUS (glargine)

Indications:

- Basal insulin is a long acting human insulin analog indicated to improve glycemic control in adults and children with type 1 or type 2 diabetes.
- Not recommended for treating diabetic ketoacidosis. Use intravenous, short-acting insulin instead.
Pharmacology:
- Insulin glargine is a human insulin analog that has been designed to have low aqueous solubility at neutral pH. At pH 4, as in the lantus injection solution, insulin glargine is completely soluble. After injection into SC tissue, the acidic solution is neutralized, leading to formation of microprecipitates from which small amounts of insulin are slowly released resulting in a relatively constant concentration/time profile over 24 hours with no obvious peak. This allows for once daily dosing. The onset of activity is 1.5 hours.

How Supplied:
- Lantus 100units/mL (U-100) is available as
  - 10mL vial
  - 3mL SoloStar pen

Dosage and Administration:
- The dose of glargine insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Should only be administered subcutaneously
- Should be administered once daily at any time of day, but at the same time each day
- Rotate injection sites within an injection area to reduce the risk of lipodystrophy

Drug Interactions:
- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
- The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:
- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
- Injection site reactions
- Lipodystrophy
- Pruritus
- Rash
- Weight gain
- edema

Precautions and Contraindications:
• Do not use during episodes of hypoglycemia.
• Pregnancy category C: use during pregnancy only if the potential benefit justifies the potential risk to the fetus
• All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
• Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
• Like all insulins, requirements may be reduced in patients with renal or hepatic impairment
• Lantus should not be mixed with any insulin
• Do not administer via an insulin pump or intravenously because severe hypoglycemia can occur
• Has not been studied in children with type 2 diabetes. Has not been studied in children with type 1 diabetes < 6 years of age.

Key advice to patients:
• Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
• Patient should be instructed on how to manage sick days or skipped meal.
• Lantus should only be used if the solution is clear and colorless with no visible particles
• Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
• Store in refrigerator
• Product is stable for 28 days after initial use (may be kept at room temperature while using)
• Do not use if product has been frozen

B. TOUJEO (glargine)

Indications:
• Basal insulin is a long acting human insulin analog indicated to improve glycemic control in adults (≥ 18 years of age) with type 1 or type 2 diabetes.
• Not recommended for treating diabetic ketoacidosis. Use intravenous, short-acting insulin instead.

Pharmacology:
• Insulin glargine is a human insulin analog that has been designed to have low aqueous solubility at neutral pH. At pH 4, as in the Toujeo injection solution, insulin glargine is completely soluble. After injection into SC tissue, the acidic solution is neutralized, leading to formation of microprecipitates from which small amounts of insulin are slowly released resulting in a relatively constant concentration/time profile over 24 hours with no obvious peak. This allows for once daily dosing. The onset of activity is 6 hours.

How Supplied:
• Toujeo 300 units/ml (U-300) is available as
  ○ 1.5 ml Solostar pen (package size of 3 or 5)
    ▪ Avg. Retail Price: $130 per pen (300 units)

Dosage and Administration:

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• The dose of glargine insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
• Should only be administered subcutaneously
• Should be administered once daily at any time of day, but at the same time each day
• Rotate injection sites within an injection area to reduce the risk of lipodystrophy

Drug Interactions:
• The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine).
• The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
• Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
• The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
• The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:
• Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
• Injection site reactions
• Lipodystrophy
• Pruritus
• Rash
• Weight gain
• Edema

Precautions and Contraindications:
• Do not use during episodes of hypoglycemia.
• Use during pregnancy only if the potential benefit justifies the potential risk to the fetus
• All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
• Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
• Like all insulins, requirements may be reduced in patients with renal or hepatic impairment
• Toujeo should not be mixed with any insulin
• Do not administer via an insulin pump or intravenously because severe hypoglycemia can occur
• Has not been studied in children with type 1 or type 2 diabetes

Key advice to patients:

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Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.

Patient should be instructed on how to manage sick days or skipped meal.

Toujeo should only be used if the solution is clear and colorless with no visible particles.

Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.

Unopened Toujeo Solostar disposable prefilled pen should be stored in a refrigerator (36°F-46°F or 2°-8°C).

Opened (in-use) Toujeo Solostar disposable prefilled pen should not be refrigerated, but should be kept at room temperature (below 86°F or 30°C) away from direct heat and sunlight.

Product is stable for 28 days after initial use

Do not use if product has been frozen

C. LEVEMIR (detemir)

Indications:

- Basal insulin is a long acting human insulin analog indicated to improve glycemic control in adults and children with type 1 or type 2 diabetes.
- Not recommended for treating diabetic ketoacidosis. Use intravenous, short-acting insulin instead.

Pharmacology:

- Insulin detemir is a recombinant, soluble, long-acting insulin analog that is produced from a chemical modification of regular insulin; a 14-carbon fatty acid (myristic acid) is covalently bound to the amino acid Lysine at position B29 and the amino acid threonine at position B30 is omitted. Fatty acid acylation enhances insulin detemir’s affinity to albumin, which allows for delayed absorption due to albumin binding in SC adipose tissue and plasma. Levemir has an approximate 24 hour duration of action. The pharmacodynamics profile is fairly consistent with no pronounce peak.

How Supplied:

- Levemir 100 units/mL (U-100) is available as
  - 10mL vial
  - 3mL prefilled pen (FlexPen)
  - 3mL FlexTouch

Dosage and Administration:

- The dose of detemir insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Should only be administered subcutaneously
- Can be administered once daily or in divided doses twice daily. Once daily administration should be given with the evening meal or at bedtime.
- Rotate injection sites within an injection area to reduce the risk of lipodystrophy

Drug Interactions:
• The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
• The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
• Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
• The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
• The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:

• Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
• Injection site reactions
• Lipodystrophy
• Pruritus
• Rash
• Weight gain
• edema

Precautions and Contraindications:

• Do not use during episodes of hypoglycemia.
• Pregnancy category C: use during pregnancy only if the potential benefit justifies the potential risk to the fetus
• All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
• Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
• Like all insulins, requirements may be reduced in patients with renal or hepatic impairment
• Lantus should not be mixed with any insulin
• Do not administer via an insulin pump or intravenously because severe hypoglycemia can occur
• Has not been studied in children with type 2 diabetes. Has not been studied in children with type 1 diabetes < 2 years of age.

Key advice to patients:

• Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
• Patient should be instructed on how to manage sick days or skipped meal.
• Leveimir should only be used if the solution is clear and colorless with no visible particles
• Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
• Store in refrigerator
• Product is stable for 42 days after initial use (may be kept at room temperature while using)
• Do not use if product has been frozen

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ULTRA-LONG-ACTING (BASAL) INSULINS

A. TRESIBA (degludec)

Indications:

- Basal insulin is a long acting human insulin analog indicated to improve glycemic control in adults (≥ 18 years of age) with type 1 or type 2 diabetes.
- Not recommended for treating diabetic ketoacidosis. Use intravenous, short-acting insulin instead.

Pharmacology:

- Insulin degludec is a long-acting basal human insulin with a relatively neutral pH of 7.6. Tresiba was designed to form multi-hexamers when injected into subcutaneous tissue resulting in a SQ insulin degludec depot. The protracted time action profile of Tresiba is predominantly due to delayed absorption of insulin degludec from the SQ tissue to the systemic circulation and to a lesser extent due to binding of insulin degludec to circulating albumin. This allows for once daily dosing. The onset of activity is approximately 1 hour.

How Supplied:

- Tresiba 100 units/ml (U-100) is available as
  - 3 ml FlexTouch pen (package size of 5)
- Tresiba 200 units/ml (U-200) is available as
  - 3 ml FlexTouch pen (package size of 3)

Dosage and Administration:

- The dose of glargine insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Should only be administered subcutaneously
- Should be administered once daily at any time of day, but at the same time each day
- Rotate injection sites within an injection area to reduce the risk of lipodystrophy

Drug Interactions:

- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine).
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:

- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
- Injection site reactions
- Lipodystrophy
- Pruritus
- Rash
- Weight gain
- Edema

Precautions and Contraindications:

- Do not use during episodes of hypoglycemia.
- Use during pregnancy only if the potential benefit justifies the potential risk to the fetus
- All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
- Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
- Like all insulins, requirements may be reduced in patients with renal or hepatic impairment
- Tresiba should not be diluted or mixed with any insulin
- Do not administer via an insulin pump or intravenously because severe hypoglycemia can occur
- Has not been studied in children with type 1 or type 2 diabetes

Key advice to patients:

- Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
- Patient should be instructed on how to manage sick days or skipped meal.
- Tresiba should only be used if the solution is clear and colorless with no visible particles.
- Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
- Unopened Tresiba Flextouch disposable prefilled pen should be stored in a refrigerator (36°F-46°F or 2°C-8°C).
- Opened (in-use) Tresiba Flextouch disposable prefilled pen should not be refrigerated, but should be kept at room temperature (below 86°F or 30°C) away from direct heat and sunlight.
- Product is stable for up to 56 days (8 weeks) after initial use, if it is kept at room temperature
- Do not use if product has been frozen
PRE-MIXED & COMBINATION INSULINS

A. HUMULIN 70/30 and NOVOLIN 70/30

Indications:

- Premixed and fixed ratio of recombinant insulin indicated to improve glycemic control in adults with type 1 or type 2 diabetes.
- In premix insulins the proportions of rapid acting and long acting insulins are fixed and do not allow for basal versus prandial dose adjustments.

Pharmacology:

- These insulins combine an intermediate-acting insulin with the more rapid onset of action of regular human insulin in a fixed ration (70% NPH, 30% regular). The onset of action ranges between 15 to 30 minutes and peaks about 3.5 hours after the dose was administered although this number varies widely between the different products marketed and patient utilization. Duration of action ranges between 18 and 24 hours.

How Supplied:

- Humulin 70/30 suspension 100units/mL (U-100) is available as
  - 10mL vials
  - 3mL vials
  - 3mL prefilled pens (Humulin 70/30 KwikPen)
- Novolin 70/30 suspension 100u/mL (U-100) is available as
  - 10mL vials

Dosage and Administration:

- The dose of insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Should only be administered subcutaneously
- Administer approximately 30-45 minutes before a meal
- Rotate the vial or pen between palms to mix before using a dose; do not shake

Drug Interactions:

- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.

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• The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:
• Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
• Injection site reactions
• Lipodystrophy
• Pruritus
• Rash
• Weight gain
• Edema

Precautions and Contraindications:
• Do not use during episodes of hypoglycemia.
• All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
• Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
• Like all insulins, requirements may be reduced in patients with renal or hepatic impairment

Key advice to patients:
• Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
• Patient should be instructed on how to manage sick days or skipped meal.
• Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
• Store in refrigerator
• Product is stable for 28 days after initial use (may be kept at room temperature while using)
• Do not use if product has been frozen
• Should only be used if uniformly cloudy

B. HUMULIN 50/50
Indications:
• Premixed and fixed ratio of recombinant insulin indicated to improve glycemic control in adults with type 1 or type 2 diabetes.
• In premix insulins the proportions of rapid acting and long acting insulins are fixed and do not allow for basal versus prandial dose adjustments.

Pharmacology:
• These insulins combine an intermediate-acting insulin with the more rapid onset of action of regular human insulin in a fixed ration (50% NPH, 50% regular). The onset of action ranges between 15 to 30 minutes and peaks 2 to 4 hours after the dose was administered although this
number varies widely between the different products marketed and patient utilization. Duration of action can be up to 24 hours.

**How Supplied:**

- Humulin 50/50 suspension 100units/mL (U-100) is available as
  - 10mL vials

**Dosage and Administration:**

- The dose of insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Should only be administered subcutaneously
- Administer approximately 30-45 minutes before a meal
- Rotate the vial between palms to mix before using a dose; do not shake

**Drug Interactions:**

- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
- The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

**Adverse Effects:**

- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
- Injection site reactions
- Lipodystrophy
- Pruritus
- Rash
- Weight gain
- Edema

**Precautions and Contraindications:**

- Do not use during episodes of hypoglycemia.
- All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
- Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
- Like all insulins, requirements may be reduced in patients with renal or hepatic impairment
Key advice to patients:

- Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
- Patient should be instructed on how to manage sick days or skipped meal.
- Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
- Store in refrigerator
- Product is stable for 28 days after initial use (may be kept at room temperature while using)
- Do not use if product has been frozen
- Should only be used if uniformly cloudy

C. HUMALOG 75/25

Indications:

- Premixed and fixed ratio of recombinant insulin indicated to improve glycemic control in adults with type 1 or type 2 diabetes.

Pharmacology:

- Humalog 75/25 combines a NPH insulin with a rapid-acting lispro in a ratio of 3 to 1. The onset of action range is about 15 minutes and peaks 1 to 4 hours after the dose was administered although this number varies widely between the different products marketed and patient utilization. Duration of action ranges between 18 and 24 hours. It has two phases of absorption. The early phase represents insulin lispro and its distinct characteristics of rapid onset. The late phase represents the prolonged action of insulin lispro protamine suspension. Humalog 75/25 has a similar glucose lowering effect as compared with Humulin 70/30 on a unit for unit basis.

How Supplied:

- Humalog 75/25 suspension 100units/mL (U-100) is available as
  - 10mL vials
  - 3mL prefilled pen (Humalog KwikPen Mix 75/25)

Dosage and Administration:

- The dose of insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Should only be administered subcutaneously
- Administer approximately 15 minutes before a meal
- Rotate the vial or pen between palms to mix before using a dose; do not shake

Drug Interactions:

- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
• Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
• The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
• The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

Adverse Effects:

• Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
• Injection site reactions
• Lipodystrophy
• Pruritus
• Rash
• Weight gain
• edema

Precautions and Contraindications:

• Do not use during episodes of hypoglycemia.
• All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
• Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
• Like all insulins, requirements may be reduced in patients with renal or hepatic impairment

Key advice to patients:

• Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
• Patient should be instructed on how to manage sick days or skipped meal.
• Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
• Store in refrigerator
• Product is stable for 28 days after initial use (may be kept at room temperature while using)
• Do not use if product has been frozen
• Should only be used if uniformly cloudy

D. NOVOLOG 70/30

Indications:

• Premixed and fixed ratio of recombinant insulin indicated to improve glycemic control in patients with type 1 or type 2 diabetes.
• In premix insulins the proportions of rapid acting and long acting insulins are fixed and do not allow for basal versus prandial dose adjustments.

Pharmacology:
NovoLog 70/30 combines a NPH insulin with a rapid-acting aspart. The onset of action range is between 10 and 20 minutes and peaks 1 to 4 hours after the dose was administered. Duration of action is up to 24 hours. The rapid absorption characteristics of NovoLog are maintained by NovoLog 70/30. The insulin aspart in the soluble component of the mix is absorbed more rapidly from the SC layers than regular human insulin. The remaining 70% is in crystalline form as NPH insulin which has a prolonged absorption profile.

**How Supplied:**

- NovoLog 70/30 suspension 100units/mL (U-100) is available as
  - 10mL vials
  - 3mL prefilled pen (NovoLog Mix 70/30 FlexPen)

**Dosage and Administration:**

- The dose of insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
- Should only be administered subcutaneously
- Type 1 DM: Administer approximately 15 minutes before a meal
- Type 2 DM: Administer dose within 15 minutes before or after starting a meal
- Rotate the vial or pen between palms to mix before using a dose; do not shake

**Drug Interactions:**

- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
- The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

**Adverse Effects:**

- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
- Injection site reactions
- Lipodystrophy
- Pruritus
- Rash
- Weight gain
- Edema

**Precautions and Contraindications:**
• Do not use during episodes of hypoglycemia.
• All insulin can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
• Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
• Like all insulins, requirements may be reduced in patients with renal or hepatic impairment

Key advice to patients:
• Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
• Patient should be instructed on how to manage sick days or skipped meal.
• Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
• Store in refrigerator
  • Product is stable for 28 days after initial use (may be kept at room temperature while using)
• Do not use if product has been frozen
• Should only be used if uniformly cloudy

E. RYZODEG 70/30

Indications:
• Premixed and fixed ratio of recombinant insulin indicated to improve glycemic control in adults with type 1 or type 2 diabetes.
• In premix insulins the proportions of rapid acting and long acting insulins are fixed and do not allow for basal versus prandial dose adjustments.
• Not recommended for treating diabetic ketoacidosis. Use intravenous, short-acting insulin instead.

Pharmacology:
• Ryzodeg 70/30 combines ultra-long-acting insulin degludec with rapid-acting insulin aspart. The onset of action is between 10-20 minutes and peaks 60-90 minutes after the dose is administered. The duration of action may extend beyond 24 hours. The rapid absorption characteristics of Ryzodeg are maintained by Ryzodeg 70/30. The insulin aspart in the soluble component of the mix is absorbed more rapidly from the SC layers than regular human insulin. The remaining 70% is in a multi-hexamer form as insulin degludec which has a prolonged absorption profile.

How Supplied:
• Ryzodeg 70/30 100 units/mL (U-100) is available as
  o 3mL FlexTouch disposable prefilled pen (package size of 5)

Dosage and Administration:
• The dose of insulin must be individualized depending on the patient’s goal blood glucose concentrations and HbA1C.
• Should only be administered subcutaneously
• Administer once or twice daily with many main meal
• Rotate injection sites within an injection area to reduce the risk of lipodystrophy
**Drug Interactions:**

- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- The use of insulin with rosiglitazone is not recommended by the manufacturer of rosiglitazone due to a significant increase in the risk for heart failure or edema. Pioglitazone should be used cautiously.
- Certain drugs may affect glucose metabolism and may necessitate dosage adjustments of insulin
- The following may increase susceptibility to hypoglycemia: oral antidiabetic agents, pramlintide, ACE inhibitors, fibrates, fluoxetine, monoamine oxidase inhibitors, salicylates, sulfonamide antibiotics.
- The following may reduce the blood-glucose lowering effect: corticosteroids, niacin, diuretics, sympathomimetic agents, isoniazid, somatropin, thyroid hormones, estrogens, oral contraceptives and atypical antipsychotics.

**Adverse Effects:**

- Hypoglycemia is the most common adverse effects associated with insulin use and may be life-threatening.
- Injection site reactions
- Lipodystrophy
- Pruritus
- Rash
- Weight gain
- Edema

**Precautions and Contraindications:**

- Do not use during episodes of hypoglycemia.
- Use during pregnancy only if the potential benefit justifies the potential risk to the fetus
- All insulins can cause hypokalemia, which if untreated, may result in respiratory paralysis, ventricular arrhythmia and death; Use caution in patients predisposed to hypokalemia
- Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
- Like all insulins, requirements may be reduced in patients with renal or hepatic impairment
- Ryzodeg 70/30 should not be diluted or mixed with any other insulin
- Do not administer via an insulin pump or intravenously because severe hypoglycemia can occur
- Has not been studied in children with type 1 or type 2 diabetes

**Key advice to patients:**

- Patients should be instructed on self-management of their disease including glucose monitoring, proper injection technique as well as management of hypoglycemia and hyperglycemia.
- Patient should be instructed on how to manage sick days or skipped meal.
- Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded.
- Ryzodeg 70/30 FlexTouch disposable prefilled pen should only be used if the solution is clear and colorless with no visible particles
- Unopened Ryzodeg 70/30 FlexTouch disposable prefilled pen should be stored in a refrigerator (36°F-46°F or 2°C-8°C).
- Opened (in-use) Ryzodeg 70/30 FlexTouch disposable prefilled pen should not be refrigerated, but should be kept at room temperature (below 86°F or 30°C) away from direct heat and sunlight.
- Product is stable for up to 28 days (4 weeks) after initial use, if it is kept at room temperature.
- Do not use if product has been frozen.