

**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 vial

The active ingredient: insulin lispro 100 units/ml

Inactive ingredients and allergens: 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: Rapid-acting insulins and insulin analogs.

Humalog is used to treat diabetes. **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 (either before or after).

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 (see 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 vial 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 or selective serotonin reuptake inhibitors)
- 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?

Always use **Humalog** according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and manner of treatment with this medicine.

Dose

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

Do not exceed the recommended dose.

- You should normally inject **Humalog** within 15 minutes of a meal. If you need to, you can inject soon after a meal. In any case, 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 **Humalog**), you may have to inject a different amount than the amount you injected 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.

Method of administration:

- **Humalog** is administered by subcutaneous injection or in an insulin infusion pump.
- Do not inject **Humalog** directly into a vein. 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.
- Before using **Humalog**, it is very important to read the detailed instructions carefully and follow them strictly. Failure to follow the instructions may result in an inaccurate insulin dose.
- The amount of insulin for injection is measured in units. It is important to recognize the markings on the pen, because the volume of injected insulin depends on the strength and is in fact the number of units per ml. Use only an appropriate syringe. Using an inappropriate syringe may result in an inaccurate insulin dose.
- Below are general instructions for injection with a disposable syringe and vials (in case of use with an insulin infusion pump, please see instructions for use enclosed in the product's package).
- Disposable needles should be discarded after use, as directed by the medical staff, in

order to prevent infections. In order to prevent the possible transmission of disease, each pen and needle must be used by a single person and should not be transferred from one to another, even if the needle has been changed.

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.

Injecting Humalog

- First wash your hands.
- Before you make an injection, clean your skin as you have been instructed. Clean the rubber stopper on the vial, but do not remove the stopper.
- Use a clean, sterile syringe and needle to pierce the rubber stopper and draw in the amount of **Humalog** you want. Your doctor will tell you how to do this. **Do not share your needles and syringes.**
- 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.
- Your doctor will tell you if you have to mix **Humalog** with one of the human insulins. For example, if you do need to inject a mixture, draw the **Humalog** into the syringe before the long acting insulin. Inject the liquid as soon as you have mixed it. Do the same thing every time. You should not normally mix **Humalog** with one of the mixtures of human insulins. You should never mix **Humalog** with insulins produced by other manufacturers or animal insulins.
- 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.

Using an insulin infusion pump

- Only certain insulin infusion pumps may be used to infuse insulin lispro. Before infusing insulin lispro, the manufacturer's instructions should be studied to ascertain the suitability or otherwise for the particular pump. Read and follow the instructions in the product literature supplied with the infusion pump.
- Be sure to use the correct reservoir and catheter for your pump.
- Changing of the infusion set (tubing and needle) must be done according to the instructions in the product information supplied with the infusion set.
- 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 doctor and consider the need to reduce or stop your insulin infusion.
- 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 doctor or clinic.
- When used with an insulin infusion pump, **Humalog** should not be mixed with any other insulin.

If you have accidentally taken a higher dose

If you take 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 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 sections 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**.
- Always carry something to show you are diabetic.
- Always carry sugar with you.

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.

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.

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 the 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.

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side ef-

fects due to drug treatment” found 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 following 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
- 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
- nausea
- 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 have nausea or are vomiting, the amount of insulin you need may change. **Even when you are not eating normally, you still need insulin.** Test your urine or blood, proceed as you would normally do when sick, 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.
- Before opening, store in the refrigerator at a temperature of 2°C - 8°C. **Do not freeze.**
- During use store below 30°C. Do not freeze.
- The insulin can be used for up to 28 days from first opening. Do not expose to sunlight or heat.

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

Using an insulin infusion pump

- When using an insulin infusion pump, replace the insulin in the reservoir at least every 7 days, even if some solution remains in the pump.
- Do not expose the insulin in the pump to a temperature greater than 37°C.

6. ADDITIONAL INFORMATION

What Humalog contains

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.

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

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

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 of solution for injection. Each vial contains 1,000 units (10 milliliters). **Humalog** 100 units/ml is supplied in a 10 ml vial.

Registration holder and address: Eli Lilly Israel Ltd., 4 HaSheizaf st., POB 4246, Ra'anana 4366411.

Name of manufacturer and address: Lilly S.A., Alcobendas, Madrid, Spain

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

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