HUMALOG® insulin lispro injection, solution
REMEDIYPACK INC.

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

HUMALOG (insulin lispro), for subcutaneous or intravenous use

Initial U.S. Approval: 1996

INDICATIONS AND USAGE
HUMALOG is a rapid acting human insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus.

DOSAGE AND ADMINISTRATION

See full prescribing information for important administration instructions. (2.1, 2.2, 2.3, 2.4)

Subcutaneous injection: Administer HUMALOG® U-100 or U-200 by subcutaneous injection within 15 minutes before a meal or immediately after a meal. (2.2)

Continuous subcutaneous infusion (Insulin Pump): Administer HUMALOG U-100 by continuous subcutaneous infusion using an insulin pump. DO NOT administer HUMALOG U-200 by continuous subcutaneous infusion. (2.2)

Infusion infusion: Administer HUMALOG U-100 by intravenous infusion ONLY after dilution and under medical supervision. DO NOT administer HUMALOG U-200 by intravenous infusion. (2.2)

The dosage of HUMALOG must be individualized based on the route of administration and the individual's metabolic needs, blood glucose monitoring results and glycemic control goal. (2.3)

Do not perform dose conversion when using the HUMALOG U-100 or U-200 KwikPens. The dose window shows the number of insulin units to be delivered and no conversion is needed. (2.1, 2.3)

Do not mix HUMALOG U-200 with any other insulin. (2.4)

DOSAGE FORMS AND STRENGTHS

HUMALOG 100 units/mL (U-100) is available as: (3)

- 10 mL vial
- 3 mL vial

HUMALOG 200 units/mL (U-200) is available as: (3)

- 3 mL Humalog KwikPen® (prefilled)
- 3 mL Humalog® Junior KwikPen® (prefilled)
- 3 mL cartridges

HUMALOG 200 units/mL (U-200) is available as: (3)

- 3 mL Humalog® (prefilled)

CONTRAINDICATIONS

Do not use during episodes of hypoglycemia. (4)

Do not use in patients with hypersensitivity to HUMALOG or any of its excipients. (4)

WARNINGS AND PRECAUTIONS

Never share a HUMALOG KwikPen, cartridge, reusable pen compatible with Lilly 3 mL cartridges, or syringe between patients, even if the needle is changed. (5.1)

Hyper- or Hypoglycemia with Changes in Insulin Regimen: Carry out under close medical supervision and increase frequency of blood glucose monitoring. (5.2)

Hypoglycemia: May be life-threatening. Monitor blood glucose and increase monitoring frequency with changes to insulin dosage, use of glucose lowering medications, meal pattern, physical activity; in patients with renal or hepatic impairment; and in patients with hypoglycemia unawareness. (5.3, 5.4, 5.7, 5.8)

Hyperglycemia Due to Medication Errors: Accidental mix-ups between insulin products can occur. Instruct patients to check insulin labels before injection. Do not transfer HUMALOG U-200 from the HUMALOG KwikPen to a syringe as overdose and severe hypoglycemia can result. (5.4)

Hypersensitivity Reactions: May be life-threatening. Discontinue HUMALOG, monitor and treat if indicated. (5.5)

Hypokalemia: May be life-threatening. Monitor potassium levels in patients at risk of hypokalemia and treat if indicated. (5.5)

Fluid Retention and Heart Failure with Concomitant Use of Thiazolidinediones (TZDs): Observe for signs and symptoms of heart failure; consider dosage reduction or discontinuation if heart failure occurs. (5.7)

Hyperglycemia and Atherosclerotic Disease Due to Insulin Pump Device Malfunction: Monitor glucose and administer HUMALOG U-100 by subcutaneous injection if pump malfunction occurs. (5.8)

ADVERSE REACTIONS

Adverse reactions associated with HUMALOG include hypoglycemia, allergic reactions, injection site reactions, lipodystrophy, pruritus, and rash. (5.1)

To report SUSPECTED ADVERSE REACTIONS, contact Eli Lilly and Company at 1-800-LillyRX (1-800-545-5979) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Drugs that Affect Glucose Metabolism: Adjustment of insulin dosage may be needed. (5.2, 5.3, 5.7, 5.8)

Anti-Adrenergic Drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine): Monitor blood glucose and increase monitoring frequency with changes to insulin dosage, use of glucose lowering medications, meal pattern, physical activity; in patients with renal or hepatic impairment; and in patients with hypoglycemia unawareness. (5.3, 5.4, 5.7, 5.8)

Drugs that May Increase the Risk of Hypoglycemia: Monitor blood glucose and increase monitoring frequency with changes to insulin dosage, use of glucose lowering medications, meal pattern, physical activity; in patients with renal or hepatic impairment; and in patients with hypoglycemia unawareness. (5.4)

Drugs that May Decrease the Blood Glucose Lowering Effect of HUMALOG: Monitor blood glucose and increase monitoring frequency with changes to insulin dosage, use of glucose lowering medications, meal pattern, physical activity; in patients with renal or hepatic impairment; and in patients with hypoglycemia unawareness. (5.5)

Drugs that May Increase or Decrease the Blood Glucose Lowering Effect of HUMALOG: Monitor blood glucose and increase monitoring frequency with changes to insulin dosage, use of glucose lowering medications, meal pattern, physical activity; in patients with renal or hepatic impairment; and in patients with hypoglycemia unawareness. (5.5)

Drugs that May Blunt Signs and Symptoms of Hypoglycemia: Monitor blood glucose and increase monitoring frequency with changes to insulin dosage, use of glucose lowering medications, meal pattern, physical activity; in patients with renal or hepatic impairment; and in patients with hypoglycemia unawareness. (5.6)

USE IN SPECIFIC POPULATIONS

Pediatric: Not studied in children with type 2 diabetes or in children with type 1 diabetes <3 years of age. (6.1)

See 17 for PATIENT COUNSELING INFORMATION, FDA-approved patient labeling and FDA-approved patient labeling. Revised: 8/2019
FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
HUMALOG is a rapidacting human insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus.

2 DOSAGE AND ADMINISTRATION
2.1 Important Administration Instructions
- Always check insulin labels before administration [see Warnings and Precautions (5.4)].
- Inspect HUMALOG visually before use. It should appear clear and colorless. Do not use HUMALOG if particulate matter or coloration is seen.
- Use HUMALOG KwikPens with caution in patients with visual impairment that may rely on audible clicks to dial their dose.
- Do NOT mix HUMALOG U-100 with other insulins when administering using a continuous subcutaneous infusion pump.
- Do NOT transfer HUMALOG U-200 from the KwikPen to a syringe for administration [see Warnings and Precautions (5.4)].
- Do NOT perform dose conversion when using any HUMALOG U-100 or U-200 KwikPens. The dose window shows the number of insulin units to be delivered and no conversion is needed.
- Do NOT mix HUMALOG U-200 with any other insulins.
- Do NOT administer HUMALOG U-200 using a continuous subcutaneous infusion pump (i.e., insulin pump).
- Do NOT administer HUMALOG U-200 intravenously.

2.2 Route of Administration
Subcutaneous Injection: HUMALOG U-100 or U-200
- Administer the dose of HUMALOG U-100 or HUMALOG U-200 within fifteen minutes before a meal or immediately after a meal by injection into the subcutaneous tissue of the abdominal wall, thigh, upper arm, or buttocks. To reduce the risk of lipodystrophy, rotate the injection site within the same region from one injection to the next [see Adverse Reactions (6)].
- HUMALOG administered by subcutaneous injection should generally be used in regimens with an intermediate- or long-acting insulin.
- The HUMALOG U-100 KwikPen and HUMALOG U-200 KwikPen each dial in 1 unit increments.

Continuous Subcutaneous Infusion (Insulin Pump): HUMALOG U-100 ONLY
- Do NOT administer HUMALOG U-200 using a continuous subcutaneous infusion pump.
- Administer HUMALOG U-100 by continuous subcutaneous infusion into the subcutaneous tissue of the abdominal wall. Rotate infusion sites within the same region to reduce the risk of lipodystrophy [see Adverse Reactions (6.1)].
- Follow healthcare professional recommendations when setting basal and meal time infusion rate.
- Do NOT dilute or mix HUMALOG U-100 when administering by continuous subcutaneous infusion.
- Change HUMALOG U-100 in the pump reservoir at least every 7 days.
- Change the infusion set and the infusion set insertion site at least every 3 days.
- Do NOT expose HUMALOG U-100 in the pump reservoir to temperatures greater than 98.6°F (37°C).
- Use HUMALOG U-100 in pump systems suitable for insulin infusion [see Patient Counseling Information (17.7)].

Intravenous Administration: HUMALOG U-100 ONLY
- Do NOT administer HUMALOG U-200 intravenously.
- Dilute HUMALOG U-100 to concentrations from 0.1 unit/mL to 1.0 unit/mL using 0.9% sodium chloride.
- Administer HUMALOG U-100 intravenously only under medical supervision with close monitoring of blood glucose and potassium levels to avoid hypoglycemia and hypokalemia [see Warnings and Precautions (5.3, 5.5), and How Supplied/Storage and Handling (16.4)].

2.3 Dosage Information
- Individualize and adjust the dosage of HUMALOG based on route of administration, the individual’s metabolic needs, blood glucose monitoring results and glycemic control goal.
- Dosage adjustments may be needed with changes in physical activity, changes in meal pattern (i.e., macronutrient content or timing of food intake), changes in renal or hepatic function or during acute...
2.4 Dosage Adjustment Due to Drug Interactions

- Dosage adjustment may be needed when HUMALOG is coadministered with certain drugs (see Drug Interactions (7)).
- Dosage adjustment may be needed when switching from another insulin to HUMALOG (see Warnings and Precautions (5.2)).
- Instructions for Mixing with Other Insulins

| HUMALOG U-100 subcutaneous injection route | HUMALOG U-100 may be mixed with NPH insulin preparations ONLY.
| HUMALOG U-100 continuous subcutaneous infusion route (Insulin Pump) | Do NOT mix HUMALOG U-100 with any other insulin.
| HUMALOG U-200 subcutaneous injection route | Do NOT mix with any other insulin.

3 DOSAGE FORMS AND STRENGTHS

HUMALOG 100 units per mL (U-100) is available as:
- 10 mL vials
- 3 mL vials
- 3 mL Humalog KwikPen (prefilled)
- 3 mL Humalog Junior KwikPen (prefilled)
- 3 mL cartridges

HUMALOG 200 units per mL (U-200) is available as:
- 3 mL Humalog KwikPen (prefilled)

4 CONTRAINDICATIONS

HUMALOG is contraindicated:
- during episodes of hypoglycemia
- in patients who are hypersensitive to HUMALOG or to any of its excipients.

5 WARNINGS AND PRECAUTIONS

5.1 Never Share a HUMALOG KwikPen, Cartridge, Reusable Pen Compatible with Lilly 3 mL Cartridges 1, or Syringe Between Patients

HUMALOG KwikPen, cartridges, and reusable pens compatible with Lilly 3 mL cartridges must never be shared between patients, even if the needle is changed. Patients using HUMALOG vials must never share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens.

5.2 Hyper- or Hypoglycemia with Changes in Insulin Regimen

Changes in insulin strength, manufacturer, type, or method of administration may affect glycemic control and predispose to hypoglycemia (see Warnings and Precautions (5.3)) or hyperglycemia. These changes should be made cautiously and under close medical supervision and the frequency of blood glucose monitoring should be increased.

5.3 Hypoglycemia

Hypoglycemia is the most common adverse reaction associated with insulin, including HUMALOG. Severe hypoglycemia can cause seizures, may be life-threatening, or cause death. Hypoglycemia can impair concentration ability and reaction time; this may place an individual and others at risk in situations where these abilities are important (e.g., driving or operating other machinery).

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

Risk Factors for Hypoglycemia

The risk of hypoglycemia after an injection is related to the duration of action of the insulin and, in general, is highest when the glucose lowering effect of the insulin is maximal. As with all insulin preparations, the glucose lowering effect time course of HUMALOG may vary in different individuals or at different times in the same individual and depends on many conditions, including the area of injection as well as the injection site blood supply and temperature (see Clinical Pharmacology (12.2)). Other factors which may increase the risk of hypoglycemia include changes in meal pattern (e.g., macronutrient content or timing of meals), changes in level of physical activity, or changes to co-administered medication (see Drug Interactions (7)). Patients with renal or hepatic impairment may be at higher risk of hypoglycemia (see Use in Specific Populations (8.6, 8.7)).

Risk Mitigation Strategies for Hypoglycemia

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

5.4 Hypoglycemia Due to Medication Errors

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

Do not transfer HUMALOG U-200 from the HUMALOG KwikPen to a syringe. The markings on the insulin syringe will not measure the dose correctly and can result in overdosage and severe hypoglycemia (see Dosage and Administration (2.1) and Warnings and Precautions (5.3)).

5.5 Hypersensitivity Reactions

Severe, life-threatening, generalized allergy, including anaphylaxis, can occur with insulin products, including HUMALOG. If hypersensitivity reactions occur, discontinue HUMALOG; treat per standard of care and monitor until symptoms and signs resolve (see Adverse Reactions (6.1)). HUMALOG is contraindicated in patients who have had hypersensitivity reactions to HUMALOG or any of its excipients (see Contraindications (4)).
5.6 Hypokalemia
All insulin products, including HUMALOG, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Untreated hypokalemia may cause respiratory paralysis, ventricular arrhythmia, and death. Monitor potassium levels in patients at risk for hypokalemia if indicated (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentrations).

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

5.8 Hyperglycemia and Ketosis Due to Insulin Pump Device Malfunction
Malfunction of the insulin pump or insulin infusion set or insulin degradation can rapidly lead to hyperglycemia and lactic acidosis. Prompt identification and correction of the cause of hyperglycemia or lactic acidosis is necessary. Interruption and reinitiation of insulin pump therapy must be trained to administer insulin by injection or via the insulin pump. Patients using continuous subcutaneous insulin infusion pump therapy must be trained to administer insulin by injection and have alternate insulin therapy available in case of pump failure (see How Supplied/Storage and Handling (16.2) and Patient Counseling Information (17.7)).

6 ADVERSE REACTIONS
Observed with HUMALOG U-100
The following adverse reactions are discussed elsewhere:
- Hypoglycemia (see Warnings and Precautions (5.3)),
- Hypokalemia (see Warnings and Precautions (5.6)).

6.1 Clinical Trial Experience
Because clinical trials are conducted under widely varying design, the adverse reaction rates reported in one clinical trial may not be easily compared with those rates reported in another clinical trial, and may not reflect the rates actually observed in clinical practice.
The frequencies of Treatment-Emergent Adverse Events during HUMALOG clinical trials in patients with type 1 diabetes mellitus and type 2 diabetes mellitus are listed in the tables below.

<table>
<thead>
<tr>
<th>Table 1: Treatment-Emergent Adverse Events in Patients with Type 1 Diabetes Mellitus (adverse events with frequency ≥5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Flu syndrome</td>
</tr>
<tr>
<td>Pharyngitis</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Cough increased</td>
</tr>
<tr>
<td>Infection</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Urinary tract infection</td>
</tr>
<tr>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Asthenia</td>
</tr>
<tr>
<td>Bronchitis</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Dysmenorrhea</td>
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<tr>
<td>Myalgia</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2: Treatment-Emergent Adverse Events in Patients with Type 2 Diabetes Mellitus (adverse events with frequency ≥5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Infection</td>
</tr>
<tr>
<td>Pharyngitis</td>
</tr>
<tr>
<td>Rhinitis</td>
</tr>
<tr>
<td>Flu syndrome</td>
</tr>
<tr>
<td>Urinary tract infection</td>
</tr>
</tbody>
</table>

**Insulin Initiation and Intensification of Glucose Control**

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

**Lipodystrophy**

Long-term use of insulin, including HUMALOG, can cause lipodystrophy at the site of repeated insulin injections or infusion. Lipodystrophy includes lipoatrophy (thinning of adipose tissue) and lipohypertrophy (thickening of adipose tissue), and may affect insulin absorption. Rotate insulin injection or infusion sites within the same region to reduce the risk of lipodystrophy (see Dosage and Administration (2.2)).

**Weight gain**

Weight gain can occur with insulin therapy, including HUMALOG, and has been attributed to the anabolic effects of insulin and the decrease in glucosuria.

**Peripheral Edema**

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

**Adverse Reaction with Continuous Subcutaneous Insulin Infusion (CSI) - HUMALOG U-100**

In a 12-week, randomized, crossover study in adult patients with type 1 diabetes (n=39), the rates of catheter occlusions and infusion site reactions were similar for HUMALOG U-100 and regular human insulin treated patients (see Table 3).
In an embryo-fetal development study in pregnant rabbits, insulin lispro doses of 0.1, 0.25, and 1 unit/kg/day were used. The 0.1 and 0.25 units/kg/day doses had no effect on fetal development. However, the 1 unit/kg/day dose caused decreased fetal weight and an increased incidence of fetal runts/litter. Although there are limited clinical studies of the use of HUMALOG in pregnancy, published studies with human insulin suggest that optimizing overall glycemic control, including postprandial control, before conception and during pregnancy improves fetal outcome.

Although there are limited clinical studies of the use of HUMALOG in pregnancy, published studies with human insulin suggest that optimizing overall glycemic control, including postprandial control, before conception and during pregnancy improves fetal outcome. In a combined fertility and embryo-fetal development study, female rats were given subcutaneous insulin lispro injections of 5 and 20 units/kg/day (0.8 and 3 times the human subcutaneous dose of 1 unit/kg/day, respectively). There were no adverse effects on female fertility, implantation, or fetal viability and no evidence for malformation. In a randomized, 16-week, open-label, parallel design study of children and adolescents with type 1 diabetes, adverse event rates related to infusion-site reactions were similar for insulin lispro and insulin aspart (21% of 100 patients versus 17% of 198 patients, respectively). In both groups, the most frequently reported infusion-site adverse events were infusion site erythema and infusion site reaction.
The mean blood glucose levels during the assessment phase for patients on HUMALOG therapy are summarized below in intervals to achieve and maintain blood glucose concentrations between 100 to 160 mg/dL. During the assessment phase, patients received intravenous HUMALOG at an initial infusion rate of 0.5 units/hour. The infusion rate of HUMALOG could be adjusted at regular timed intervals to achieve and maintain blood glucose concentrations between 200 to 260 mg/dL during a one to three hours run-in phase. The run-in phase was followed by a 6-hour assessment phase. During the assessment phase, patients received intravenous HUMALOG at an initial infusion rate of 0.5 units/hour. The infusion rate of HUMALOG could be adjusted at regular timed intervals to achieve and maintain blood glucose concentrations between 200 to 260 mg/dL during a one to three hours run-in phase. The run-in phase was followed by a 6-hour assessment phase. During the assessment phase, patients received intravenous HUMALOG at an initial infusion rate of 0.5 units/hour.

Table 4: Mean Blood Glucose Concentrations (mg/dL) During Intravenous Infusions of HUMALOG U-100

<table>
<thead>
<tr>
<th>Time from Start of Infusion (minutes)</th>
<th>Mean Blood Glucose (mg/dL) Intravenous ⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>224 ± 16</td>
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</table>
with type 1 diabetes (n=789) and adult patients with type 2 diabetes (n=722). The safety and efficacy of HUMALOG U-100 were studied in children, adolescent, and adult patients with type 2 diabetes.

11 CLINICAL STUDIES

In standard biological assays in fasted rabbits, 0.2 unit/kg of insulin lispro injected subcutaneously had a faster time to maximum glucose lowering effect than 0.1 unit/kg of regular human insulin (1 versus 1.5 hours, respectively). When administered intravenously, HUMALOG and regular human insulin demonstrated similar dose-dependent clearance, with a mean clearance of 23.0 mL/min/kg and 21.4 mL/min/kg, respectively (0.1 unit/kg dose), and 9.6 mL/min/kg and 9.4 mL/min/kg, respectively (0.2 unit/kg dose). Accordingly, HUMALOG demonstrated a mean 1/2 time to maximum effect of 0.85 hours (51 minutes) and 0.92 hours (55 minutes), respectively for 0.1 unit/kg and 0.2 unit/kg doses, and regular human insulin mean 1/2 time to maximum effect of 0.79 hours (47 minutes) and 1.28 hours (77 minutes), respectively for 0.1 unit/kg and 0.2 unit/kg doses.

Specific Populations

The effects of age, gender, race, obesity, pregnancy, or smoking on the pharmacokinetics of HUMALOG have not been studied.

Renal Impairment — Type 2 diabetic patients with varying degree of renal impairment showed no difference in pharmacokinetics of regular insulin and HUMALOG. However, the sensitivity of the patients to insulin did change, with an increased response to insulin as the renal function declined. Some studies with human insulin have shown increased circulating levels of insulin in patients with renal impairment. Careful glucose monitoring and dose adjustments of insulin, including HUMALOG, may be necessary in patients with renal dysfunction.

Hepatic Impairment — Type 2 diabetic patients with impaired hepatic function showed no effect on the pharmacokinetics of HUMALOG as compared to patients with no hepatic dysfunction. However, some studies with human insulin have shown increased circulating levels of insulin in patients with liver failure. Careful glucose monitoring and dose adjustments of insulin, including HUMALOG, may be necessary in patients with hepatic dysfunction.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Standard 2-year carcinogenicity studies in animals have not been performed. In Fischer 344 rats, a 12-month repeat-dose toxicity study was conducted with insulin lispro at subcutaneous doses of 20 and 200 units/kg/day (approximately 3 and 32 times the human subcutaneous dose of 1 unit/kg/day, based on unit/body surface area). Insulin lispro did not produce important target organ toxicity including mammary tumors at any dose. Insulin lispro was not mutagenic in the following genetic toxicity assays: bacterial mutation, unscheduled DNA synthesis, mouse lymphoma, chromosomal aberration and micronucleus assays.

Male fertility was not compromised when male rats given subcutaneous insulin lispro injections of 5 and 20 units/kg/day (0.8 and 3 times the human subcutaneous dose of 1 unit/kg/day, based on unit/body surface area) for 6 months were mated with untreated female rats. In a combined fertility, perinatal, and postnatal study in male and female rats given 1, 5, and 20 units/kg/day subcutaneously (0.16, 0.8, and 3 times the human subcutaneous dose of 1 unit/kg/day, based on unit/body surface area), mating and fertility were not adversely affected in either gender at any dose.

13.2 Animal Toxicology and/or Pharmacology

In standard biological assays in fasted rabbits, 0.2 unit/kg of insulin lispro injected subcutaneously had the same glucose-lowering effect and had a more rapid onset of action as 0.2 unit/kg of regular human insulin.

14 CLINICAL STUDIES

The safety and efficacy of HUMALOG U-100 were studied in children, adolescent, and adult patients with type 1 diabetes (n=789) and adult patients with type 2 diabetes (n=722).
14.1 Type 1 Diabetes – Adults and Adolescents

A 12-month, randomized, parallel, open-label, active-controlled study was conducted in patients with type 1 diabetes to assess the safety and efficacy of HUMALOG (N=81) compared with Humulin® R [human insulin injection (100 units per mL)] (n=86). HUMALOG was administered by subcutaneous injection immediately prior to meals and Humulin R was administered 30 to 45 minutes before meals. Humulin® U [ULTRALENTE® human insulin (rDNA origin) extended zinc suspension] was administered once or twice daily at the basal insulin. There was a 2- to 4-week run-in period with Humulin R and Humulin U before randomization. Most patients were Caucasian (97%). Forty-seven percent of the patients were male. The mean age was 31 years (range 12 to 70 years). Glycemic control, the total daily doses of HUMALOG and Humulin R, and the incidence of severe hypoglycemia (as determined by the number of events that were not self-treated) were similar in the two treatment groups. There were no episodes of diabetic ketoacidosis in either treatment group.

<table>
<thead>
<tr>
<th>Table 5: Type 1 Diabetes Mellitus – Adults and Adolescents</th>
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</thead>
<tbody>
<tr>
<td>Treatment Duration Treatment in Combination with:</td>
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<tr>
<td>-----------------------------------------------------------</td>
</tr>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Baseline HbA1c (%)</td>
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<tr>
<td>Change from baseline HbA1c (%)</td>
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<tr>
<td>Treatment Difference in HbA1c</td>
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<tr>
<td>Baseline short-acting insulin dose (units/kg/day)</td>
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<tr>
<td>End-of-Study short-acting insulin dose (units/kg/day)</td>
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<tr>
<td>Change from baseline short-acting insulin dose (units/kg/day)</td>
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<tr>
<td>Baseline Body weight (kg)</td>
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<tr>
<td>Weight change from baseline (kg)</td>
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<tr>
<td>Patients with severe hypoglycemia (n, %)</td>
</tr>
</tbody>
</table>

* Values are Mean ± SD

Severe hypoglycemia refers to hypoglycemia for which patients were not able to self-treat.

14.2 Type 2 Diabetes – Adults

A 6-month, randomized, parallel, open-label, active-controlled study was conducted in insulin-treated patients with type 2 diabetes (n=722) to assess the safety and efficacy of HUMALOG for 3 months followed by Humulin R for 3 months or the reverse sequence. HUMALOG was administered by subcutaneous injection immediately before meals and Humulin R was administered 30 to 45 minutes before meals. Humulin® N [NPH human insulin (rDNA origin) isophane suspension] or Humulin U was administered once or twice daily as the basal insulin. All patients participated in a 2- to 4-week run-in period with Humulin R and Humulin N or Humulin U. Most of the patients were Caucasian (88%), and the numbers of men and women in each group were approximately equal. The mean age was 58.6 years (range 23.8 to 85 years). The average body mass index (BMI) was 28.2 kg/m² (range 23.8 to 85 years). The majority of patients used Humulin N (84%) compared with Humulin U (16%) as their basal insulin. The reductions from baseline in HbA1c and the incidence of severe hypoglycemia (as determined by the number of events that were not self-treated) were similar between the two treatment groups of the combined groups (see Table 6).

<table>
<thead>
<tr>
<th>Table 6: Type 2 Diabetes Mellitus — Adults</th>
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<tbody>
<tr>
<td>Baseline</td>
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<tr>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>HbA1c (%)</td>
</tr>
<tr>
<td>Change from baseline HbA1c (%)</td>
</tr>
<tr>
<td>Short-acting insulin dose (units/kg/day)</td>
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<tr>
<td>Change from baseline short-acting insulin dose (units/kg/day)</td>
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<tr>
<td>Body weight (kg)</td>
</tr>
<tr>
<td>Weight change from baseline</td>
</tr>
<tr>
<td>Patients with severe hypoglycemia (n, %)</td>
</tr>
</tbody>
</table>

* Values are Mean ± SD

Severe hypoglycemia refers to hypoglycemia for which patients were not able to self-treat.

14.3 Type 1 Diabetes – Pediatric and Adolescents

An 8-month, crossover study of adolescents with type 1 diabetes (n=463), aged 9 to 19 years, compared two subcutaneous multiple-dose treatment regimens: HUMALOG or Humulin R, both administered with Humulin N (NPH human insulin) as the basal insulin. HUMALOG achieved glycemic control comparable to Humulin R, as measured by HbA1c (see Table 7), and both treatment groups had a comparable incidence of hypoglycemia. In a 9-month, crossover study of prepubescent children (n=60) with type 1 diabetes, aged 3 to 11 years, HUMALOG administered immediately after meals and Humulin R administered 30 minutes before meals resulted in similar glycemic control, as measured by HbA1c, and incidence of hypoglycemia, regardless of treatment group.

<table>
<thead>
<tr>
<th>Table 7: Pediatric Subcutaneous Administration of HUMALOG in Type 1 Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>HbA1c (%)</td>
</tr>
<tr>
<td>Change from baseline HbA1c (%)</td>
</tr>
<tr>
<td>Short-acting insulin dose (units/kg/day)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
</tr>
<tr>
<td>Weight change from baseline (kg)</td>
</tr>
<tr>
<td>Patients with severe hypoglycemia (n, %)</td>
</tr>
</tbody>
</table>

* Values are Mean ± SD

Severe hypoglycemia refers to hypoglycemia that required glucagon or glucose injection or resulted in coma.

14.4 Type 1 Diabetes – Adults Continuous Subcutaneous Insulin Infusion

To evaluate the administration of HUMALOG U-100 via external insulin pumps, two open-label, crossover design studies were performed in patients with type 1 diabetes. One study involved 39 patients, aged 19 to 58 years, treated for 24 weeks with HUMALOG or regular human insulin. After 12 weeks of treatment, the mean HbA1c values decreased from 7.8% to 7.2% in the HUMALOG-treated
14.5 Type 1 Diabetes – Pediatric Continuous Subcutaneous Insulin Infusion

A randomized, 16-week, open-label, parallel design, study of children and adolescents with type 1 diabetes (n=298) aged 4 to 18 years compared two subcutaneous infusion regimens administered via an external insulin pump: insulin aspart (n=198) or HUMALOG U-100 (n=100). These two treatments resulted in comparable changes from baseline in HbA1c and comparable rates of hypoglycemia after 16 weeks of treatment (see Table 8). Infusion site reactions were similar between groups.

Table 8: Pediatric Insulin Pump Study in Type 1 Diabetes (16 weeks; n=298)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HUMALOG</th>
<th>Aspart</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>100</td>
<td>198</td>
</tr>
<tr>
<td>Baseline HbA1c (%) a</td>
<td>8.2 ± 0.8</td>
<td>8.0 ± 0.9</td>
</tr>
<tr>
<td>Change from Baseline HbA1c (%)</td>
<td>-0.1 ± 0.7</td>
<td>-0.1 ± 0.8</td>
</tr>
<tr>
<td>Treatment Difference in HbA1c, Mean (95% confidence interval)</td>
<td>0.1 (-0.3, 0.1)</td>
<td></td>
</tr>
<tr>
<td>Baseline insulin dose (units/kg/24 hours) a</td>
<td>0.9 ± 0.3</td>
<td>0.9 ± 0.3</td>
</tr>
<tr>
<td>End-of-Study insulin dose (units/kg/24 hours) a</td>
<td>0.9 ± 0.2</td>
<td>0.9 ± 0.2</td>
</tr>
<tr>
<td>Patients with severe hypoglycemia (n, %) b</td>
<td>8 (8%)</td>
<td>19 (10%)</td>
</tr>
<tr>
<td>Diabetic ketoacidosis (n, %)</td>
<td>0 (0)</td>
<td>0 (0.5%)</td>
</tr>
<tr>
<td>Baseline body weight (kg) a</td>
<td>55.5 ± 19.0</td>
<td>54.1 ± 19.7</td>
</tr>
<tr>
<td>Weight Change from baseline (kg) a</td>
<td>1.6 ± 2.1</td>
<td>1.8 ± 2.1</td>
</tr>
</tbody>
</table>

a Values are Mean ± SD
b Severe hypoglycemia refers to hypoglycemia associated with central nervous system symptoms and requiring the intervention of another person or hospitalization.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

HUMALOG is available as:

<table>
<thead>
<tr>
<th>HUMALOG</th>
<th>Total Volume</th>
<th>Concentration</th>
<th>Total Units Available in Presentation</th>
<th>NDC Number</th>
<th>Max Dose per Injection</th>
<th>Dose Increment</th>
<th>Package Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-100 vial</td>
<td>10 mL</td>
<td>100 units/mL</td>
<td>1000 units</td>
<td>0002-7500-01</td>
<td>n/a</td>
<td>n/a</td>
<td>1 vial</td>
</tr>
<tr>
<td>U-100 vial</td>
<td>3 mL</td>
<td>100 units/mL</td>
<td>300 units</td>
<td>0002-7500-17</td>
<td>n/a</td>
<td>n/a</td>
<td>1 vial</td>
</tr>
<tr>
<td>U-100 cartridge</td>
<td>3 mL</td>
<td>100 units/mL</td>
<td>300 units</td>
<td>0002-7516-59</td>
<td>n/a</td>
<td>n/a</td>
<td>5 cartridges</td>
</tr>
<tr>
<td>U-100 KwikPen</td>
<td>3 mL</td>
<td>100 units/mL</td>
<td>300 units</td>
<td>0002-8799-59</td>
<td>60 units</td>
<td>1 unit</td>
<td>5 pens</td>
</tr>
<tr>
<td>U-100 Junior KwikPen</td>
<td>3 mL</td>
<td>100 units/mL</td>
<td>300 units</td>
<td>0002-7714-59</td>
<td>30 units</td>
<td>0.5 units</td>
<td>5 pens</td>
</tr>
<tr>
<td>U-200 KwikPen</td>
<td>3 mL</td>
<td>200 units/mL</td>
<td>600 units</td>
<td>0002-7712-27</td>
<td>60 units</td>
<td>1 unit</td>
<td>2 pens</td>
</tr>
</tbody>
</table>

Each prefilled KwikPen, cartridge, and reusable pen compatible with Lilly 3 mL cartridges is for use by a single patient. HUMALOG KwikPen, cartridges, and reusable pens compatible with Lilly 3 mL cartridges must never be shared between patients, even if the needle is changed. Patients using HUMALOG vials must never share needles or syringes with another person.

16.2 Storage and Handling

Do not use after the expiration date.

Unopened HUMALOG should be stored in a refrigerator (36°F to 46°F [2°C to 8°C]), but not in the freezer. Do not use HUMALOG if it has been frozen. In-use HUMALOG vials, cartridges, and HUMALOG KwikPen should be stored at room temperature, below 86°F (30°C) and must be used within 28 days or be discarded, even if they still contain HUMALOG. Protect from direct heat and light. See table below:

<table>
<thead>
<tr>
<th>HUMALOG U-100</th>
<th>Not In-Use (Unopened)</th>
<th>In-Use (Opened)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room Temperature (Below 86°F [30°C])</td>
<td>Room Temperature, (Below 86°F [30°C])</td>
<td></td>
</tr>
<tr>
<td>Not In-Use (Unopened) Refrigerated</td>
<td>In-Use (Opened) Refrigerated</td>
<td></td>
</tr>
<tr>
<td>10 mL vial</td>
<td>28 days</td>
<td>Until expiration date</td>
</tr>
<tr>
<td>3 mL vial</td>
<td>28 days</td>
<td>Until expiration date</td>
</tr>
<tr>
<td>3 mL cartridge</td>
<td>28 days</td>
<td>Until expiration date</td>
</tr>
<tr>
<td>3 mL Humalog KwikPen (prefilled)</td>
<td>28 days</td>
<td>Until expiration date</td>
</tr>
<tr>
<td>3 mL Humalog Junior KwikPen (prefilled)</td>
<td>28 days</td>
<td>Until expiration date</td>
</tr>
</tbody>
</table>

Use in an External Insulin Pump — Change the HUMALOG U-100 in the reservoir at least every 7 days, change the infusion set and the infusion set insertion site at least every 3 days or after exposure to temperatures that exceed 98.6°F (37°C). A HUMALOG 3 mL cartridge used in the D-Tron pumps should be discarded after 7 days, even if it still contain HUMALOG. However, as with other external insulin pumps, the infusion set should be replaced and a new infusion set insertion site should be selected at least every 3 days.

Diluted HUMALOG U-100 for Subcutaneous Injection — Diluted HUMALOG may remain in patient use for 28 days when stored at 41°F (5°C) and for 14 days when stored at 86°F (30°C). Do not dilute HUMALOG U-100 contained in a cartridge or HUMALOG used in an external insulin pump.

16.3 Preparation and Handling

Diluted HUMALOG U-100 for Subcutaneous Injection — HUMALOG may be diluted with Sterile...
Diluent for HUMALOG for subcutaneous injection. Diluting one part HUMALOG to nine parts diluent will yield a concentration one-tenth that of HUMALOG (equivalent to U-10). Diluting one part HUMALOG to one part diluent will yield a concentration one-half that of HUMALOG (equivalent to U-50).

16.4 Administration for Intravenous Administration
Infusion bags prepared with HUMALOG U-100 are stable when stored in a refrigerator (2°C to 8°C [36°F to 46°F]) for 48 hours and then may be used at room temperature for up to an additional 48 hours [see Dosage and Administration (2.2)].

17 PATIENT COUNSELING INFORMATION
Advising the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

17.1 Never Share a HUMALOG KwikPen, Cartridge, Reusable Pen Compatible with Lilly 3 mL Cartridges, or Syringe Between Patients
Advisors that they must never share a HUMALOG KwikPen, cartridge, or reusable pen compatible with Lilly 3 mL cartridges with another person, even if the needle is changed. Advertisers advise patients using HUMALOG vials not to share needles or syringes with another person. Sharing poses a risk for transmission of blood-borne pathogens.

17.2 Hypoglycemia
Instruct patients on self-management procedures including glucose monitoring, proper injection technique, and management of hypoglycemia and hyperglycemia, especially at initiation of HUMALOG therapy. Instruct patients on handling of special situations such as intercurrent conditions (illness, stress, or emotional disturbances), an inadequate or skipped insulin dose, inadvertent administration of an increased insulin dose, inadequate food intake, and skipped meals. Instruct patients on the management of hypoglycemia.
Inform patients that their ability to concentrate and react may be impaired as a result of hypoglycemia. Advise patients who have frequent hypoglycemia or reduced or absent warning signs of hypoglycemia to use caution when driving or operating machinery [see Warnings and Precautions (5.3)].

17.3 Hypersensitivity Reactions
Advise patients that hypersensitivity reactions have occurred with HUMALOG. Inform patients on the symptoms of hypersensitivity reactions [see Warnings and Precautions (5.5)].

17.4 Medication Errors
Instruct patients to always check the insulin label before each injection to avoid mix-ups between insulin products.
Inform patients that HUMALOG U-200 contains 2 times as much insulin in 1 mL as HUMALOG U-100.
Inform patients that the HUMALOG U-200 KwikPen dose window shows the number of units of HUMALOG U-200 to be injected and that no dose conversion is required.
Instruct patients to NOT transfer HUMALOG U-200 from the HUMALOG KwikPen to a syringe. The markings on the syringe will not measure the dose correctly and this can result in overdosage and severe hypoglycemia.

17.5 Administration Instruction for HUMALOG U-200
Instruct patients to NOT mix HUMALOG U-200 with any other insulin.

17.6 Women of Reproductive Potential
Advise females of reproductive potential with diabetes to inform their doctor if they are pregnant or are contemplating pregnancy [see Use in Specific Populations (8.1)].

17.7 Instructions For Patients Using Continuous Subcutaneous Insulin Pumps
Patients using external pump infusion therapy should be trained appropriately.
The following insulin pumps have been tested in HUMALOG clinical trials conducted by Eli Lilly and Company.
• Disetronic® and H-Tron® plus V100, D-Tron® and D-Tronplus® with Disetronic Rapid infusion sets
• MiniMed® Models 506, 507 and 508 and Polyfin® infusion sets
HUMALOG is recommended for use in pump systems for insulin infusion such as MiniMed, Disetronic, and other equivalent pumps. Before using HUMALOG in a pump system, read the pump label to make sure the pump is indicated for continuous delivery of fast-acting insulin. HUMALOG is recommended for use in any reservoir and infusion sets that are compatible with insulin and the specific pump. Please see recommended reservoir and infusion sets in the pump manual. Do not use HUMALOG U-200 in an external insulin pump.

To avoid insulin degradation, infusion set occlusion, and loss of the preservative (metacresol), insulin in the reservoir should be replaced at least every 7 days; infusion sets and infusion set insertion sites should be changed at least every 3 days.
Insulin exposed to temperatures higher than 98.6°F (37°C) should be discarded. The temperature of the insulin may exceed ambient temperature when the pump housing, cover, tubing or sport case is exposed to sunlight or radiant heat. Infusion sites that are erythematous, pruritic, or thickened should be reported to the healthcare professional, and a new site selected because continued inflation may increase the skin reaction or alter the absorption of HUMALOG.

In cases of pump malfunction or insulin degradation can lead to rapid hyperglycemia and ketosis. This is especially pertinent for rapid acting insulin analogs that are more rapidly absorbed through skin and have a shorter duration of action. Prompt identification and correction of the cause of hyperglycemia or ketosis is necessary. Problems include pump malfunction, infusion set occlusion, leakage, disconnection or kinking, and degraded insulin. Less commonly, hypoglycemia from pump malfunction may occur. If these problems cannot be promptly corrected, patients should resume therapy with subcutaneous insulin injection and contact their healthcare professionals [see Dosage and Administration (2.2) and How Supplied/Storage and Handling (16.2)].

1 3 mL cartridge is for use in Eli Lilly and Company’s HumaPen®, Luxura®, HD insulin delivery device, and Disetronic D-TRON® and D-TRON® Plus pumps.
2 Humalog®, Humalog® KwikPen®, Humalog® Junior KwikPen®, HumaPen®, HumPen®, Luxura® and HumaPen® Luxura® are trademarks of Eli Lilly and Company.
3 D-Tron®, H-Tron®, D-Tron®, and D-Tronplus® are registered trademarks of Roche Diagnostics GmbH.
4 MiniMed® and Polyfin® are registered trademarks of MiniMed, Inc.

Other product and company names may be the trademarks of their respective owners.

Literature revised November 2018
HUMALOG® (hu-ma-log)
(insulin lispro injection)

What is HUMALOG?
• HUMALOG is a man-made fast-acting insulin used to control high blood sugar in adults and children with diabetes mellitus.
• It is not known if HUMALOG is safe and effective in children younger than 3 years of age or when used to treat children with type 2 diabetes mellitus.

Who should not use HUMALOG?
Do not use HUMALOG if you:
• are having an episode of low blood sugar (hypoglycemia).
• have an allergy to HUMALOG or any of the ingredients in HUMALOG.

Before using HUMALOG, tell your healthcare provider about all of your medical conditions, including if you:
• have kidney or liver problems.
• take any other medicines, especially ones commonly called TZDs (thiazolidinediones).
• have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with HUMALOG.
• have any other medical conditions. Some medical conditions can affect your insulin needs and your dose of HUMALOG.
• are pregnant or plan to become pregnant. Talk to your healthcare provider if you are pregnant or plan to become pregnant. You and your healthcare provider should decide about the best way to manage your diabetes while you are pregnant.
• are breastfeeding or plan to breastfeed. It is not known if HUMALOG passes into your breast milk. You and your healthcare provider should decide if you will use HUMALOG while you breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription or over-the-counter medicines, vitamins, or herbal supplements.

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

How should I use HUMALOG?
• Read the Instructions for Use that come with your HUMALOG.
• Do not share your Humalog KwikPen, cartridges, reusable pen compatible with Lilly 3 mL cartridges, or syringes with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.
• Use HUMALOG exactly as your healthcare provider tells you to.
• HUMALOG starts acting fast, so inject it up to 15 minutes before or right after you eat a meal.
• Know the type and strength of insulin you use. Do not change the type of insulin you use unless your healthcare provider tells you to. The amount of insulin and the best time for you to take your insulin may need to change if you take a different type of insulin.
• Check your blood sugar levels. Ask your healthcare provider what your blood sugars should be and when you should check your blood sugar level.

What should I avoid while using HUMALOG?
While using HUMALOG do not:
• Drive or operate heavy machinery, until you know how HUMALOG affects you.
• Drink alcohol or use prescription or over-the-counter medicines that contain alcohol.

What are the possible side effects of HUMALOG?
HUMALOG may cause serious side effects, including:
• low blood sugar (hypoglycemia). Signs and symptoms that may indicate low blood sugar include:
  • dizziness or light-headedness, sweating, confusion, headache, blurred vision, slurred speech, shakiness, fast heartbeat, hunger, amnesia, irritability, or mood changes.
• Your HUMALOG dose may need to change because of:
  • change in level of physical activity or exercise, weight gain or loss, change in diet, illness.
• serious allergic reactions (whole body allergic reaction). Get medical help right away, if you have any of these symptoms of an allergic reaction:
  • a rash over your whole body, trouble breathing, a fast heartbeat, sweating, feel faint.
• low potassium in your blood (hypokalemia).
• heart failure. Taking certain diabetes pills called thiazolidinediones or “TZDs” with HUMALOG may cause heart failure in some people. This can happen even if you have never had heart failure or heart problems before. If you already have heart failure it may get worse while you take TZDs with HUMALOG. Your healthcare provider should monitor you closely while you are taking TZDs with HUMALOG. Tell your healthcare provider if you have any new or worse symptoms of heart failure including:
  • shirrness of breath
  • swelling of your ankles or feet
  • sudden weight gain.

Treatment with TZDs and HUMALOG may need to be adjusted or stopped by your healthcare provider if you have new or worse heart failure.

The most common side effects of HUMALOG include:
• low blood sugar (hypoglycemia), reaction at the injection site, skin thickening or pits at the injection site (lipodystrophy), itching (pruritis), rash.

These are not all the possible side effects of HUMALOG.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of HUMALOG.
• Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about HUMALOG that is written for health professionals.
• Do not use HUMALOG for a condition for which it was not prescribed. Do not give or share HUMALOG with other people, even if they also have diabetes. It may harm them.

What are the ingredients in HUMALOG?
Active ingredient: insulin lispro
Inactive ingredients: glycerin, dibasic sodium phosphate, metacresol, zinc oxide (zinc ion), trace
amounts of phenol and water for injection

The brands listed are trademarks of their respective owners and are not trademarks of Eli Lilly and Company.

Humalog® and Humalog KwikPen® are registered trademarks of Eli Lilly and Company.

Marketed by: Lilly USA, LLC, Indianapolis, IN 46285, USA

For more information, go to www.humalog.com or call 1-800-545-5979.

This Patient Information has been approved by the U.S. Food and Drug Administration

Patient Information revised: December 2018

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This Patient Information has been approved by the U.S. Food and Drug Administration

For more information, go to www.humalog.com or call 1-800-545-5979.

Marketed by: Lilly USA, LLC, Indianapolis, IN 46285, USA

Company.

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^ Instructions for Use

HUMALOG® (HU-ma-log)

(Insulin lispro injection)

Read the Instructions for Use before you start taking HUMALOG and each time you get a new HUMALOG vial. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

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

Supplies needed to give your injection

Preparing your HUMALOG dose

- a HUMALOG vial
- a U-100 insulin syringe and needle
- 2 alcohol swabs
- 1 sharps container for throwing away used needles and syringes. See “Disposing of used needles and syringes” at the end of these instructions.

<table>
<thead>
<tr>
<th>Step 1: If you are using a new vial, pull off the plastic Protective Cap, but do not remove the Rubber Stopper.</th>
<th>Step 2: Wipe the Rubber Stopper with an alcohol swab.</th>
<th>Step 3: Hold the syringe with the needle pointing up. Pull down on the Plunger until the tip of the Plunger reaches the line for the number of units for your prescribed dose.</th>
<th>Step 4: Push the Plunger all the way in (Example Dose: 20 units shown).</th>
<th>Step 5: Turn the vial and syringe upside down and slowly pull the Plunger down until the tip is a few units past the line for your prescribed dose.</th>
<th>Step 6: If there are air bubbles, tap the syringe gently a few times to let any air bubbles rise to the top. (Example Dose: 20 units shown).</th>
<th>Step 7: Slowly push the Plunger up until the tip reaches the line for your prescribed dose. Check the syringe to make sure that you have the right dose. (Example Dose: 20 units shown).</th>
<th>Step 8: Pull the Plunger up out of the vial’s Rubber Stopper.</th>
</tr>
</thead>
<tbody>
<tr>
<td>If you are using a new vial, pull off the plastic Protective Cap, but do not remove the Rubber Stopper.</td>
<td>Wipe the Rubber Stopper with an alcohol swab.</td>
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<td>If there are air bubbles, tap the syringe gently a few times to let any air bubbles rise to the top. (Example Dose: 20 units shown).</td>
<td>Slowly push the Plunger up until the tip reaches the line for your prescribed dose. Check the syringe to make sure that you have the right dose. (Example Dose: 20 units shown).</td>
<td>Pull the Plunger up out of the vial’s Rubber Stopper.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If you use HUMALOG with NPH insulin: Giving your HUMALOG injection with a syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPH insulin is the only type of insulin that can be mixed with HUMALOG. Do not mix HUMALOG with any other type of insulin.</td>
</tr>
<tr>
<td>HUMALOG should be drawn up into the syringe first, before you draw up your NPH insulin. Talk to your healthcare provider if you are not sure about the right way to mix HUMALOG and NPH insulin.</td>
</tr>
</tbody>
</table>

Giving your HUMALOG using an insulin pump

- Inject your insulin exactly as your healthcare provider has shown you.
- HUMALOG starts acting fast, to give your injection within 15 minutes before or right after you eat a meal.
- Change (rotate) your injection site for each injection.
- Dispose of used needles and syringes
  - Change your insertion site every 3 days.
  - Change the insulin in the reservoir at least every 7 days, even if you have not used all of the insulin.
  - Do not dilute or mix HUMALOG with any other type of insulin in your insulin pump.
  - See your insulin pump manual for instructions or talk to your healthcare provider.
  - Put your used needles and syringes in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and syringes in your household trash.
  - If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
    - How should I store HUMALOG?
    - All unopened HUMALOG vials:
      - made of a heavy-duty plastic,
      - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
      - upright and stable during use,
      - leak-resistant, and
      - properly labeled to warn of hazardous waste inside the container.
    - When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at: http://www.fda.gov/safesharpsdisposal.
    - Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

After HUMALOG vials have been opened:

- Store all unopened vials in the refrigerator.
- Do not freeze. Do not use if it has been frozen.
- Keep away from heat and out of direct light.
- Unopened vials can be used until the expiration date on the canister and label, if they have been stored in the refrigerator.
- Unopened vials should be thrown away after 28 days, if they are stored at room temperature.

General information about the safe and effective use of HUMALOG

- Store opened vials in the refrigerator or at room temperature below 86°F (30°C) for up to 28 days.
- Keep vials away from heat and out of direct light.
- Throw away all opened vials after 28 days of use, even if there is insulin left in the vial.
If you have any questions or problems with your HUMALOG, contact Lilly at 1-800-Lilly-Rx (1-800-545-5979) or call your healthcare provider for help. For more information on HUMALOG and insulin, go to www.humalog.com.

These Instructions for Use have been approved by the U.S. Food and Drug Administration. Humalog® is a registered trademark of Eli Lilly and Company.

Step 9:
Choose your injection site.
HUMALOG is injected under the skin (subcutaneously) of your stomach area (abdomen), buttocks, upper legs or upper arms.
Wipe the skin with an alcohol swab. Let the injection site dry before you inject your dose.

Step 10:
Insert the needle into your skin.

Step 11:
Push down on the Plunger to inject your dose.
The needle should stay in your skin for at least 5 seconds to make sure you have injected all of your insulin dose.

Step 12:
Pull the needle out of your skin.
You may see a drop of insulin at the needle tip. This is normal and does not affect the dose you just received.
If you see blood after you take the needle out of your skin, press the injection site with a piece of gauze or an alcohol swab. Do not rub the area.
Do not recap the needle. Recapping the needle can lead to a needle stick injury.

Keep HUMALOG vials, syringes, needles, and all medicines out of the reach of children.
Always use a new syringe or needle for each injection.
Do not reuse or share your syringes or needles with other people. You may give other people a serious infection or get a serious infection from them.

- Wash your hands with soap and water.
- Check the HUMALOG label to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- HUMALOG should look clear and colorless. Do not use HUMALOG if it is thick, cloudy, or colored, or if you see lumps or particles in it.
- Do not use HUMALOG past the expiration date printed on the label or 28 days after you first use it.
- Always use a new syringe or needle for each injection to help ensure sterility and prevent blocked needles. Do not reuse or share your syringes or needles with other people. You may give other people a serious infection or get a serious infection from them.

**Patient Information**

**HUMALOG KwikPen® insulin lispro injection U-200 (200 units per mL)**

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

**What is HUMALOG?**
- HUMALOG is a rapid-acting man-made insulin used to control high blood sugar in adults and children with diabetes mellitus.
- This HUMALOG KwikPen (“Pen”) contains 2 times as much insulin (200U/mL) in 1 mL as standard insulin (100U/mL).
- It is not known if HUMALOG is safe and effective in children less than 3 years of age.
- It is not known if HUMALOG is safe and effective in children with type 2 diabetes.

**Who should not take HUMALOG?**
Do not take HUMALOG if you:
- are having an episode of low blood sugar (hypoglycemia).
What should I tell my healthcare provider before using HUMALOG?
Before using HUMALOG, tell your healthcare provider about all your medical conditions, including if you:
- have liver or kidney problems.
- take other medicines, especially ones called TZDs (thiazolidinediones).
- have heart failure or other heart problems. If you have heart failure, it may get worse while you take TZDs with HUMALOG.
- are pregnant, planning to become pregnant, or breastfeeding. It is not known if HUMALOG may harm your unborn or breastfeeding baby.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Before you start using HUMALOG, talk to your healthcare provider about how blood sugar and how to manage it.

How should I use HUMALOG KwikPen?
- Read the detailed Instructions for Use that come with your HUMALOG KwikPen.
- Use HUMALOG KwikPen exactly as your healthcare provider tells you to. Your healthcare provider should tell you how much HUMALOG to use and when to use it.
- Know the amount of HUMALOG you use. Do not change the amount of HUMALOG you use unless your healthcare provider tells you to.
- Check your insulin label each time you give your injection to make sure you are using the correct insulin.
- HUMALOG comes in a KwikPen which is a disposable prefilled pen that you must use to give your HUMALOG. The dose window on your pen shows your dose of HUMALOG. Do not make any dose changes unless your healthcare provider tells you to.
- Do not use a syringe to remove HUMALOG from your KwikPen disposable prefilled pen.
- Do not re-use needles. Always use a new needle for each injection. Re-use of needles increases your risk of having blocked needles, which may cause you to get the wrong dose of HUMALOG. Using a new needle for each injection also lowers your risk of getting an infection. If your needle is blocked, follow the instructions in the “General information about the safe and effective use of your Pen” section of the Instructions for Use.
- HUMALOG is a rapid-acting insulin. Take HUMALOG within 15 minutes before eating or right after eating a meal.
- Inject HUMALOG under your skin (subcutaneously). Do not use HUMALOG KwikPen (“Pen”) in an insulin pump or inject HUMALOG KwikPen into your vein (intravenously).
- Change (rotate) your injection site with each dose.
- Do not mix the HUMALOG in the HUMALOG KwikPen with any other type of insulin or liquid medicine.
- Check your blood sugar levels. Ask your healthcare provider what your blood sugar should be and when you should check your blood sugar levels.

Keep HUMALOG KwikPen and all medicines out of reach of children.

Your dose of HUMALOG may need to change because of:
- change in physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of other medicines you take.

What should I avoid while using HUMALOG KwikPen?
While using HUMALOG KwikPen do not:
- drive or operate heavy machinery, until you know how HUMALOG KwikPen affects you
- drink alcohol or use over-the-counter medicines that contain alcohol

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

Get emergency help if you have:
- trouble breathing, shortness of breath, fast heartbeat, swelling of your face, tongue, or throat, sweating, extreme drowsiness, dizziness, confusion.

The most common side effects of HUMALOG include:
- low blood sugar (hypoglycemia), allergic reactions, including reactions at your injection site, skin thickening or rash at the injection site (lipodystrophy), itching, and rash.

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

General Information about the safe and effective use of HUMALOG KwikPen.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use HUMALOG for a condition for which it was not prescribed. Do not give HUMALOG to other people, even if they have the same symptoms that you have. It may harm them.

This Patient Information leaflet summarizes the most important information about HUMALOG KwikPen. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about HUMALOG that is written for healthcare providers. For more information go to www.humalog.com or call 1-800-LillyRx (1-800-545-5979).

What are the ingredients in HUMALOG U-2007
Active ingredient: insulin lispro.
Inactive ingredient: glycerin, tromethamine, metacresol, zinc oxide (zinc ion), trace amounts of phenol and water for injection.

Humalog® and Humalog KwikPen® are registered trademarks of Eli Lilly and Company.
Marketed by: Lilly USA, LLC, Indianapolis, IN 46285, USA

For more information, go to www.humalog.com.
Patient Information issued: May 26, 2015
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Instructions for Use

HUMALOG® Junior KwikPen®

insulin Impro injection

100 units/ml, 3 ml pen

Read the instructions for Use before you start using HUMALOG and each time you get another HUMALOG® Junior KwikPen®. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Do not share your HUMALOG Junior KwikPen with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.

HUMALOG Junior KwikPen ("Pen") is a disposable prefilled pen containing 300 units of HUMALOG.

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

How to recognize your HUMALOG Junior KwikPen:

- You can give yourself more than 1 dose from the Pen.
- Each turn of the Dose Knob dials 0.5 (1/2) unit of insulin. You can give from 0.5 (1/2) to 30 units in a single injection.
- If your dose is more than 30 units, you will need to give more than 1 injection.
- The Plunger will only reach the end of the cartridge when you have used all 300 units in the Pen.
- If you do not have a FDA-cleared sharps disposal container, you may use a puncture-resistant lid, without sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at http://www.fda.gov/safesharpsdisposal
- Do not store used needles. For more information about sharps disposal in the state that you live in, go to the FDA’s website at http://www.fda.gov/safesharpsdisposal
- The used Pen may be discarded in the trash, unless your community guidelines permit this. Do not recycle the container.

Instructions for Use

Preparing your Pen

- HUMALOG Junior KwikPen
- Pen compatible Needle [BD (Becton, Dickinson and Company) Pen Needles recommended]
- Alcohol swab
- Gauze

Priming your Pen

Prime before each injection.

Selecting your dose

You can give from 0.5 (1/2) to 30 units in a single injection.

After your injection

Disposing of Pens and Needles

- Put your used needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - Storing your Pen
  - Unused Pens
    - Made of a heavy-duty plastic, can be closed with a tight-fitting, puncture-resistant lid, without sharp being able to come out, upright and stable during use, leak-resistant, and properly labeled to warn of hazardous waste inside the container.
  - When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at http://www.fda.gov/safesharpsdisposal
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle the container.

- After you receive your insulin by turning the Dose Knob, You will receive your insulin by turning the Dose Knob.
- If you still do not see insulin, repeat the priming steps 6 to 8, but not more than 4 times.
- If you still do not see insulin, change the Needle and repeat the priming steps 6 to 8.
- Small air bubbles are normal and will not affect your dose.

- Pull the Needle out of your skin.
- A drop of insulin at the Needle tip is normal. It will not affect your dose.
- Check the number in the Dose Window.
- If you see "0" in the Dose window, you have received the full amount you dialed.
- If you do not see "0" in the Dose window, do not redial. Insert the Needle into your skin and finish your injection.
- If you still do not think you received the full amount you dialed for your injection, do not start over or repeat that injection. Monitor your blood glucose as instructed.

- Carefully replace the Outer Needle Shield.
- Do not store the Pen with the Needle attached to prevent leaking, blocking the Needle, and air from entering the Pen.

- Replace the Pen Cap by lining up the Cap Clip with the Dose Indicator and pushing straight on.

- Do not store the Pen in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Do not freeze your insulin. Do not use if it has been frozen.
- Unused Pen may be used until the expiration date printed on the Label, if the Pen has been kept in the refrigerator.
- General information about the safe and effective use of your Pen
  - Store the Pen at room temperature (up to 86°F [30°C]). Keep away from heat and light.

- Do not share your HUMALOG Junior KwikPen with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.

- The used Pen may be discarded in the trash, unless your community guidelines permit this. Do not recycle the container.

- After you receive your insulin by turning the Dose Knob, You will receive your insulin by turning the Dose Knob.
- If you still do not see insulin, repeat the priming steps 6 to 8.
- Small air bubbles are normal and will not affect your dose.

- Pull the Needle out of your skin.
- A drop of insulin at the Needle tip is normal.
- Check the number in the Dose Window.
- If you see "0" in the Dose window, you have received the full amount you dialed.
- If you do not see "0" in the Dose window, do not redial. Insert the Needle into your skin and finish your injection.
- If you still do not think you received the full amount you dialed for your injection, do not start over or repeat that injection. Monitor your blood glucose as instructed.

- Carefully replace the Outer Needle Shield.
- Do not store the Pen with the Needle attached to prevent leaking, blocking the Needle, and air from entering the Pen.

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- The used Pen may be discarded in the trash, unless your community guidelines permit this. Do not recycle the container.

- After you receive your insulin by turning the Dose Knob, You will receive your insulin by turning the Dose Knob.
- If you still do not see insulin, repeat the priming steps 6 to 8.
- Small air bubbles are normal and will not affect your dose.

- Pull the Needle out of your skin.
- A drop of insulin at the Needle tip is normal.
- Check the number in the Dose Window.
- If you see "0" in the Dose window, you have received the full amount you dialed.
- If you do not see "0" in the Dose window, do not redial. Insert the Needle into your skin and finish your injection.
- If you still do not think you received the full amount you dialed for your injection, do not start over or repeat that injection. Monitor your blood glucose as instructed.

- Carefully replace the Outer Needle Shield.
- Do not store the Pen with the Needle attached to prevent leaking, blocking the Needle, and air from entering the Pen.

- Replace the Pen Cap by lining up the Cap Clip with the Dose Indicator and pushing straight on.

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- Pull the Needle out of your skin.
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- Check the number in the Dose Window.
- If you see "0" in the Dose window, you have received the full amount you dialed.
- If you do not see "0" in the Dose window, do not redial. Insert the Needle into your skin and finish your injection.
- If you still do not think you received the full amount you dialed for your injection, do not start over or repeat that injection. Monitor your blood glucose as instructed.

- Carefully replace the Outer Needle Shield.
- Do not store the Pen with the Needle attached to prevent leaking, blocking the Needle, and air from entering the Pen.

- Replace the Pen Cap by lining up the Cap Clip with the Dose Indicator and pushing straight on.

- Do not store the Pen in the refrigerator at 36°F to 46°F (2°C to 8°C).
- Do not freeze your insulin. Do not use if it has been frozen.
- Unused Pen may be used until the expiration date printed on the Label, if the Pen has been kept in the refrigerator.
- General information about the safe and effective use of your Pen
  - Store the Pen at room temperature (up to 86°F [30°C]). Keep away from heat and light.
Instructed by your healthcare provider. If you normally need to give 2 injections for your full dose, be sure to give your second injection.

- The Plunger only moves a little with each injection and you may not notice that it moves.
- If you see blood after you take the Needle out of your skin, press the injection site lightly with a piece of gauze or an alcohol swab. Do not rub the area.

If you need help with dividing up your dose the right way, ask your healthcare provider.

You must use a new Needle for each injection and repeat the priming step. The Pen will not let you dial more than the number of units left in the Pen.

If you need to inject more than the number of units left in the Pen, you may either:

- inject the amount left in your Pen and then use a new Pen to give the rest of your dose, or
- get a new Pen and inject the full dose.

It is normal to see a small amount of insulin left in the Pen that you can not inject. Inject your insulin as your healthcare provider has shown you.

- Change (rotate) your injection site for each injection.
- Do not try to change your dose while injecting.


Step 9: Turn the Dose Knob to select the number of units you need to inject.

- The Dose Indicator should line up with your dose.
- The Pen dials 0.5 (½) unit at a time.
- The Dose Knob clicks as you turn it.
- Do not dial your dose by counting the clicks. You may dial the wrong dose. This may lead to you getting too much insulin or not enough insulin.
- The dose can be corrected by turning the Dose Knob in either direction until the correct dose lines up with the Dose Indicator.
- The whole unit numbers (for example, 4) are printed on the dial.
- The half units are shown as lines between the whole unit numbers.
- Always check the number in the Dose Window to make sure you have dialed the correct dose.

- Wash your hands with soap and water.
- Check the Pen to make sure you are taking the right type of insulin. This is especially important if you use more than 1 type of insulin.
- Do not use your Pen past the expiration date printed on the Label or for more than 28 days after you first start using the Pen.
- Always use a new needle for each injection to help prevent infections and blocked needles. Do not reuse or share your needles with other
people. You may give other people a serious infection or get a serious infection from them.

- Priming your Pen means removing the air from the Needle and Cartridge that may collect during normal use and ensures that the Pen is working correctly.
- If you do not prime before each injection, you may get too much or too little insulin.

Step 1:
- Pull the Pen Cap straight off.
- Do not remove the Pen Label.
- Wipe the Rubber Seal with an alcohol swab.

Step 2:
- Check the liquid in the Pen. HUMALOG should look clear and colorless. Do not use if it is cloudy, colored, or has particles or clumps in it.

Step 3:
- Select a new Needle.
- Pull off the Paper Tab from the Outer Needle Shield.

Step 4:
- Push the capped Needle straight onto the Pen and twist the Needle on until it is tight.

Step 5:
- Pull off the Outer Needle Shield. Do not throw it away.
- Pull off the Inner Needle Shield and throw it away.

DRUG: Humalog
GENERIC: Insulin lispro
 DOSAGE: INJECTION, SOLUTION
 ADMINISTRATION: INTRAVENOUS
NDC: 70518-2264-0
PACKAGING: 10 mL in 1 VIAL
OUTER PACKAGING: 1 in 1 CARTON
ACTIVE INGREDIENT(S):
- Insulin lispro 100[iU] in 1mL.
INACTIVE INGREDIENT(S):
- Glycerin
- Water
- Hydrochloric acid
- Phenol
- Meuacerol
- Sodium Phosphate, Dibasic
- Sodium hydroxide
- Zinc

HUMALOG
insulin lispro injection, solution

Product Information
Product Type: HUMAN PRESCRIPTION DRUG
Route of Administration: INTRAVENOUS, SUBCUTANEOUS

Active Ingredients

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Inactive Ingredients

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Packaging

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**Labeler** - REMEDYREPACK INC. (829572556)

Revised: 8/2019

REMEDYREPACK INC.