

**PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS'
REGULATIONS (PREPARATIONS) - 1986**

This medicine is dispensed by a physician's prescription only

HUMALOG

Solution for injection in a cartridge

The active ingredient and its quantity: insulin lispro 100 units/ml

Inactive ingredients and allergens in the preparation: see chapter 2, section "Important information about some of the ingredients of this medicine" and chapter 6 "Additional information".

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, please contact your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Humalog is used for the treatment of adults and children who have diabetes and need insulin in order to maintain a balance of blood sugar levels.

Therapeutic group: Drugs used in diabetes, insulins and analogues for injection, fast-acting.

Humalog works more quickly than normal human insulin because the insulin molecule has been changed slightly.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog is a substitute for your own insulin and is used to control glucose in the long term. It works very quickly and lasts a shorter time than soluble insulin (2 to 5 hours). You should normally use Humalog within 15 minutes of a meal.

Your doctor may tell you to use Humalog as well as a longer-acting insulin. Each kind of insulin comes with another patient information leaflet to tell you about it. Do not change your insulin unless your doctor tells you to. Be very careful if you do change insulin.

Humalog is suitable for use in adults and children. Humalog may be used in children when an advantage is expected compared to soluble insulin, for example, in the timing of injection in relation to meals.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- you are **allergic** (hypersensitive) to the active ingredient (insulin lispro) or any of the other ingredients of this medicine (listed in section 6).
- you think **hypoglycemia** (low blood sugar) is starting. Further in this leaflet it tells you how to deal with mild hypoglycemia (see section 3: If you have accidentally taken a higher dose).

Special warnings regarding the use of this medicine

- Always check the pack and the cartridge label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog that your doctor has told you to use.
- If your blood sugar levels are well controlled by your current insulin therapy, you may not feel the warning symptoms when your blood sugar is falling too low. Warning signs are listed later in this leaflet. You must think carefully about when to have your meals, how often to exercise and how much to do. You must also keep a close watch on your blood sugar levels by testing your blood glucose often.
- A few people who have had hypoglycemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycemia or have difficulty recognizing it, please discuss this with your doctor.
- If you answer YES to any of the following questions, tell your doctor, pharmacist or diabetes nurse
 - Have you recently become ill?
 - Do you have trouble with your kidneys or liver?
 - Are you exercising more than usual?
- The amount of insulin you need may also change if you drink alcohol.
- You should also tell your doctor, pharmacist or diabetes nurse if you are planning to go abroad. The time difference between countries may mean that you have to have your injections and meals at different times from when you are at home.
- Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible, if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localized swelling (edema).

Skin changes at the injection site

The injection site should be rotated to prevent skin changes such as lumps under the skin. The insulin may not work very well if you inject into a lumpy area (See 'How should you use the medicine?'). Contact your doctor if you are currently injecting into a lumpy area before you start injecting a different area. Your doctor may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

Drug interactions

If you are taking or have recently taken any other medicines, including non-prescription medicines and nutritional supplements, tell your doctor or pharmacist (see section "Special warnings regarding the use of this medicine").

Your insulin needs may change if you are taking:

- contraceptive pills
- steroids
- thyroid hormone replacement therapy
- oral hypoglycemics
- acetyl salicylic acid
- sulpha antibiotics
- octreotide
- 'beta2 stimulants' (for example ritodrine, salbutamol or terbutaline)
- beta-blockers
- some antidepressants [Monoamine Oxidase Inhibitors (MAOIs) or Selective Serotonin Reuptake Inhibitors (SSRIs)]
- danazol
- some angiotensin converting enzyme (ACE) inhibitors (for example captopril, enalapril)
- angiotensin II receptor blockers

Pregnancy and breastfeeding

Are you pregnant or thinking about becoming pregnant, or are you breastfeeding? The amount of insulin you need usually falls during the first three months of pregnancy and increases for the remaining six months. If you are breastfeeding, you may need to alter your insulin intake or diet. Ask your doctor for advice.

Driving and using machines

Your ability to concentrate and react may be reduced if you have hypoglycemia. Please keep this possible problem in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery).

You should contact your doctor about the advisability of driving if you have:

- frequent episodes of hypoglycemia
- reduced or absent warning signs of hypoglycemia

Important information about some of the ingredients of this medicine

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

The 3 ml cartridge is only for use in Lilly 3 ml pens. It is not for use in 1.5 ml pens.

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and manner of treatment with this medicine. To prevent the possible transmission of disease, each cartridge must be used by you only, even if the needle on the pen is changed.

The dose and manner of treatment will be determined only by your doctor.

Do not exceed the recommended dose.

Dose

- You should normally inject Humalog within 15 minutes of a meal. If you need to, you can inject soon after a meal. But your doctor will have told you exactly how much to use, when to use it, and how often. These instructions are only for you. Follow them exactly and visit your diabetes clinic regularly.
- If you change the type of insulin you use (for example from a human or animal insulin to a Humalog product), you may have to take more or less than before. This might just be for the first injection or it may be a gradual change over several weeks or months.
- Inject Humalog under the skin. You should only inject it into a muscle if your doctor has told you to.

Preparing Humalog

Humalog is already dissolved in water, so you do not need to mix it. But you must use it **only** if it looks like water. It must be clear, have no color and no solid pieces in it. Check each time you inject yourself.

Getting the pen ready to use

- First wash your hands. Disinfect the rubber membrane of the cartridge.
- **You must only use Humalog cartridges in Lilly insulin pens. Please make sure that Humalog or Lilly cartridges are mentioned in the leaflet accompanying your pen. The 3 ml cartridge only fits the Lilly 3 ml pens.**
- Follow the instructions that come with the pen. Put the cartridge into the pen.

- You will set the dose to 1 or 2 units. Then hold the pen with the needle pointing up and tap the side of the pen so that any air bubbles float to the top. With the pen still pointing up, press the injection mechanism. Do this until a drop of Humalog comes out of the needle. There may still be some small air bubbles left in the pen. These are harmless, but if the air bubble is too big, it may make the dose of your injection less accurate.

Injecting Humalog

- Before you make an injection, clean your skin as you have been instructed. Inject under the skin, as you were taught. Do not inject directly into a vein. After your injection, leave the needle in the skin for 5 seconds to make sure you have taken the whole dose. Do not rub the area you have just injected. Make sure you inject at least 1 cm from the last injection and that you 'rotate' the places you inject, as you have been taught. It doesn't matter which injection site you use, either upper arm, thigh, buttock or abdomen, your Humalog injection will still work quicker than soluble human insulin.
- You must not administer Humalog by the intravenous route. Inject Humalog as your physician or nurse has taught you. Only your physician can administer Humalog by the intravenous route. He will only do this under special circumstances such as surgery or if you are ill and your glucose levels are too high.

After Injecting

- As soon as you have done the injection, take the needle off the pen using the outer needle cap. This will keep the Humalog sterile and prevent leaking. It will also stop air going back into the pen and the needle clogging up. **Do not share your needles. Do not share your pen.** Replace the cap on your pen. Leave the cartridge in the pen.

Further injections

- Before every injection, dial 1 or 2 units and press the injection mechanism with the pen pointing up until a drop of Humalog comes out of the needle. You can see how much Humalog is left by looking at the gauge on the side of the cartridge. The distance between each mark on the gauge is about 20 units. If there is not enough for your dose, change the cartridge.

Do not mix any other insulin in a Humalog cartridge. Once the cartridge is empty, do not use it again.

If you have accidentally taken a higher dose

If you use more Humalog than you need or are unsure how much you have injected, a low blood sugar may occur. Check your blood sugar.

If your blood sugar is low (**mild hypoglycemia**), eat glucose tablets, sugar or drink a sugary drink. Then eat fruit, biscuits or a sandwich, as your doctor has advised you, and have some rest. This will often get you over mild hypoglycemia or a minor insulin overdose.

If you get worse and your breathing is shallow and your skin gets pale, tell your doctor at once. A glucagon injection can treat quite severe hypoglycemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon, you will have to go to the hospital. Ask your doctor to tell you about glucagon.

If a child has accidentally swallowed the medicine, proceed immediately to a doctor or hospital Emergency Room, and bring the package of the medicine with you.

If you forgot to take the medicine

If you take less Humalog than you need or are unsure how much you have injected, a high blood sugar may occur. Check your blood sugar.

If hypoglycemia (low blood sugar) or hyperglycemia (high blood sugar) is not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death (see A and B in chapter 4 “side effects”).

Three simple steps to avoid hypoglycemia and hyperglycemia are:

- Always keep spare syringes and a spare vial of Humalog, or a spare pen and cartridges, in case you lose your pen or cartridges or they get damaged.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

If you stop taking this medicine

If you take less Humalog than you need, a high blood sugar may occur. Do not change your insulin unless your doctor tells you to.

Treatment should be continued as recommended by the doctor.

Even if there is an improvement in your health condition, do not stop treatment with this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose each time you take your medicine. Wear glasses if you need them.

If you have further questions regarding the use of this medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

Like all medicines, this medicine can cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not suffer from any of them.

Systemic allergy is rare ($\geq 1/10,000$ to $<1/1,000$). The symptoms are as follows:

- rash over the whole body
- difficulty in breathing
- wheezing
- blood pressure dropping
- heart beating fast
- sweating

If you think you are having this sort of insulin allergy with Humalog, tell your doctor at once.

Local allergy is common ($\geq 1/100$ to $<1/10$). Some people get redness, swelling or itching around the area of the insulin injection. This usually clears up in anything from a few days to a few weeks. If this happens to you, tell your doctor.

Lipodystrophy is uncommon ($\geq 1/1,000$ to $<1/100$). If you inject insulin too often at the same place, the fatty tissue may either shrink (lipoatrophy) or thicken (lipohypertrophy). Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). The insulin may not work very well if you inject into a lumpy area. Change the injection site with each injection to help prevent these skin changes.

Edema (e.g. swelling in arms, ankles; fluid retention) has been reported, particularly at the start of insulin therapy or during a change in therapy to improve control of your blood glucose.

If a side effect occurs, if one of the side effects gets worse, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link “Reporting side effects due to drug treatment” located on the Home Page of the Ministry of Health’s website

(www.health.gov.il), which directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

Common problems of diabetes

A. Hypoglycemia

Hypoglycemia (low blood sugar) means there is not enough sugar in the blood. This can be caused if:

- you take too much Humalog or other insulin
- you miss or delay meals or change your diet
- you exercise or work too hard just before or after a meal
- you have an infection or illness (especially diarrhea or vomiting)
- there is a change in your need for insulin or
- you have trouble with your kidneys or liver which gets worse.

Alcohol and some medicines can affect your blood sugar levels.

The first symptoms of low blood sugar usually come on quickly and include the following:

- tiredness
- nervousness or shakiness
- headache
- rapid heartbeat
- feeling sick
- cold sweat

While you are not confident about recognizing your warning symptoms, avoid situations, e.g. driving a car, in which you or others would be put at risk by hypoglycemia.

B. Hyperglycemia and diabetic ketoacidosis

Hyperglycemia (too much sugar in the blood) means that your body does not have enough insulin.

Hyperglycemia can be brought about by:

- not taking your Humalog or other insulin
- taking less insulin than your doctor tells you to
- eating a lot more than your diet allows
- fever, infection or emotional stress

Hyperglycemia can lead to diabetic ketoacidosis. The first symptoms come on slowly over many hours or days. The symptoms include the following:

- feeling sleepy
- flushed face
- thirst
- no appetite
- fruity smell on the breath
- feeling or being sick

Severe symptoms are heavy breathing and a rapid pulse. **Get medical help immediately.**

C. Illness

If you are ill, especially if you feel sick or are sick, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, follow your 'sick rules', and tell your doctor.

5. HOW TO STORE THIS MEDICINE?

Avoid poisoning! This medicine and all other medicines must be stored in a closed place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.

Do not use this medicine after the expiry date (exp. date) which is stated on the carton and label. The expiry date refers to the last day of that month.

Storage conditions:

Before opening, store in the refrigerator at a temperature of 2°C - 8°C. Do not freeze.

Keep your cartridge in use at room temperature (below 30°C) and discard after 28 days. Do not put it near heat or in the sun. Do not keep your pen or the cartridges you are using in the fridge. The pen with the inserted cartridge should not be stored with the needle attached.

Keep out of the sight and reach of children.

Do not use this medicine if you notice it is colored or it has solid pieces in it. You must use it **only** if it looks like water. Check this each time you inject yourself.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, the medicine also contains:

glycerine, metacresol, dibasic sodium phosphate, zinc oxide, water for injection, hydrochloric acid, sodium hydroxide.

The active substance is insulin lispro. Insulin lispro is made in the laboratory by a 'recombinant DNA technology' process. It is a changed form of human insulin and so is different from other human and animal insulins. Insulin lispro is closely related to human insulin which is a natural hormone made by the pancreas.

What the medicine looks like and contents of the pack

Humalog is a sterile, clear, colorless aqueous solution for injection and contains 100 units of insulin lispro in each milliliter (100 units/ml) solution for injection. Each cartridge contains 300 units (3 milliliters).

The cartridges come in packs of 5.

Registration holder and address:

Eli Lilly Israel Ltd., 4 HaSheizaf St., POB 4246, Ra'anana 4366411

Manufacturer name and address:

Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana (IN) 46285, USA

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 102-83-28580-00

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