

PART III: CONSUMER INFORMATION

HUMALOG® VIALS

(insulin lispro injection)

Solution for Injection, 100 units/mL, Lilly Standard

This leaflet is part III of a three-part "Product Monograph" published when HUMALOG® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about HUMALOG®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Insulin is a hormone produced by the pancreas, a large gland that lies near the stomach. This hormone is necessary for the body's correct use of food, especially sugar. Diabetes occurs when the pancreas does not make enough insulin to meet your body's needs.

To control your diabetes, your doctor has prescribed injections of insulin to keep your blood glucose at a near-normal level.

What it does:

Insulin lispro is a recombinant DNA sourced human insulin analogue. HUMALOG consists of zinc-insulin lispro crystals dissolved in a clear fluid. HUMALOG is used to control high blood sugar (glucose) in people with diabetes. HUMALOG takes effect more rapidly and has a shorter duration of activity as compared to regular insulin.

The rapid onset of activity requires HUMALOG to be given within 15 minutes before a meal. When necessary, HUMALOG may be given shortly after a meal instead (within 20 minutes of the start of the meal). The time course of action of any insulin may vary to some extent in different individuals or at different times in the same individual. As with all insulin preparations, the duration of action of HUMALOG is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Proper control is important. Uncontrolled diabetes (hyperglycemia) over a long period of time can result in a number of serious problems such as blindness, kidney failure, poor circulation/heart attacks, strokes and/or nerve damage. These problems can be prevented or reduced by good diabetes management. This will require close and constant cooperation with your diabetes healthcare team including: yourself, your doctor and your diabetes educators (nurses, dietitians, social workers, pharmacists and other healthcare professionals). Thus, you can lead an active, healthy and productive life by eating a balanced daily diet, exercising regularly, and taking your insulin injections as prescribed.

You have been instructed to test your blood and/or your urine regularly for glucose. If your blood tests consistently show above- or below-normal glucose levels or your urine tests

consistently show the presence of glucose, your diabetes is not properly controlled and you must let your doctor know.

When it should not be used:

- When your blood sugar is too low (hypoglycemia). After treating your low blood sugar, follow your healthcare provider's instructions on the use of HUMALOG.
- If you are allergic to anything in HUMALOG. A complete list of ingredients in HUMALOG is provided below.

What the medicinal ingredient is:

HUMALOG contains 100 units/mL of Human Insulin Analogue.

HUMALOG contains insulin lispro injection.

What the non-medicinal ingredients are:

HUMALOG contains glycerol, dibasic sodium phosphate, m-cresol, zinc (as ion) and water for injection. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

What dosage forms it comes in:

HUMALOG:

- Vial: 10 mL
- Vial: 3 mL

Also available in:

HUMALOG:

- Cartridge: 3.0 mL
- KwikPen, 3.0 mL prefilled pen

HUMALOG MIX25:

- Cartridge, 3.0 mL
- KwikPen, 3.0 mL prefilled pen

HUMALOG MIX50:

- Cartridge, 3.0 mL
- KwikPen, 3.0 mL prefilled pen

DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND DIRECTION.

Always keep an extra supply of HUMALOG as well as a spare syringe and needle on hand. Always wear identification to indicate that you have diabetes so that appropriate treatment can be given if complications occur away from home.

When you receive your insulin from the pharmacy, always check to see that:

1. The name HUMALOG appears on the carton and bottle (vial) label.
2. The carton and bottle (vial) label is correct for your type of insulin.
3. The insulin strength is U-100.

- The expiration date on the package will allow you to use the insulin before that date.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Hypoglycemia or low blood sugar is the most common adverse effect experienced by insulin users. Blood glucose monitoring is recommended for all patients with diabetes. Uncorrected hypoglycemic or hyperglycemic reactions can cause loss of consciousness, coma or even death. Information on how to recognize these symptoms is provided below.
- This Lilly human insulin analogue differs from other insulins because it has a unique structure, a very quick onset of action and a short duration of activity. HUMALOG should be given within 15 minutes before a meal or when necessary shortly after a meal instead (within 20 minutes of the start of the meal). The short duration of action of HUMALOG means that if you have Type 1 diabetes you also need to use a longer acting human insulin, such as HUMULIN N to give the best glucose control (except when using an insulin infusion pump).
- HUMALOG should not be used if it is not water-clear and colourless or if it has formed a deposit of solid particles on the wall of the vial.
- Any change of insulin should be made cautiously and only under medical supervision. Changes in purity, strength, brand (manufacturer), type (regular, NPH, etc), species (beef, pork, beef-pork, human), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.
- Mixing of HUMALOG with either animal insulins or insulin preparations produced by other manufacturers is not recommended.
- Patients taking HUMALOG may require a change in dosage from that used with other insulins. If an adjustment is needed, it may occur with the first dose or over a period of several weeks.
- Insulin infusion pump: when used in an insulin infusion pump, HUMALOG should not be diluted or mixed with any other insulin. Carefully read and follow the insulin infusion pump manufacturer's instructions and this insert before using HUMALOG.

BEFORE you use HUMALOG talk to your doctor or pharmacist if:

- You have trouble with your kidneys or liver, your doctor may decide to alter your insulin dose.
- You drink alcohol (including wine and beer): watch for signs of hypoglycemia and never drink alcohol on an empty stomach.
- You exercise more than usual or if you want to change your usual diet. Exercise may lower your body's need for insulin during and for some time after the activity. Exercise may

also speed up the effect of an insulin dose, especially if the exercise involves the area of injection site.

- You are ill. Illness, especially with nausea and vomiting, may cause your insulin requirements to change. Even if you are not eating, you will still require insulin. You and your doctor should establish a sick day plan for you to use in case of illness. When you are sick, test your blood/urine frequently.
- You are travelling across more than 2 time zones. You should consult your doctor concerning adjustments in your insulin schedule.
- You are pregnant. HUMALOG can be used in pregnancy if clinically indicated. Data on a large number of exposed pregnancies do not indicate any adverse effect of HUMALOG on pregnancy or on the health of the foetus/newborn. Good control of diabetes is especially important for you and your unborn baby. Pregnancy may make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or are nursing a baby, consult your doctor.
- When you use other medicines. Many medicines affect the way glucose works in your body and this may influence your insulin dose. Listed below are the most common medicines, which may affect your insulin treatment. Talk to your doctor or pharmacist if you take, or change any other medicines, even those not prescribed.

INTERACTIONS WITH THIS MEDICATION

Insulin requirements may be increased if you are taking other drugs with hyperglycemic activity, such as oral contraceptives (for example, birth control pills, injections and patches), corticosteroids, or thyroid replacement therapy. Insulin requirements may be decreased in the presence of agents such as oral antidiabetic agents, salicylates (aspirin), sulfa antibiotics, certain antidepressants (monoamine oxidase inhibitors), beta-blockers, alcohol, ACE-inhibitors and angiotensin II receptor blockers. Always discuss any medications you are taking with your doctor.

The use of thiazolidinediones (such as rosiglitazone and pioglitazone), alone or in combination with other antidiabetic agents (including insulin), has been associated with heart failure and swelling of the lower extremities. Please contact your physician immediately if you develop symptoms of shortness of breath, fatigue, exercise intolerance, or swelling of the lower extremities while you are on these agents.

PROPER USE OF THIS MEDICATION

HUMALOG

HUMALOG is a sterile solution. HUMALOG should be given by subcutaneous injection, or by continuous subcutaneous insulin infusion pump. The concentration of

HUMALOG in 3 mL vials or 10 mL vials is 100 units/mL (U-100).

When used as a meal-time insulin, HUMALOG should be given within 15 minutes before a meal, or when necessary shortly after a meal instead (within 20 minutes of the start of the meal).

HUMALOG is a clear and colourless liquid with a water-like appearance and consistency. Do not use if it appears cloudy, thickened, or slightly coloured or if solid particles are visible. Always check the appearance of your vial of HUMALOG before using, and if you note anything unusual in its appearance or notice your insulin requirements changing markedly, consult your doctor.

Injection Procedure

Correct Syringe:

Doses of insulin are measured in units. HUMALOG is available in 100 units/mL (U-100). It is important that you understand the markings on your syringe, because the volume of HUMALOG you inject depends on the strength, that is, the number of units/mL. For this reason, you should always use a syringe marked for U-100 insulin preparations. Failure to use the proper syringe can lead to a mistake in dosage, causing serious problems for you, such as a blood glucose level that is too low or too high.

Syringe Use:

To help avoid contamination and possible infection, follow these instructions exactly.

Disposable plastic syringes and needles should be used only once and then discarded. **NEEDLES AND SYRINGES MUST NOT BE SHARED.**

Reusable glass syringes and needles must be sterilized before each injection. **Follow the package directions supplied with your syringe.**

Preparing the Dose:

1. Wash your hands.
2. Inspect the HUMALOG in the vial. It should look clear and colourless. Do not use HUMALOG if it appears cloudy, thickened, or slightly coloured or if solid particles are visible.
3. Flip off the plastic protective cap but do not remove the stopper if using a new vial.
4. Wipe the top of the vial with an alcohol swab.
5. If you are mixing insulins, refer to the instructions for mixing below.
6. Remove the cover from the needle. Draw air into the syringe equal to your HUMALOG dose. Put the needle through the rubber top of the HUMALOG vial and inject the air into the vial.
7. Turn the vial and syringe upside down. Hold the vial and syringe firmly in one hand.
8. Making sure the tip of the needle is in the HUMALOG, withdraw the correct dose into the syringe.

9. Before removing the needle from the vial, check your syringe for air bubbles, which reduce the amount of HUMALOG. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push them out with the plunger and withdraw the correct dose.
10. Remove the needle from the vial and lay the syringe down so that the needle does not touch anything.

Mixing Humalog With Longer-Acting Insulin Formulations

MIXING HUMALOG WITH EITHER ANIMAL INSULINS OR INSULIN PREPARATIONS PRODUCED BY OTHER MANUFACTURERS IS NOT RECOMMENDED.

1. HUMALOG should be mixed with longer-acting insulins (HUMULIN N) only on the advice of your doctor.
2. Draw air into your syringe equal to the amount of longer-acting HUMULIN insulin you are taking. Insert the needle into the longer-acting insulin vial and inject the air, taking care not to come in contact with the insulin in the vial. Withdraw the needle.
3. Now inject air into your HUMALOG vial in the same manner, but do not withdraw the needle.
4. Turn the vial and syringe upside down.
5. Making sure the tip of the needle is in the HUMALOG, withdraw the correct dose of HUMALOG into the syringe.
6. Before removing the needle from the vial of HUMALOG, check your syringe for air bubbles, which reduce the amount of HUMALOG in it. If bubbles are present, hold the syringe straight up and tap its side until the bubbles float to the top. Push them out with the plunger and withdraw the correct dose. Gently roll or shake the long acting HUMULIN vial until the insulin is mixed.
7. Remove the needle from the vial of HUMALOG and insert it into the vial of the longer-acting HUMULIN insulin. Turn the vial and syringe upside down. Making sure the tip of the needle is in the insulin, withdraw your dose of longer-acting HUMULIN insulin.
8. Remove the needle and lay the syringe down so that the needle does not touch anything.

Follow your doctor's instructions on mixing your insulin just before giving your injection. HUMALOG should be injected immediately after mixing. It is important to be consistent in your method.

Syringes from different manufacturers may vary in the amount of space between the bottom line and the needle. Because of this, do not change the sequence of mixing, or the model and brand of syringe or needle that the doctor has prescribed.

Injection:

Cleanse the skin with alcohol where the injection is to be made. Stabilize the skin by spreading it or pinching up a large area. Insert the needle as instructed by your doctor. Push the plunger in as far as it will go. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area. To avoid tissue damage, give the next injection at a site at least 1 cm (0.5 inches) from the previous injection site.

Use of HUMALOG in an Insulin Infusion Pump:

1. Minimed, Accu-Check and other equivalent Health Canada approved insulin infusion pumps may be used to infuse HUMALOG. Read and follow the instructions that accompany the infusion pump.
2. Be sure to use the correct reservoir and catheter for the pump.
3. Change the HUMALOG in the reservoir at least every 14 days. Change the infusion set as recommended in pump manufacturers' instructions (typically every 3 days is recommended) or as directed by your healthcare professional. Use aseptic technique when inserting the infusion set.
4. In the event of a hypoglycemic episode, the infusion should be stopped until the episode is resolved. If repeated or severe low blood glucose levels occur, notify your health care professional and consider the need to reduce or temporarily stop your insulin infusion.
5. A pump malfunction or obstruction of the infusion set can result in a rapid rise in glucose levels. If an interruption to insulin flow is suspected, follow the instructions in the product literature and if appropriate, notify your health care professional.
6. When used with an insulin infusion pump, HUMALOG should not be mixed with any other insulin.

Usual dose

Your doctor has told you which insulin to use, how much, and when and how often to inject it. Because each patient's case of diabetes is different, this schedule has been individualized for you.

Your usual HUMALOG dose may be affected by changes in your food, activity, or work schedule. Carefully follow your doctor's instructions to allow for these changes. Other things that may affect your HUMALOG dose are illness, pregnancy, medication, exercise and travel.

Overdose

Hypoglycemia (too little glucose in the blood) is one of the most frequent adverse events experienced by insulin users. It can be brought about by:

1. Missing or delaying meals
2. Taking too much insulin
3. Exercising or working more than usual
4. An infection or illness (especially with diarrhea or vomiting)
5. A change in the body's need for insulin

6. Diseases of the adrenal, pituitary, or thyroid gland, or progression of kidney or liver disease
7. Interactions with other drugs that lower blood glucose, such as oral hypoglycemics, salicylates, sulfa antibiotics, and certain antidepressants
8. Consumption of alcoholic beverages

Dietary Implications:

If a usual meal cannot be obtained at the appropriate time, then to avoid hypoglycemia, you should take the amount of carbohydrate prescribed for this meal in the form of orange juice, syrup, candy, or bread and milk, without changing your insulin dosage. If it becomes necessary to omit a meal on account of nausea and vomiting, you should test your blood sugar level and notify your doctor.

Mild to moderate hypoglycemia may be treated by eating foods or drinks that contain sugar. Patients should always carry a quick source of sugar, such as candy mints or glucose tablets. More severe hypoglycemia may require the assistance of another person. Patients who are unable to take sugar orally or who are unconscious should be treated with intravenous administration of glucose at a medical facility or should be given an injection of glucagon (either intramuscular or subcutaneous). The patient should be given oral carbohydrates as soon as consciousness is recovered.

In case of drug overdose, contact a healthcare practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Hypoglycemia:

One of the most frequent adverse events experienced by insulin users is hypoglycemia (see PROPER USE OF THIS MEDICATION).

Diabetic Acidosis and Coma:

Diabetic acidosis may develop if your body has too little insulin. (This is the opposite of insulin reaction, which is the result of too much insulin in the blood). Diabetic acidosis may be brought on if you omit your insulin or take less than the doctor has prescribed, eat significantly more than your diet calls for, or develop a fever or infection. With acidosis, urine tests show a large amount of sugar and acetone.

The first symptoms of diabetic acidosis usually come on gradually, over a period of hours or days, and include a drowsy feeling, flushed face, thirst, and loss of appetite. Heavy breathing and a rapid pulse are more severe symptoms.

If uncorrected, loss of consciousness, coma, or death can result. Therefore, it is important that you obtain medical assistance immediately.

Lipoatrophy:

Rarely, administration of insulin subcutaneously can result in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue). If you notice either of these conditions, consult your doctor. A change in your injection technique may help alleviate the problem.

Allergy to Insulin:

Patients occasionally experience redness, swelling, and itching at the site of injection of insulin. This condition, called local allergy, usually clears up in a few days to a few weeks. If you have local reactions, contact your doctor, who may recommend a change in the type or species of insulin.

Less common, but potentially more serious, is generalized allergy to insulin, which may cause rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalized allergy may be life threatening. If you think you are having a generalized allergic reaction to insulin, notify a doctor immediately. Your doctor may recommend skin testing, that is, injecting small doses of other insulins into the skin, in order to select the best insulin for you to use. Patients who have had severe generalized allergic reactions to insulin should be skin tested with each new preparation to be used before treatment with that preparation is started.

This is not a complete list of side effects. For any unexpected effects while taking HUMALOG, contact your doctor or pharmacist.

HOW TO STORE IT

Prior to first use, HUMALOG insulin vials should be stored in a refrigerator between 2° and 8°C. Do not freeze. Do not expose to excessive heat or sunlight. The vial of HUMALOG that you are currently using can be kept unrefrigerated, for up to 28 days, as long as it is kept as cool as possible (below 30°C) and away from direct heat and light. Vials in use, or not refrigerated, should be discarded after 28 days even if they still contain HUMALOG. Do not use HUMALOG if it has been frozen.

DO NOT USE A VIAL OF HUMALOG AFTER THE EXPIRATION DATE STAMPED ON THE LABEL.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your healthcare professionals or pharmacist first, or Eli Lilly Canada Inc at: 1-888-545-5972 or visit the website at www.lilly.ca

The information in this document is current as of the last revision date shown below. For the most current information please visit our website or contact us directly.

This leaflet was prepared by Eli Lilly Canada Inc., Toronto, Ontario, M1N 2E8.

HUMALOG is distributed by: Eli Lilly Canada Inc.

You may need to read this package insert again. Please do not throw it away until you have finished your medicine.

Last revised: June 5, 2012

PART III: CONSUMER INFORMATION

HUMALOG® CARTRIDGES

(insulin lispro injection)

Solution for Injection, 100 units/mL, Lilly Standard

and HUMALOG® KWIKPEN™

(insulin lispro injection)

Solution for Injection, 100 units/mL, Lilly Standard

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ABOUT THIS MEDICATION

What the medication is used for:

Insulin is a hormone produced by the pancreas, a large gland that lies near the stomach. This hormone is necessary for the body's correct use of food, especially sugar. Diabetes occurs when the pancreas does not make enough insulin to meet your body's needs.

To control your diabetes, your doctor has prescribed injections of insulin to keep your blood glucose at a near-normal level.

What it does:

Insulin lispro is a recombinant DNA sourced human insulin analogue. HUMALOG consists of zinc-insulin lispro crystals dissolved in a clear fluid. HUMALOG is used to control high blood sugar (glucose) in people with diabetes. HUMALOG takes effect more rapidly and has a shorter duration of activity as compared to regular insulin.

The rapid onset of activity requires HUMALOG to be given within 15 minutes before a meal. When necessary, HUMALOG may be given shortly after a meal instead (within 20 minutes of the start of the meal). The time course of action of any insulin may vary to some extent in different individuals or at different times in the same individual. As with all insulin preparations, the duration of action of HUMALOG is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Proper control is important. Uncontrolled diabetes (hyperglycemia) over a long period of time can result in a number of serious problems such as blindness, kidney failure, poor circulation/heart attacks, strokes and/or nerve damage. These problems can be prevented or reduced by good diabetes management. This will require close and constant cooperation with your diabetes healthcare team including: yourself, your doctor and your diabetes educators (nurses, dietitians, social workers, pharmacists and other healthcare professionals). Thus, you can lead an active, healthy and productive life by eating a balanced daily diet, exercising regularly, and taking your insulin injections as prescribed.

You have been instructed to test your blood and/or your urine regularly for glucose. If your blood tests consistently show above- or below-normal glucose levels or your urine tests consistently show the presence of glucose, your diabetes is not properly controlled and you must let your doctor know.

When it should not be used:

- When your blood sugar is too low (hypoglycemia). After treating your low blood sugar, follow your healthcare provider's instructions on the use of HUMALOG.
- If you are allergic to anything in HUMALOG. A complete list of ingredients in HUMALOG is provided below.

What the medicinal ingredient is:

HUMALOG contains 100 units/mL of Human Insulin Analogue.

HUMALOG contains insulin lispro injection.

What the non-medicinal ingredients are:

HUMALOG contains glycerol, dibasic sodium phosphate, m-cresol, zinc (as ion) and water for injection. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

What dosage forms it comes in:

HUMALOG:

- Cartridge: 3.0 mL
- KwikPen, 3.0 mL prefilled pen

Also available in:

HUMALOG:

- Vial: 10 mL
- Vial: 3 mL

HUMALOG MIX25:

- Cartridge, 3.0 mL
- KwikPen, 3.0 mL prefilled pen

HUMALOG MIX50:

- Cartridge, 3.0 mL
- KwikPen, 3.0 mL prefilled pen

HUMALOG prefilled pens and cartridges are available in boxes of 5. HUMALOG cartridges are designed for use with Lilly injector systems. The cartridge or prefilled pen containing HUMALOG is not designed to allow any other insulin to be mixed in the cartridge or for the cartridge or prefilled pen to be reused.

For guidance on the use of the Pen (prefilled, disposable insulin injector), please refer to the separate Instructions for Use enclosed within the packaging.

DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND DIRECTION.

Always keep an extra supply of HUMALOG as well as a spare syringe and needle on hand. Always wear identification to indicate that you have diabetes so that appropriate treatment can be given if complications occur away from home.

When you receive your insulin from the pharmacy, always check to see that:

1. The name HUMALOG appears on the carton and cartridge or prefilled pen label.
2. The carton and cartridge or prefilled pen label is correct for your type of insulin.
3. The insulin strength is U-100.
4. The expiration date on the package will allow you to use the insulin before that date.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Hypoglycemia or low blood sugar is the most common adverse effect experienced by insulin users. Blood glucose monitoring is recommended for all patients with diabetes. Uncorrected hypoglycemic or hyperglycemic reactions can cause loss of consciousness, coma or even death. Information on how to recognize these symptoms is provided below.
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- HUMALOG should not be used if it is not water-clear and colourless or if it has formed a deposit of solid particles on the wall of the cartridge.
- Any change of insulin should be made cautiously and only under medical supervision. Changes in purity, strength, brand (manufacturer), type (regular, NPH, etc), species (beef, pork, beef-pork, human), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.
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- Insulin infusion pump: when used in an insulin infusion pump, HUMALOG should not be diluted or mixed with any other insulin. Carefully read and follow the insulin infusion pump manufacturer's instructions and this insert before using HUMALOG.

BEFORE you use HUMALOG talk to your doctor or pharmacist if:

- You have trouble with your kidneys or liver, your doctor may decide to alter your insulin dose.
- You drink alcohol (including wine and beer): watch for signs of hypoglycemia and never drink alcohol on an empty stomach.
- You exercise more than usual or if you want to change your usual diet. Exercise may lower your body's need for insulin during and for some time after the activity. Exercise may also speed up the effect of an insulin dose, especially if the exercise involves the area of injection site.
- You are ill. Illness, especially with nausea and vomiting, may cause your insulin requirements to change. Even if you are not eating, you will still require insulin. You and your doctor should establish a sick day plan for you to use in case of illness. When you are sick, test your blood/urine frequently.
- You are travelling across more than 2 time zones. You should consult your doctor concerning adjustments in your insulin schedule.
- You are pregnant. HUMALOG can be used in pregnancy if clinically indicated. Data on a large number of exposed pregnancies do not indicate any adverse effect of HUMALOG on pregnancy or on the health of the foetus/newborn. Good control of diabetes is especially important for you and your unborn baby. Pregnancy may make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or are nursing a baby, consult your doctor.
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The use of thiazolidinediones (such as rosiglitazone and pioglitazone), alone or in combination with other antidiabetic agents (including insulin), has been associated with heart failure and swelling of the lower extremities. Please contact your physician immediately if you develop

symptoms of shortness of breath, fatigue, exercise intolerance, or swelling of the lower extremities while you are on these agents.

PROPER USE OF THIS MEDICATION

HUMALOG

HUMALOG is a sterile solution. HUMALOG should be given by subcutaneous injection, or by continuous subcutaneous insulin infusion pump. The concentration of HUMALOG in 3.0 mL cartridges or prefilled pens is 100 units/mL (U-100).

When used as a meal-time insulin, HUMALOG should be given within 15 minutes before a meal, or when necessary shortly after a meal instead (within 20 minutes of the start of the meal).

HUMALOG is a clear and colourless liquid with a water-like appearance and consistency. Do not use if it appears cloudy, thickened, or slightly coloured or if solid particles are visible. Always check the appearance of your cartridge or prefilled pen of HUMALOG before using, and if you note anything unusual in its appearance or notice your insulin requirements changing markedly, consult your doctor.

Injection Procedure

Preparing a Cartridge of HUMALOG for Insertion in a Pen:

1. Wash your hands.
2. Before inserting the HUMALOG cartridge into the pen, inspect it to make sure the contents look clear and colourless. Do not use the HUMALOG cartridge if it appears cloudy, thickened, or slightly coloured or if solid particles are visible.
3. Follow the pen manufacturer's directions carefully for loading the cartridge into the pen.

Injecting the Dose:

1. Wash your hands.
2. Use an alcohol swab to wipe the exposed rubber surface on the metal cap end of the cartridge or prefilled pen.
3. Inspect the HUMALOG in the cartridge. It should look clear and colourless. Do not use HUMALOG if it appears cloudy, thickened, or slightly coloured or if solid particles are visible.
4. Follow pen manufacturer's directions for attaching needle.
5. Hold the pen with needle pointing straight up. If there are large bubbles, tap the side of the pen until they float to the top. Remove the bubbles and the air in the needle by setting the pen to a 2-unit dose and depressing the plunger. Repeat this step if necessary until a drop of HUMALOG appears at the end of the needle.
6. To avoid tissue damage, injection sites can be rotated so that the same site is not used more than approximately once a month.
7. Cleanse the skin with alcohol where the injection is to be made.

8. With one hand, stabilize the skin by spreading it or pinching up a large area.
9. Insert the needle as instructed by your doctor.
10. To inject HUMALOG, follow the pen manufacturer's instructions.
11. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.
12. Immediately after an injection, remove the needle from the pen. This will guard against contamination and prevent leakage, re-entry of air, and potential needle clogs. Dispose of the needle in a responsible manner. Do not reuse needle. **NEEDLES, CARTRIDGES, AND PENS MUST NOT BE SHARED.**
13. Use the gauge on the side of the 3.0 mL cartridge to help you judge how much HUMALOG remains. The distance between each mark is approximately 20 units for 3.0 mL cartridges. When the leading edge of the plunger reaches the last mark on the gauge there is approximately 20 units of HUMALOG remaining in the cartridge. You may continue to use the cartridge until the plunger will no longer advance. See injection instructions accompanying the pen to ensure that a complete dose is obtained.

Use of HUMALOG in an Insulin Infusion Pump:

1. Minimed, Accu-Check and other equivalent Health Canada approved insulin infusion pumps may be used to infuse HUMALOG. Read and follow the instructions that accompany the infusion pump.
2. Be sure to use the correct reservoir and catheter for the pump.
3. Change the HUMALOG in the reservoir at least every 14 days. Change the infusion set as recommended in pump manufacturers' instructions (typically every 3 days is recommended) or as directed by your healthcare professional. Use aseptic technique when inserting the infusion set.
4. In the event of a hypoglycemic episode, the infusion should be stopped until the episode is resolved. If repeated or severe low blood glucose levels occur, notify your health care professional and consider the need to reduce or temporarily stop your insulin infusion.
5. A pump malfunction or obstruction of the infusion set can result in a rapid rise in glucose levels. If an interruption to insulin flow is suspected, follow the instructions in the product literature and if appropriate, notify your health care professional.
6. When used with an insulin infusion pump, HUMALOG should not be mixed with any other insulin.

Usual dose

Your doctor has told you which insulin to use, how much, and when and how often to inject it. Because each patient's case of diabetes is different, this schedule has been individualized for you.

Your usual HUMALOG dose may be affected by changes in your food, activity, or work schedule. Carefully follow your doctor's instructions to allow for these changes. Other things that may affect your HUMALOG dose are illness, pregnancy, medication, exercise and travel.

Overdose

Hypoglycemia (too little glucose in the blood) is one of the most frequent adverse events experienced by insulin users. It can be brought about by:

1. Missing or delaying meals
2. Taking too much insulin
3. Exercising or working more than usual
4. An infection or illness (especially with diarrhea or vomiting)
5. A change in the body's need for insulin
6. Diseases of the adrenal, pituitary, or thyroid gland, or progression of kidney or liver disease
7. Interactions with other drugs that lower blood glucose, such as oral hypoglycemics, salicylates, sulfa antibiotics, and certain antidepressants
8. Consumption of alcoholic beverages

Dietary Implications:

If a usual meal cannot be obtained at the appropriate time, then to avoid hypoglycemia, you should take the amount of carbohydrate prescribed for this meal in the form of orange juice, syrup, candy, or bread and milk, without changing your insulin dosage. If it becomes necessary to omit a meal on account of nausea and vomiting, you should test your blood sugar level and notify your doctor.

Mild to moderate hypoglycemia may be treated by eating foods or drinks that contain sugar. Patients should always carry a quick source of sugar, such as candy mints or glucose tablets. More severe hypoglycemia may require the assistance of another person. Patients who are unable to take sugar orally or who are unconscious should be treated with intravenous administration of glucose at a medical facility or should be given an injection of glucagon (either intramuscular or subcutaneous). The patient should be given oral carbohydrates as soon as consciousness is recovered.

In case of drug overdose, contact a healthcare practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Hypoglycemia:

One of the most frequent adverse events experienced by insulin users is hypoglycemia (see PROPER USE OF THIS MEDICATION).

Diabetic Acidosis and Coma:

Diabetic acidosis may develop if your body has too little insulin. (This is the opposite of insulin reaction, which is the result of too much insulin in the blood). Diabetic acidosis may be brought on if you omit your insulin or take less than the doctor has prescribed, eat significantly more than your diet calls for, or develop a fever or infection. With acidosis, urine tests show a large amount of sugar and acetone.

The first symptoms of diabetic acidosis usually come on gradually, over a period of hours or days, and include a drowsy feeling, flushed face, thirst, and loss of appetite. Heavy breathing and a rapid pulse are more severe symptoms.

If uncorrected, loss of consciousness, coma, or death can result. Therefore, it is important that you obtain medical assistance immediately.

Lipoatrophy:

Rarely, administration of insulin subcutaneously can result in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue). If you notice either of these conditions, consult your doctor. A change in your injection technique may help alleviate the problem.

Allergy to Insulin:

Patients occasionally experience redness, swelling, and itching at the site of injection of insulin. This condition, called local allergy, usually clears up in a few days to a few weeks. If you have local reactions, contact your doctor, who may recommend a change in the type or species of insulin.

Less common, but potentially more serious, is generalized allergy to insulin, which may cause rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalized allergy may be life threatening. If you think you are having a generalized allergic reaction to insulin, notify a doctor immediately. Your doctor may recommend skin testing, that is, injecting small doses of other insulins into the skin, in order to select the best insulin for you to use. Patients who have had severe generalized allergic reactions to insulin should be skin tested with each new preparation to be used before treatment with that preparation is started.

This is not a complete list of side effects. For any unexpected effects while taking HUMALOG, contact your doctor or pharmacist.

HOW TO STORE IT

Prior to first use, HUMALOG insulin cartridges or prefilled pens should be stored in a refrigerator between 2° and 8°C. Do not freeze. Do not expose to excessive heat or sunlight. The pen and cartridge of HUMALOG that you are currently using should not be refrigerated but should be kept as cool as possible (below 30°C) and away from direct heat and light. Do not use HUMALOG if it has been frozen. Cartridges or

prefilled pens in use, or not refrigerated, should be discarded after 28 days, even if they still contain HUMALOG.

DO NOT USE A CARTRIDGE OR PREFILLED PEN OF HUMALOG AFTER THE EXPIRATION DATE STAMPED ON THE LABEL.

Dispose of used needles in a puncture-resistant container or as directed by your healthcare professional.

Dispose of used pens as instructed by your healthcare professional and without the needle attached.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at
www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your healthcare professionals or pharmacist first, or Eli Lilly Canada Inc at:

1-888-545-5972 or visit the website at www.lilly.ca

The information in this document is current as of the last revision date shown below. For the most current information please visit our website or contact us directly.

This leaflet was prepared by Eli Lilly Canada Inc., Toronto, Ontario, M1N 2E8.

HUMALOG is distributed by: Eli Lilly Canada Inc.

You may need to read this package insert again. Please do not throw it away until you have finished your medicine.

Last revised: June 5, 2012

PART III: CONSUMER INFORMATION

HUMALOG® MIX25® CARTRIDGES

(25% insulin lispro injection, 75% insulin lispro protamine suspension)

Suspension for Injection, 100 units/mL, Lilly Standard

and HUMALOG® MIX25® KWIKPEN™

(25% insulin lispro injection, 75% insulin lispro protamine suspension)

Suspension for Injection, 100 units/mL, Lilly Standard

This leaflet is part III of a three-part "Product Monograph" published when HUMALOG® MIX25® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about HUMALOG® MIX25®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Insulin is a hormone produced by the pancreas, a large gland that lies near the stomach. This hormone is necessary for the body's correct use of food, especially sugar. Diabetes occurs when the pancreas does not make enough insulin to meet your body's needs.

To control your diabetes, your doctor has prescribed injections of insulin to keep your blood glucose at a near-normal level.

What it does:

Insulin lispro is a recombinant DNA sourced human insulin analogue. HUMALOG MIX25 is a mixture of fast-acting (insulin lispro) and longer-acting (insulin lispro protamine) man-made insulins. HUMALOG MIX25 is used to control high blood sugar (glucose) in people with diabetes. HUMALOG MIX25 takes effect more rapidly and has a shorter duration of activity as compared to regular insulin.

The rapid onset of activity requires HUMALOG MIX25 to be given within 15 minutes before a meal. The time course of action of any insulin may vary to some extent in different individuals or at different times in the same individual. As with all insulin preparations, the duration of action of HUMALOG MIX25 is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Proper control is important. Uncontrolled diabetes (hyperglycemia) over a long period of time can result in a number of serious problems such as blindness, kidney failure, poor circulation/heart attacks, strokes and/or nerve damage. These problems can be prevented or reduced by good diabetes management. This will require close and constant cooperation with your diabetes healthcare team including: yourself, your doctor and your diabetes educators (nurses, dietitians, social workers, pharmacists and other healthcare professionals). Thus, you can lead an active, healthy and productive life by eating a

balanced daily diet, exercising regularly, and taking your insulin injections as prescribed.

You have been instructed to test your blood and/or your urine regularly for glucose. If your blood tests consistently show above- or below-normal glucose levels or your urine tests consistently show the presence of glucose, your diabetes is not properly controlled and you must let your doctor know.

When it should not be used:

- When your blood sugar is too low (hypoglycemia). After treating your low blood sugar, follow your healthcare provider's instructions on the use of HUMALOG MIX25 insulin.
- If you are allergic to anything in HUMALOG MIX25. A complete list of ingredients in HUMALOG MIX25 insulin is provided below.

What the medicinal ingredient is:

HUMALOG MIX25 insulin contains 100 units/mL of Human Insulin Analogue.

HUMALOG MIX25 contains a mix of insulin lispro injection (25%) and insulin lispro protamine suspension (75%).

What the non-medicinal ingredients are:

HUMALOG MIX25 contains glycerol, dibasic sodium phosphate, m-cresol, zinc (as ion) and water for injection. Hydrochloric acid or sodium hydroxide may be added to adjust pH. HUMALOG MIX25 also contains liquefied phenol, protamine sulphate, and zinc oxide.

What dosage forms it comes in:

HUMALOG MIX25:

- Cartridge, 3.0 mL
- KwikPen, 3.0 mL prefilled pen

Also available in:

HUMALOG:

- Vial: 10 mL
- Vial: 3 mL
- Cartridge: 3.0 mL
- KwikPen, 3.0 mL prefilled pen

HUMALOG MIX50:

- Cartridge, 3.0 mL
- KwikPen, 3.0 mL prefilled pen

HUMALOG MIX25 prefilled pens and cartridges are available in boxes of 5. HUMALOG MIX25 cartridges are designed for use with Lilly injector systems. The cartridge or prefilled pen containing HUMALOG MIX25 is not designed to allow any other insulin to be mixed in the cartridge or for the cartridge or prefilled pen to be reused.

For guidance on the use of the Pen (prefilled, disposable insulin injector), please refer to the separate Instructions for Use enclosed within the packaging.

DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND DIRECTION.

Always keep an extra supply of HUMALOG MIX25 as well as a spare syringe and needle on hand. Always wear identification to indicate that you have diabetes so that appropriate treatment can be given if complications occur away from home.

When you receive your insulin from the pharmacy, always check to see that:

1. The name HUMALOG MIX25 appears on the carton and cartridge or prefilled pen label.
2. The carton and cartridge or prefilled pen label is correct for your type of insulin.
3. The insulin strength is U-100.
4. The expiration date on the package will allow you to use the insulin before that date.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Hypoglycemia or low blood sugar is the most common adverse effect experienced by insulin users. Blood glucose monitoring is recommended for all patients with diabetes. Uncorrected hypoglycemic or hyperglycemic reactions can cause loss of consciousness, coma or even death. Information on how to recognize these symptoms is provided below.
- This Lilly human insulin analogue differs from other insulins because it has a unique structure, a very quick onset of action and a short duration of activity. HUMALOG MIX25 should be given within 15 minutes before a meal.
- HUMALOG MIX25 is a white suspension and should be administered by subcutaneous injection only. HUMALOG MIX25 must not be administered intravenously.
- Any change of insulin should be made cautiously and only under medical supervision. Changes in purity, strength, brand (manufacturer), type (regular, NPH, etc), species (beef, pork, beef-pork, human), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.
- Mixing of HUMALOG MIX25 with either animal insulins or insulin preparations produced by other manufacturers is not recommended.
- Patients taking HUMALOG MIX25 may require a change in dosage from that used with other insulins. If an adjustment is needed, it may occur with the first dose or over a period of several weeks.

BEFORE you use HUMALOG MIX25 talk to your doctor or pharmacist if:

- You have trouble with your kidneys or liver, your doctor may decide to alter your insulin dose.
- You drink alcohol (including wine and beer): watch for signs of hypoglycemia and never drink alcohol on an empty stomach.
- You exercise more than usual or if you want to change your usual diet. Exercise may lower your body's need for insulin during and for some time after the activity. Exercise may also speed up the effect of an insulin dose, especially if the exercise involves the area of injection site.
- You are ill. Illness, especially with nausea and vomiting, may cause your insulin requirements to change. Even if you are not eating, you will still require insulin. You and your doctor should establish a sick day plan for you to use in case of illness. When you are sick, test your blood/urine frequently.
- You are travelling across more than 2 time zones. You should consult your doctor concerning adjustments in your insulin schedule.
- You are pregnant. HUMALOG MIX25 can be used in pregnancy if clinically indicated. Data on a large number of exposed pregnancies do not indicate any adverse effect of HUMALOG MIX25 on pregnancy or on the health of the foetus/newborn. Good control of diabetes is especially important for you and your unborn baby. Pregnancy may make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or are nursing a baby, consult your doctor.
- When you use other medicines. Many medicines affect the way glucose works in your body and this may influence your insulin dose. Listed below are the most common medicines, which may affect your insulin treatment. Talk to your doctor or pharmacist if you take, or change any other medicines, even those not prescribed.

INTERACTIONS WITH THIS MEDICATION

Insulin requirements may be increased if you are taking other drugs with hyperglycemic activity, such as oral contraceptives (for example, birth control pills, injections and patches), corticosteroids, or thyroid replacement therapy. Insulin requirements may be decreased in the presence of agents such as oral antidiabetic agents, salicylates (aspirin), sulfa antibiotics, certain antidepressants (monoamine oxidase inhibitors), beta-blockers, alcohol, ACE-inhibitors and angiotensin II receptor blockers. Always discuss any medications you are taking with your doctor.

The use of thiazolidinediones (such as rosiglitazone and pioglitazone), alone or in combination with other antidiabetic agents (including insulin), has been associated with heart failure and swelling of the lower extremities. Please contact your physician immediately if you develop symptoms of shortness of breath, fatigue, exercise

intolerance, or swelling of the lower extremities while you are on these agents.

PROPER USE OF THIS MEDICATION

HUMALOG MIX25

The 3.0 mL cartridge is only for use in 3.0 mL pens.

Preparing a Cartridge of HUMALOG MIX25 for Insertion in a Pen

1. Wash your hands.
2. Cartridges containing HUMALOG MIX25 should be rotated in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Cartridges contain a small glass bead to assist mixing. Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose.
3. Inspect HUMALOG MIX25 cartridge before inserting it into the pen. Do not use the HUMALOG MIX25 cartridge if clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance.
4. Follow the pen manufacturer's directions carefully for loading the cartridge into the pen.

Injecting the Dose:

1. Wash your hands.
2. Use an alcohol swab to wipe the exposed rubber surface on the metal cap end of the cartridge or prefilled pen.
3. Inspect the HUMALOG MIX25 in the cartridge. It should look uniformly cloudy or milky.
4. Follow pen manufacturer's directions for attaching needle.
5. Hold the pen with needle pointing straight up. If there are large bubbles, tap the side of the pen until they float to the top. Remove the bubbles and the air in the needle by setting the pen to a 2-unit dose and depressing the plunger. Repeat this step if necessary until a drop of HUMALOG MIX25 appears at the end of the needle.
6. To avoid tissue damage, injection sites can be rotated so that the same site is not used more than approximately once a month.
7. Cleanse the skin with alcohol where the injection is to be made.
8. With one hand, stabilize the skin by spreading it or pinching up a large area.
9. Insert the needle as instructed by your doctor.
10. To inject HUMALOG MIX25, follow the pen manufacturer's instructions.
11. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.
12. Immediately after an injection, remove the needle from the pen. This will guard against contamination and prevent leakage, re-entry of air, and potential needle clogs. Dispose of the needle in a responsible manner. Do not reuse needle.

NEEDLES, CARTRIDGES, AND PENS MUST NOT BE SHARED.

13. Use the gauge on the side of the 3.0 mL cartridge to help you judge how much HUMALOG MIX25 remains once it is in use. The distance between each mark is approximately 20 units for 3.0 mL cartridges. When the leading edge of the plunger reaches the last mark on the gauge there is approximately 20 units of HUMALOG MIX25 remaining in the cartridge. You may continue to use the cartridge until the plunger will no longer advance. See injection instructions accompanying the pen to ensure that a complete dose is obtained.

Usual dose

Your doctor has told you which insulin to use, how much, and when and how often to inject it. Because each patient's case of diabetes is different, this schedule has been individualized for you.

Your usual HUMALOG MIX25 dose may be affected by changes in your food, activity, or work schedule. Carefully follow your doctor's instructions to allow for these changes. Other things that may affect your HUMALOG MIX25 dose are illness, pregnancy, medication, exercise and travel.

Overdose

Hypoglycemia (too little glucose in the blood) is one of the most frequent adverse events experienced by insulin users. It can be brought about by:

1. Missing or delaying meals
2. Taking too much insulin
3. Exercising or working more than usual
4. An infection or illness (especially with diarrhea or vomiting)
5. A change in the body's need for insulin
6. Diseases of the adrenal, pituitary, or thyroid gland, or progression of kidney or liver disease
7. Interactions with other drugs that lower blood glucose, such as oral hypoglycemics, salicylates, sulfa antibiotics, and certain antidepressants
8. Consumption of alcoholic beverages

Dietary Implications:

If a usual meal cannot be obtained at the appropriate time, then to avoid hypoglycemia, you should take the amount of carbohydrate prescribed for this meal in the form of orange juice, syrup, candy, or bread and milk, without changing your insulin dosage. If it becomes necessary to omit a meal on account of nausea and vomiting, you should test your blood sugar level and notify your doctor.

Mild to moderate hypoglycemia may be treated by eating foods or drinks that contain sugar. Patients should always carry a quick source of sugar, such as candy mints or glucose tablets. More severe hypoglycemia may require the assistance of another person. Patients who are unable to take sugar orally or who are unconscious should be treated with

intravenous administration of glucose at a medical facility or should be given an injection of glucagon (either intramuscular or subcutaneous). The patient should be given oral carbohydrates as soon as consciousness is recovered.

In case of drug overdose, contact a healthcare practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Hypoglycemia:

One of the most frequent adverse events experienced by insulin users is hypoglycaemia (see PROPER USE OF THIS MEDICATION).

Diabetic Acidosis and Coma:

Diabetic acidosis may develop if your body has too little insulin. (This is the opposite of insulin reaction, which is the result of too much insulin in the blood). Diabetic acidosis may be brought on if you omit your insulin or take less than the doctor has prescribed, eat significantly more than your diet calls for, or develop a fever or infection. With acidosis, urine tests show a large amount of sugar and acetone.

The first symptoms of diabetic acidosis usually come on gradually, over a period of hours or days, and include a drowsy feeling, flushed face, thirst, and loss of appetite. Heavy breathing and a rapid pulse are more severe symptoms.

If uncorrected, loss of consciousness, coma, or death can result. Therefore, it is important that you obtain medical assistance immediately.

Lipoatrophy:

Rarely, administration of insulin subcutaneously can result in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue). If you notice either of these conditions, consult your doctor. A change in your injection technique may help alleviate the problem.

Allergy to Insulin:

Patients occasionally experience redness, swelling, and itching at the site of injection of insulin. This condition, called local allergy, usually clears up in a few days to a few weeks. If you have local reactions, contact your doctor, who may recommend a change in the type or species of insulin.

Less common, but potentially more serious, is generalized allergy to insulin, which may cause rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalized allergy may be life threatening. If you think you are having a generalized allergic reaction to insulin, notify a doctor immediately. Your doctor may recommend skin testing, that is, injecting small doses of other insulins into the skin, in order to select the best insulin for you to use. Patients who have had severe generalized allergic reactions to insulin should be skin tested with each new

preparation to be used before treatment with that preparation is started.

This is not a complete list of side effects. For any unexpected effects while taking HUMALOG MIX25, contact your doctor or pharmacist.

HOW TO STORE IT

Prior to first use, HUMALOG MIX25 cartridges or prefilled pens should be stored in a refrigerator between 2° and 8°C. Do not freeze. Do not expose to excessive heat or sunlight. The pen and cartridge of HUMALOG MIX25 that you are currently using should not be refrigerated but should be kept as cool as possible (below 30°C) and away from direct heat and light. Do not use HUMALOG MIX25 if it has been frozen. Cartridges or prefilled pens in use, or not refrigerated, should be discarded after 28 days, even if they still contain HUMALOG MIX25.

DO NOT USE A CARTRIDGE OR PREFILLED PEN OF HUMALOG MIX25 AFTER THE EXPIRATION DATE STAMPED ON THE LABEL. Dispose of used needles in a puncture-resistant container or as directed by your healthcare professional.

Dispose of used pens as instructed by your healthcare professional and without the needle attached.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your healthcare professionals or pharmacist first, or Eli Lilly Canada Inc at: 1-888-545-5972 or visit the website at www.lilly.ca

The information in this document is current as of the last revision date shown below. For the most current information please visit our website or contact us directly.

This leaflet was prepared by Eli Lilly Canada Inc., Toronto, Ontario, M1N 2E8. HUMALOG MIX25 is distributed by: Eli Lilly Canada Inc.

You may need to read this package insert again. Please do not throw it away until you have finished your medicine.

Last revised: June 5, 2012

PART III: CONSUMER INFORMATION

HUMALOG MIX50® CARTRIDGES

(50% insulin lispro injection, 50% insulin lispro protamine suspension)

Suspension for Injection, 100 units/mL, Lilly Standard

and HUMALOG MIX50® KWIKPEN™

(50% insulin lispro injection, 50% insulin lispro protamine suspension)

Suspension for Injection, 100 units/mL, Lilly Standard

This leaflet is part III of a three-part "Product Monograph" published when HUMALOG MIX50® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about HUMALOG MIX50®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Insulin is a hormone produced by the pancreas, a large gland that lies near the stomach. This hormone is necessary for the body's correct use of food, especially sugar. Diabetes occurs when the pancreas does not make enough insulin to meet your body's needs.

To control your diabetes, your doctor has prescribed injections of insulin to keep your blood glucose at a near-normal level.

What it does:

Insulin lispro is a recombinant DNA sourced human insulin analogue. HUMALOG MIX50 is a mixture of fast-acting (insulin lispro) and longer-acting (insulin lispro protamine) man-made insulins. HUMALOG MIX50 is used to control high blood sugar (glucose) in people with diabetes. HUMALOG MIX50 takes effect more rapidly and has a shorter duration of activity as compared to regular insulin.

The rapid onset of activity requires HUMALOG MIX50 to be given within 15 minutes before a meal. The time course of action of any insulin may vary to some extent in different individuals or at different times in the same individual. As with all insulin preparations, the duration of action of HUMALOG MIX50 is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Proper control is important. Uncontrolled diabetes (hyperglycemia) over a long period of time can result in a number of serious problems such as blindness, kidney failure, poor circulation/heart attacks, strokes and/or nerve damage. These problems can be prevented or reduced by good diabetes management. This will require close and constant cooperation with your diabetes healthcare team including: yourself, your doctor and your diabetes educators (nurses, dietitians, social workers, pharmacists and other healthcare professionals). Thus, you can lead an active, healthy and productive life by eating a

balanced daily diet, exercising regularly, and taking your insulin injections as prescribed.

You have been instructed to test your blood and/or your urine regularly for glucose. If your blood tests consistently show above- or below-normal glucose levels or your urine tests consistently show the presence of glucose, your diabetes is not properly controlled and you must let your doctor know.

When it should not be used:

- When your blood sugar is too low (hypoglycemia). After treating your low blood sugar, follow your healthcare provider's instructions on the use of HUMALOG MIX50 insulin.
- If you are allergic to anything in HUMALOG MIX50. A complete list of ingredients in HUMALOG MIX50 insulin is provided below.

What the medicinal ingredient is:

HUMALOG MIX50 insulin contains 100 units/mL of Human Insulin Analogue.

HUMALOG MIX50 contains a mix of insulin lispro injection (50%) and insulin lispro protamine suspension (50%).

What the non-medicinal ingredients are:

HUMALOG MIX50 contains glycerol, dibasic sodium phosphate, m-cresol, zinc (as ion) and water for injection. Hydrochloric acid or sodium hydroxide may be added to adjust pH. HUMALOG MIX50 also contains liquefied phenol, protamine sulphate, and zinc oxide.

What dosage forms it comes in:

HUMALOG MIX50:

- Cartridge, 3.0 mL
- KwikPen, 3.0 mL prefilled pen

Also available in:

HUMALOG:

- Vial: 10 mL
- Vial: 3 mL
- Cartridge: 3.0 mL
- KwikPen, 3.0 mL prefilled pen

HUMALOG MIX25:

- Cartridge, 3.0 mL
- KwikPen, 3.0 mL prefilled pen

HUMALOG MIX50 prefilled pens and cartridges are available in boxes of 5. HUMALOG MIX50 cartridges are designed for use with Lilly injector systems. The cartridge or prefilled pen containing HUMALOG MIX50 is not designed to allow any other insulin to be mixed in the cartridge or for the cartridge or prefilled pen to be reused.

For guidance on the use of the Pen (prefilled, disposable insulin injector), please refer to the separate Instructions for Use enclosed within the packaging.

DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND DIRECTION.

Always keep an extra supply of HUMALOG MIX50 as well as a spare syringe and needle on hand. Always wear identification to indicate that you have diabetes so that appropriate treatment can be given if complications occur away from home.

When you receive your insulin from the pharmacy, always check to see that:

1. The name HUMALOG MIX50 appears on the carton and cartridge or prefilled pen label.
2. The carton and cartridge or prefilled pen label is correct for your type of insulin.
3. The insulin strength is U-100.
4. The expiration date on the package will allow you to use the insulin before that date.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Hypoglycemia or low blood sugar is the most common adverse effect experienced by insulin users. Blood glucose monitoring is recommended for all patients with diabetes. Uncorrected hypoglycemic or hyperglycemic reactions can cause loss of consciousness, coma or even death. Information on how to recognize these symptoms is provided below.
- This Lilly human insulin analogue differs from other insulins because it has a unique structure, a very quick onset of action and a short duration of activity. HUMALOG MIX50 should be given within 15 minutes before a meal.
- HUMALOG MIX50 is a white suspension and should be administered by subcutaneous injection only. HUMALOG MIX50 must not be administered intravenously.
- Any change of insulin should be made cautiously and only under medical supervision. Changes in purity, strength, brand (manufacturer), type (regular, NPH, etc), species (beef, pork, beef-pork, human), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.
- Mixing of HUMALOG MIX50 with either animal insulins or insulin preparations produced by other manufacturers is not recommended.
- Patients taking HUMALOG MIX50 may require a change in dosage from that used with other insulins. If an adjustment is needed, it may occur with the first dose or over a period of several weeks.

BEFORE you use HUMALOG MIX50 talk to your doctor or pharmacist if:

- You have trouble with your kidneys or liver, your doctor may decide to alter your insulin dose.
- You drink alcohol (including wine and beer): watch for signs of hypoglycemia and never drink alcohol on an empty stomach.
- You exercise more than usual or if you want to change your usual diet. Exercise may lower your body's need for insulin during and for some time after the activity. Exercise may also speed up the effect of an insulin dose, especially if the exercise involves the area of injection site.
- You are ill. Illness, especially with nausea and vomiting, may cause your insulin requirements to change. Even if you are not eating, you will still require insulin. You and your doctor should establish a sick day plan for you to use in case of illness. When you are sick, test your blood/urine frequently.
- You are travelling across more than 2 time zones. You should consult your doctor concerning adjustments in your insulin schedule.
- You are pregnant. HUMALOG MIX50 can be used in pregnancy if clinically indicated. Data on a large number of exposed pregnancies do not indicate any adverse effect of HUMALOG MIX50 on pregnancy or on the health of the foetus/newborn. Good control of diabetes is especially important for you and your unborn baby. Pregnancy may make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or are nursing a baby, consult your doctor.
- When you use other medicines. Many medicines affect the way glucose works in your body and this may influence your insulin dose. Listed below are the most common medicines, which may affect your insulin treatment. Talk to your doctor or pharmacist if you take, or change any other medicines, even those not prescribed.

INTERACTIONS WITH THIS MEDICATION

Insulin requirements may be increased if you are taking other drugs with hyperglycemic activity, such as oral contraceptives (for example, birth control pills, injections and patches), corticosteroids, or thyroid replacement therapy. Insulin requirements may be decreased in the presence of agents such as oral antidiabetic agents, salicylates (aspirin), sulfa antibiotics, certain antidepressants (monoamine oxidase inhibitors), beta-blockers, alcohol, ACE-inhibitors and angiotensin II receptor blockers. Always discuss any medications you are taking with your doctor.

The use of thiazolidinediones (such as rosiglitazone and pioglitazone), alone or in combination with other antidiabetic agents (including insulin), has been associated with heart failure and swelling of the lower extremities. Please contact your physician immediately if you develop symptoms of shortness of breath, fatigue, exercise

intolerance, or swelling of the lower extremities while you are on these agents.

PROPER USE OF THIS MEDICATION

HUMALOG MIX50

The 3.0 mL cartridge is only for use in 3.0 mL pens.

Preparing a Cartridge of HUMALOG MIX50 for Insertion in a Pen

1. Wash your hands.
2. Cartridges containing HUMALOG MIX50 should be rotated in the palms of the hands ten times and inverted 180° ten times immediately before use to resuspend insulin until it appears uniformly cloudy or milky. If not, repeat the above procedure until contents are mixed. Cartridges contain a small glass bead to assist mixing. Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose.
3. Inspect HUMALOG MIX50 cartridge before inserting it into the pen. Do not use the HUMALOG MIX50 cartridge if clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance.
4. Follow the pen manufacturer's directions carefully for loading the cartridge into the pen.

Injecting the Dose:

1. Wash your hands.
2. Use an alcohol swab to wipe the exposed rubber surface on the metal cap end of the cartridge or prefilled pen.
3. Inspect the HUMALOG MIX50 in the cartridge. It should look uniformly cloudy or milky.
4. Follow pen manufacturer's directions for attaching needle.
5. Hold the pen with needle pointing straight up. If there are large bubbles, tap the side of the pen until they float to the top. Remove the bubbles and the air in the needle by setting the pen to a 2-unit dose and depressing the plunger. Repeat this step if necessary until a drop of HUMALOG MIX50 appears at the end of the needle.
6. To avoid tissue damage, injection sites can be rotated so that the same site is not used more than approximately once a month.
7. Cleanse the skin with alcohol where the injection is to be made.
8. With one hand, stabilize the skin by spreading it or pinching up a large area.
9. Insert the needle as instructed by your doctor.
10. To inject HUMALOG MIX50, follow the pen manufacturer's instructions.
11. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.
12. Immediately after an injection, remove the needle from the pen. This will guard against contamination and prevent leakage, re-entry of air, and potential needle clogs. Dispose of the needle in a responsible manner. Do not reuse needle.

NEEDLES, CARTRIDGES, AND PENS MUST NOT BE SHARED.

13. Use the gauge on the side of the 3.0 mL cartridge to help you judge how much HUMALOG MIX50 remains once it is in use. The distance between each mark is approximately 20 units for 3.0 mL cartridges. When the leading edge of the plunger reaches the last mark on the gauge there is approximately 20 units of HUMALOG MIX50 remaining in the cartridge. You may continue to use the cartridge until the plunger will no longer advance. See injection instructions accompanying the pen to ensure that a complete dose is obtained.

Usual dose

Your doctor has told you which insulin to use, how much, and when and how often to inject it. Because each patient's case of diabetes is different, this schedule has been individualized for you.

Your usual HUMALOG MIX50 dose may be affected by changes in your food, activity, or work schedule. Carefully follow your doctor's instructions to allow for these changes. Other things that may affect your HUMALOG MIX50 dose are illness, pregnancy, medication, exercise and travel.

Overdose

Hypoglycemia (too little glucose in the blood) is one of the most frequent adverse events experienced by insulin users. It can be brought about by:

1. Missing or delaying meals
2. Taking too much insulin
3. Exercising or working more than usual
4. An infection or illness (especially with diarrhea or vomiting)
5. A change in the body's need for insulin
6. Diseases of the adrenal, pituitary, or thyroid gland, or progression of kidney or liver disease
7. Interactions with other drugs that lower blood glucose, such as oral hypoglycemics, salicylates, sulfa antibiotics, and certain antidepressants
8. Consumption of alcoholic beverages

Dietary Implications:

If a usual meal cannot be obtained at the appropriate time, then to avoid hypoglycemia, you should take the amount of carbohydrate prescribed for this meal in the form of orange juice, syrup, candy, or bread and milk, without changing your insulin dosage. If it becomes necessary to omit a meal on account of nausea and vomiting, you should test your blood sugar level and notify your doctor.

Mild to moderate hypoglycemia may be treated by eating foods or drinks that contain sugar. Patients should always carry a quick source of sugar, such as candy mints or glucose tablets. More severe hypoglycemia may require the assistance of another person. Patients who are unable to take

sugar orally or who are unconscious should be treated with intravenous administration of glucose at a medical facility or should be given an injection of glucagon (either intramuscular or subcutaneous). The patient should be given oral carbohydrates as soon as consciousness is recovered.

In case of drug overdose, contact a healthcare practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Hypoglycemia:

One of the most frequent adverse events experienced by insulin users is hypoglycaemia (see PROPER USE OF THIS MEDICATION).

Diabetic Acidosis and Coma:

Diabetic acidosis may develop if your body has too little insulin. (This is the opposite of insulin reaction, which is the result of too much insulin in the blood). Diabetic acidosis may be brought on if you omit your insulin or take less than the doctor has prescribed, eat significantly more than your diet calls for, or develop a fever or infection. With acidosis, urine tests show a large amount of sugar and acetone.

The first symptoms of diabetic acidosis usually come on gradually, over a period of hours or days, and include a drowsy feeling, flushed face, thirst, and loss of appetite. Heavy breathing and a rapid pulse are more severe symptoms.

If uncorrected, loss of consciousness, coma, or death can result. Therefore, it is important that you obtain medical assistance immediately.

Lipoatrophy:

Rarely, administration of insulin subcutaneously can result in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue). If you notice either of these conditions, consult your doctor. A change in your injection technique may help alleviate the problem.

Allergy to Insulin:

Patients occasionally experience redness, swelling, and itching at the site of injection of insulin. This condition, called local allergy, usually clears up in a few days to a few weeks. If you have local reactions, contact your doctor, who may recommend a change in the type or species of insulin.

Less common, but potentially more serious, is generalized allergy to insulin, which may cause rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, fast pulse, or sweating. Severe cases of generalized allergy may be life threatening. If you think you are having a generalized allergic reaction to insulin, notify a doctor immediately. Your doctor may recommend skin testing, that is, injecting small doses of other insulins into the skin, in order to select the best insulin for you to use. Patients who have had severe generalized

allergic reactions to insulin should be skin tested with each new preparation to be used before treatment with that preparation is started.

This is not a complete list of side effects. For any unexpected effects while taking HUMALOG MIX50, contact your doctor or pharmacist.

HOW TO STORE IT

Prior to first use, HUMALOG MIX50 cartridges or prefilled pens should be stored in a refrigerator between 2° and 8°C. Do not freeze. Do not expose to excessive heat or sunlight. The pen and cartridge of HUMALOG MIX50 that you are currently using should not be refrigerated but should be kept as cool as possible (below 30°C) and away from direct heat and light. Do not use HUMALOG MIX50 if it has been frozen. Cartridges or prefilled pens in use, or not refrigerated, should be discarded after 28 days, even if they still contain HUMALOG MIX50.

DO NOT USE A CARTRIDGE OR PREFILLED PEN OF HUMALOG MIX50 AFTER THE EXPIRATION DATE STAMPED ON THE LABEL. Dispose of used needles in a puncture-resistant container or as directed by your healthcare professional.

Dispose of used pens as instructed by your healthcare professional and without the needle attached.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your healthcare professionals or pharmacist first, or Eli Lilly Canada Inc at:

1-888-545-5972 or visit the website at www.lilly.ca

The information in this document is current as of the last revision date shown below. For the most current information please visit our website or contact us directly.

This leaflet was prepared by Eli Lilly Canada Inc., Toronto, Ontario, M1N 2E8. HUMALOG MIX50 is distributed by: Eli Lilly Canada Inc.

You may need to read this package insert again. Please do not throw it away until you have finished your medicine.

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