

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 is a sterile suspension containing 50% insulin lispro injection and 50% insulin lispro protamine suspension. It is available in:

- Cartridge, 3 mL
- KwikPen, 3 mL prefilled pen

Other HUMALOG products include:

- HUMALOG 100 units/mL (insulin lispro injection)
- HUMALOG 200 units/mL KwikPen (insulin lispro injection)
- HUMALOG MIX25 (25% insulin lispro injection, 75% insulin lispro protamine suspension)

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 i.e. a spare pen and cartridge or prefilled pen 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 mL cartridge is only for use in 3 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 or if the cartridge is cracked or broken.
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. Prepare the injection site as directed by your healthcare professional.
8. Insert the needle as instructed by your doctor.
9. To inject HUMALOG MIX50, follow the pen manufacturer's instructions.
10. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.
11. 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 closable, puncture-resistant sharps container (like a biohazard container) or as directed by your healthcare professional. Do not reuse needle. **NEEDLES, CARTRIDGES, AND PENS MUST NOT BE SHARED.**

To prevent the possible transmission of disease, never share a HUMALOG MIX50 pen or cartridge between patients, even if the needle on the delivery device is changed.

12. Use the gauge on the side of the 3 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 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.

Inspection of Cartridge:

DO NOT USE a cartridge or KwikPen of HUMALOG MIX50 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. A cartridge or KwikPen that is cracked or broken should be returned to the place of purchase for exchange.

If you notice anything unusual in the appearance or effect of your insulin, consult your healthcare professional.

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 0701D
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.

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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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