

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is to be supplied by a physician's prescription only

HUMALOG MIX 25[®]

KWIKPEN

Suspension for Injection

HUMALOG MIX 50[®]

KWIKPEN

Suspension for Injection

Active ingredient and its quantity:

Each cartridge contains:

Insulin lispro 100 units/ml

25% insulin lispro (fast-acting/free)

and 75% insulin lispro protamine suspension

(prolonged action)

Each cartridge contains:

Insulin lispro 100 units/ml

50% insulin lispro (fast-acting/free)

and 50% insulin lispro protamine suspension

(prolonged action)

Each KwikPen delivers 1 – 60 units in steps of 1 unit.

For a list of the inactive ingredients, please see section 6.

Read this patient leaflet carefully in its entirety before using this medicine. This leaflet contains concise information regarding 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?

For the treatment of adults and children who have diabetes and need insulin to maintain the balance of blood sugar levels.

Therapeutic group: Insulins and insulin analogs.

Humalog Mix 25 KwikPen and Mix 50 KwikPen are used to treat diabetes. These are premixed suspensions. Their active substance is insulin lispro. 25% or 50% of the insulin lispro in Humalog Mix 25 KwikPen and Humalog Mix 50 KwikPen is dissolved in water and it works more quickly than normal human insulin because the insulin molecule has been changed slightly. 75% or 50% of the insulin lispro in Humalog Mix 25 KwikPen and Humalog Mix 50 KwikPen is available in a suspension together with protamine sulphate, so that its action is prolonged.

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog Mix KwikPen is a substitute for your own insulin and is used to control glucose in the long term. Humalog Mix 25 KwikPen and Mix 50 KwikPen work very quickly and longer than soluble insulin. You should normally use Humalog Mix KwikPen within 15 minutes of a meal.

Your doctor may tell you to use Humalog Mix 25 or 50 KwikPen 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.

The KwikPen is a pre-filled pen containing 3 ml (300 units, 100 units/ml) of insulin lispro. One KwikPen contains multiple doses of insulin. The KwikPen dials 1 unit at a time. **The number of units are displayed in the dose window, always check this before your injection.** You can give from 1 to 60 units in a single injection. **If your dose is more than 60 units, you will need to give yourself more than one injection.**

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

- you are allergic to 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 take more Humalog Mix KwikPen than you need).

Special warnings regarding the use of this medicine:

- Always check the pack and the label of the pre-filled pen for the name and type of the insulin when you get it from your pharmacy. Make sure you get the Humalog Mix KwikPen 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 them, 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).
- This Pen is not recommended for use by the blind or visually impaired without the help of someone trained to use the Pen.

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 to use Humalog Mix KwikPen). 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 other medicines, including nonprescription medications and nutritional supplements, inform your doctor or pharmacist.

Your insulin needs may change if you are taking:

- contraceptive pills
- steroids
- thyroid hormone replacement therapy
- oral hypoglycemics
- acetyl salicylic acid
- sulpham antibiotics
- octreotide
- "beta₂ stimulants" (for example ritodrine, salbutamol or terbutaline)
- beta-blockers, or
- 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?

Always use according to the doctor's instructions. You should check with your doctor or pharmacist if you are not sure. The dosage and manner of treatment will be determined only by the doctor.

Do not exceed the recommended dose.

To prevent the possible transmission of disease, each pen must be used by you only, even if the needle is changed.

Dose

- You should normally inject Humalog Mix KwikPen 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.
- Humalog Mix KwikPen is only suitable for injecting just under the skin. Speak to your doctor if you need to inject your insulin by another method.

Preparing Humalog Mix KwikPen

- The KwikPen 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. The cartridges should be examined frequently and should not be used 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. Check each time you inject yourself.

Getting the KwikPen ready to use (Please see user manual)

- First wash your hands.
- Read the instructions on how to use your pre-filled insulin pen. Please follow the instructions carefully. Here are some reminders.
- Use a clean needle. (Needles are not included).
- Prime your KwikPen before each use. This checks that insulin comes out and clears the air bubbles from your KwikPen. There may still be some small air bubbles left in the pen - these are harmless. But if the air bubbles are too large it may affect the insulin dose.

Injecting Humalog Mix KwikPen

- 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 five 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 where you last injected and that you 'rotate' the places you inject, as you have been taught.

After injecting

- As soon as you have done the injection, unscrew the needle from the KwikPen using the outer needle cap. This will keep the insulin sterile and stop it leaking. It also stops air entering the pen and your needle clogging. **Do not share your needles.** Do not share your pen. Replace the cap on the pen.

Further injections

- Every time you use a KwikPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the KwikPen with the needle pointing up. The scale on the cartridge shows about how many units you have left.
- Do not mix any other insulin in your pen. Once the KwikPen is empty, do not use it again. Please get rid of it carefully - your pharmacist or diabetes nurse will tell you how to do this.

If you take more Humalog Mix KwikPen than you should

If you take more Humalog Mix KwikPen 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, 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 you forget to use Humalog Mix KwikPen

If you take less Humalog Mix KwikPen 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 section 4 “Possible Side Effects”).

Three simple steps to avoid hypoglycemia or hyperglycemia are:

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

If you stop using Humalog Mix KwikPen

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

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

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

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

4. SIDE EFFECTS

As with any medicine, Humalog Mix KwikPen may cause side effects in some users. Do not be alarmed while reading the list of side effects. You may not experience 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 Mix KwikPen, 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 you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

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

website (www.health.gov.au), which refers to an online form for reporting side effects, or by entering the following link:

<https://sideeffects.health.gov.au>

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 Mix KwikPen 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 diarrhoea 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; or
- 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 THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine should be kept 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 the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

- Before the first use store your Humalog Mix KwikPen in a refrigerator (2°C – 8°C). Do not freeze.
- Keep your Humalog Mix KwikPen 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 the KwikPen that you are using in the fridge. The KwikPen should not be stored with the needle attached.
- Do not use this medicine if you notice clumps of material are present or if solid white particles stick to the bottom or wall of the cartridge, giving it a frosted appearance. Check each time you inject yourself.
- Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. ADDITIONAL INFORMATION

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, Humalog Mix KwikPen also contains:

Glycerol, dibasic sodium phosphate, metacresol, liquefied phenol, protamine sulphate, zinc oxide, hydrochloric acid solution 10%, sodium hydroxide solution 10%, water for injection.

What does the medicine look like and what are the contents of the pack:

Humalog Mix 25 KwikPen and Humalog Mix 50 KwikPen are white, sterile suspensions. Each cartridge contains 300 units (3 mL). Each pack contains 5 prefilled injector pens.

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

Name of Manufacturer and address: Eli Lilly & Company Ltd., Indianapolis, Indiana, USA

Revised in April 2021 according to MoH guidelines.

Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:

Humalog Mix 25 KwikPen: 143-45-33217-00

Humalog Mix 50 KwikPen: 143-46-33218-00