### 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>Ultra Rapid-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technosphere insulin</td>
<td>Afrezza</td>
<td>1-2 min</td>
<td>15-20 min</td>
<td>2 – 2 ½ hrs</td>
<td>Inhaled through the mouth and absorbed via the lungs. Meal time insulin to prevent post meal spikes. Can be used in both type 1 and type 2 diabetes; can be used alone in type 2s with meals and with basal insulin (injectable or via pump) for both type 1 and type 2.</td>
</tr>
<tr>
<td><strong>Rapid-Acting</strong></td>
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<td></td>
</tr>
<tr>
<td>lispro</td>
<td>Humalog</td>
<td>15-30 min</td>
<td>30-90 min</td>
<td>3-6 hrs</td>
<td>Taken by injection via an insulin vial and syringe, insulin pen, or insulin pump. Used as meal time insulin to prevent post meal spikes, and/or to correct high glucose levels. Take at the same time or within 10 minutes before eating. Can be used alone in type 2s with meals, and with basal for both type1 and type 2. *Cannot be mixed in same syringe/pen with Long-Acting insulins.</td>
</tr>
<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>3-4 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Short-Acting</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<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>Regular insulin is taken by injection via an insulin vial and syringe. Used as meal time insulin to prevent post meal spikes, and/or to correct high glucose levels. Take 30 – 60 minutes before eating. Can be used alone in type 2s with meals, and with basal insulin for both type1 and type 2. *Cannot be mixed in same syringe/pen with Long-Acting insulins.</td>
</tr>
<tr>
<td></td>
<td>Novolin R</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular insulin (concentrated)</td>
<td>Humulin R U-500</td>
<td>30 min</td>
<td>2.5 hours</td>
<td>Up to 24 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Intermediate-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPH insulin</td>
<td>Humulin N</td>
<td>2-4 hrs</td>
<td>4-12 hrs</td>
<td>12-18 hrs</td>
<td>Taken by injection via an insulin vial and syringe or insulin pen. Intermediate acting insulin covers basal insulin needs for about half the day or overnight. It is often used in combination with rapid or short acting insulin.</td>
</tr>
<tr>
<td></td>
<td>Novolin N</td>
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<td></td>
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<tr>
<td><strong>Long-Acting</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>glargine</td>
<td>Lantus</td>
<td>1-1 ½ hrs</td>
<td>No peak; insulin is delivered at</td>
<td>20-24 hrs</td>
<td>Taken by injection via an insulin vial and syringe or insulin pen. Long-acting insulin covers basal insulin needs for a</td>
</tr>
<tr>
<td>detemir</td>
<td>Levemir</td>
<td>1-2 hrs</td>
<td></td>
<td>Up to 24 hrs</td>
<td></td>
</tr>
</tbody>
</table>
a steady level

full day. Can be used alone in type 2 diabetes, or with an ultra-rapid, rapid or short acting insulin in type 1s and type 2s.

*It is never to be mixed with other types of insulins in the same syringe or pen.

<table>
<thead>
<tr>
<th>Pre-Mixed or Combination</th>
<th>Brand Name</th>
<th>Onset Time</th>
<th>Peak Time</th>
<th>Duration</th>
<th>Taken by injection via vial and insulin syringe or insulin pen.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Insulin Isophane suspension + regular human insulin injection</td>
<td>Humulin 70/30</td>
<td>30 min</td>
<td>2-4 hrs</td>
<td>14-24 hrs</td>
<td>Taken by injection via vial and insulin syringe or insulin pen.</td>
</tr>
<tr>
<td></td>
<td>Novolin 70/30</td>
<td>30 min</td>
<td>2 ½ hrs</td>
<td>Up to 24 hrs</td>
<td></td>
</tr>
<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>Insulin lispro protamine suspension + insulin lispro injection</td>
<td>Humalog 50/50</td>
<td>15-30 min</td>
<td>45-120 min</td>
<td>12-24 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Humalog 75/25</td>
<td>15 min</td>
<td>30 min – 2</td>
<td>16-20 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>½ hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin aspart protamine suspension + insulin aspart</td>
<td>NovoLog 70/30</td>
<td>10-20 min</td>
<td>1-4 hrs</td>
<td>18-24 hrs</td>
<td></td>
</tr>
</tbody>
</table>

*These products are a combination of intermediate and rapid or short acting insulin in one vial 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, depending on the type of mealtime insulin.
**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. Insulins are categorized based on the onset, peak, and duration of effect.

**ULTRA RAPID-ACTING INSULINS**

**A. AFREZZA (technosphere insulin)**

**Indications:**

- Afrezza is an inhaled, very rapid acting human insulin indicated to improve prandial glycemic control in adults with type 1 or type 2 diabetes. Most type 2 patients lack first phase insulin release so Afrezza should be an ideal insulin for newly diagnosed type 2 patients. It can also be used with a long-acting basal insulin to treat type 1 and type 2 patients who need a basal-bolus regimen.

**Pharmacology:**

- Afrezza is unique in that it is administered by oral inhalation directly into the lungs which avoids having to inject insulin subcutaneously. Afrezza is designed to be absorbed immediately after inhalation and peaks within 15 minutes. It has a much shorter duration of activity and is out of the body in terms of effect quickly thereby decreasing the incidence of hypoglycemia (low blood sugars). Afrezza should be given right before or during the meal.

**How Supplied:**

- Afrezza 100 units (U-100) is available as
  - Cartridges with 4 units of insulin or 8 units of insulin with an inhalation device called a Dreamboat
Dosage and Administration:

- Afrezza should only be administered via oral inhalation using the Dreamboat Device. For doses exceeding 8 units, inhalations from multiple cartridges are necessary.
- Afrezza can be used to administer a correction dose if the patient’s blood glucose level is too high.
- Administer within 15 minutes before a meal or immediately after a meal. Can adjust insulin dose to the amount of carbohydrates eaten.
- The cartridges and inhaler should be kept at room temperature for 10 minutes prior to use; storage in refrigerator is recommended.

Drug Interactions:

- Fluid retention and heart failure can occur with concomitant use of thiazolidinediones (TZDs)
- The signs of hypoglycemia may be masked in patients taking anti-adrenergic drugs (beta-blockers, clonidine, guanethidine, and reserpine)
- 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.
- Bronchodilators and inhaled steroids

Adverse Effects:

- Acute bronchospasm has been observed in patients with asthma and COPD
- Hypoglycemia is the most common adverse reaction associated with insulin use and may be life threatening. An advantage of Afrezza is that there is less hypoglycemia than with other rapid-acting insulins.
- Cough is a common side effect when patients first begin to use the product. This effect usually diminishes with continued use.
- Throat irritation
- Weight gain occurs with the use of most insulins but slightly less so with Afrezza

Precautions and Contraindications:

- Before starting Afrezza, a medical history, physical exam and spirometry (FEV1) should be performed in all patients to identify potential lung disease.
- Contraindicated in smokers and patients with Asthma or Chronic Obstructive Pulmonary Disease. Black Box Warning required by the FDA alerting to the possibility of acute bronchospasm and avoidance of use in Asthma and COPD.
- 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)
Afrezza has not been studied in patients younger than 18 years of age
Pregnancy Category C

Key Advice for Patients:

- Patients should be instructed on self-management of their disease including glucose monitoring, proper inhalation technique as well as management of hypoglycemia and hyperglycemia.
- Patient should be instructed on how to manage sick days or skipped meals.
- Inhaler cartridges should be refrigerated
- Before use, cartridges and inhaler should be at room temperature for 10 minutes
- The package insert for Afrezza will soon be available at www.afrezza.com

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 6 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
    - Avg. Retail Price: $221.00
  - 3mL vials
    - Avg. Retail Price: $66.35
  - 3mL cartridges
    - Avg. Retail Price: $82.22
  - 3mL pre-filled pen (Humalog Kwik-Pen)
    - Avg. Retail Price: $85.46 per pen (300 units)
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.
- 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.
- 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 within 15 minutes prior to or immediately after a meal due to its rapid onset.

How Supplied:
• NovoLog 100units/mL (U-100) is available as
  o 10mL vials
    • Avg. Retail Price: $221.00
  o 3mL cartridges
  o 3mL NovoLog FlexPen
    • Avg. Retail Price: $86.00 per pen (300 units)
  o 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.
- 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, 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 3-4 hours. Concentrations are higher after abdominal administration than those following deltoid or thigh injections. Apidra should be given within 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
    - Avg. Retail Price: $188.11
  - 3mL SoloStar prefilled syringe
    - Avg. Retail Price: $72.63 per pen (300 units)

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.
- Injection site reactions
- Lipodystrophy
- Pruritus
- Rash
- Weight gain
- Edema

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
  - Avg. Retail Price: $119.58
- Humulin R 100units/mL (u-100) is available as 10mL vials
  - Avg. Retail Price: $115.00

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.
- 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 effect 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
• 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.

***Walmart carries its own brand of short-acting insulin that is $25.00 for a 10mL vial***

http://www.relion.com/diabetes/insulin

B. HUMULIN R U-500 (CONCENTRATED)

Indications:

• Humulin R U-500 is indicated as an adjunct to diet and exercise to improve glycemic control in adults and children with type 1 diabetes.
• Humulin R U-500 is useful for the treatment of insulin resistant patients with diabetes requiring daily doses of more than 200 units.

Pharmacology:
- Humulin R U-500 contains 500 units of insulin in each milliliter making it 5 times more concentrated than Humulin R U-100. Humulin R U-500 takes effect within 30 minutes, has a peak similar to that observed with U-100 regular human insulin and has a relatively long duration of action following a single dose (up to 24 hours) as compared with U-100 insulins.

**How Supplied:**

- Humulin R 500 units/mL (U-500) is available as
  - 20mL vials
    - Avg. Retail Price: $1197.60

**Dosage and Administration:**

- Humulin R U-500 is usually given two or three times daily before meals. Dosage and timing will be individualized to the patient but a meal should follow within 30 minutes of administration.
- Humulin R U-500 should not be mixed with other insulins, as there are no data to support such use.
- It is extremely important that the patient understand the amount of insulin to be injected as normal syringes are marked in units and intended for U-100 insulin. The following table contains conversion information using both U-100 insulin and tuberculin syringes to help avoid dose confusion.

<table>
<thead>
<tr>
<th>Humulin R U-500 dose (units)</th>
<th>U-100 insulin syringe (unit markings)</th>
<th>Tuberculin syringe (volume in mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>5</td>
<td>0.05</td>
</tr>
<tr>
<td>50</td>
<td>10</td>
<td>0.1</td>
</tr>
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<td>75</td>
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<tr>
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</table>

- For doses other than those listed above refer to the following formulas:
  - U-100 insulin syringe:
    - Divide prescribed dose (actual units) by 5 = Unit markings in a U-100 insulin syringe
  - Tuberculin syringe:
• Divide prescribed dose (actual units) by 500 = volume (mL) in a tuberculin syringe
• Here are some guidelines from the National Institutes of Health:

<table>
<thead>
<tr>
<th>If patient needs:</th>
<th>Use:</th>
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<tbody>
<tr>
<td>less than 200 units a day</td>
<td>Humulin R U-100</td>
</tr>
<tr>
<td>200-300 units a day</td>
<td>Humulin R U-500 BID</td>
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<tr>
<td>300-750 units a day</td>
<td>Humulin R U-500 TID</td>
</tr>
<tr>
<td>750-2,000 units a day</td>
<td>Humulin R U-500 TID plus a 4th dose at bed time</td>
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</table>

• If a new patient says they are taking Humulin R….we need to be sure which one we are talking about.

**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.
• Injection site reactions
• Lipodystrophy
• Pruritus
• Rash
• Weight gain
• Edema

**Precautions and Contraindications:**

• **Humulin R U-500 is highly concentrated and contains 5 times as much insulin in 1mL as standard U-100 (100 units/mL) insulin.**
• 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
- Humulin R U-500 should not be mixed with any other insulin.

**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 31 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; Humulin R U-500 should look clear and colorless.

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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
    - Avg. Retail Price: $119.00
- Humulin N 100units/mL (u-100) is available as
  - 10mL vials
    - Avg. Retail Price: $119.00
  - 3mL vials
  - 3mL prefilled pens (Humulin N KwikPen)
    - Avg. Retail Price: $76.00 per pen (300 units)
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
- 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
- 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.

***Walmart has its own brand of NPH insulin for $25.00 for a 10mL vial***

http://www.relion.com/diabetes/insulin

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
  o 10mL vial
    • Avg. Retail Price: $266.00
  o 3mL SoloStar pen
    • Avg. Retail Price: $80.00 per pen (300 units)

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. 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
  - 10 mL vial
    - Avg. Retail Price: $266.00
  - 3 mL prefilled pen (FlexPen)
    - Avg. Retail Price: $80.00 per pen (300 units)
  - 3 mL 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 B: 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
- Levemir 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.
- Levemir 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

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
  o 10mL vials
    ▪ Avg. Retail Price: $119.00
  o 3mL vials
  o 3mL prefilled pens (Humulin 70/30 KwikPen)
    ▪ Avg. Retail Price: $76.00 per pen (300 units)
• Novolin 70/30 suspension 100u/mL (U-100) is available as
  o 10mL vials
    ▪ Avg. Retail Price: $119.00

***Walmart has its own brand of 70/30 insulin that is $25.00 for a 10mL vial***

http://www.relion.com/diabetes/insulin

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.
• 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
  - Avg. Retail Price: $119.00

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 50/50

Indications:

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

Pharmacology:

- Humalog 50/50 is a mixture of insulin lispro solution (50%), a rapid acting blood glucose lowering agent and insulin lispro protamine suspension (50%), an intermediate acting blood glucose lowering agent. Humalog 50/50 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. Onset of action is 50-30 minutes and peak serum concentrations are seen 45 to 120 minutes after dose was administered. Duration of action is anywhere from 12 to 24 hours depending on the patient. Direct comparison of Humalog 50/50 and Humulin 50/50 was not performed. However, a cross study comparison suggests that Humalog 50/50 has a more rapid absorption than Humulin 50/50 while having a similar duration of action.

How Supplied:

- Humalog 50/50 suspension 100units/mL (U-100) is available as
  - 10mL vials
    - Avg. Retail Price: $229.20
  - Pre-filled Pen for injection (Humalog Kwikpen Mix 50/50)
    - Avg. Retail Price: $85.46 per pen (3mL)

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.

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 100 units/mL (U-100) is available as
  - 10mL vials
    - Avg. Retail Price: $229.00
  - 3mL prefilled pen (Humalog KwikPen Mix 75/25)
    - Avg. Retail Price: $85.46 per pen (3mL)

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
    - Avg. Retail Price: $230.10
  - 3mL prefilled pen (NovoLog Mix 70/30 FlexPen)
    - Avg. Retail Price: $85.70 per pen (300 units)

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

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