PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

HUMALOG MIX 25 100 units/ml suspension for injection

Insulin lispro (25 % insulin lispro and 75 % insulin lispro protamine suspension)

Contains sugar (glycerol 16 mg/ml)

HUMALOG MIX 50 100 units/ml suspension for injection

Insulin lispro (50 % insulin lispro and 50 % insulin lispro protamine suspension)

Contains sugar (glycerol 16 mg/ml)

Read all of this leaflet carefully before you start using HUMALOG MIX 25 and HUMALOG MIX 50

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse, or other health care provider.
- HUMALOG MIX 25 or HUMALOG MIX 50 has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What HUMALOG MIX 25 and HUMALOG MIX 50 is and what it is used for
2. What you need to know before you use HUMALOG MIX 25 or HUMALOG MIX 50
3. How to use HUMALOG MIX 25 and HUMALOG MIX 50
4. Possible side effects

5. How to store HUMALOG MIX 25 and HUMALOG MIX 50

6. Contents of the pack and other information

1. What HUMALOG MIX 25 and HUMALOG MIX 50 are and what they are used for

HUMALOG MIX 25 and HUMALOG MIX 50 are used to treat diabetes. HUMALOG MIX 25 and HUMALOG MIX 50 are a substitute for your own insulin and are used to control glucose in the long term. HUMALOG MIX 25 and HUMALOG MIX 50 work very quickly and longer than soluble insulin. You should normally use HUMALOG MIX 25 or HUMALOG MIX 50 within 15 minutes of a meal.

Your doctor may tell you to use HUMALOG MIX 25 or HUMALOG MIX 50 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.

2. What you need to know before you use HUMALOG MIX 25 or HUMALOG MIX 50

Do not use HUMALOG MIX 25 or HUMALOG MIX 50:

- If you are hypersensitive (allergic) to insulin lispro or any of the other ingredients of HUMALOG MIX 25 or HUMALOG MIX 50 (listed in section 6).
- If you are experiencing hypoglycaemia (low blood sugar).

Warnings and precautions

- Always check the pack and the vial, cartridge or pen label for the name and type of the insulin when you get it from your pharmacy. Make sure you get the HUMALOG MIX 25 or HUMALOG MIX 50 that your doctor has told you to use. Check the dialled units on the dose counter of the pen to ensure you are getting the correct dose. The Humalog

Pen is not recommended for use by blind or visually impaired without the help of someone trained to use the Pen.

- 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.
- A few people who have had hypoglycaemia after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have hypoglycaemia or have difficulty recognising it, please discuss this with your doctor.
- Any change of insulin should be made cautiously and only under medical supervision.
- If you suffer from kidney or liver impairment, your dose may need to be adjusted.
- If you have recently become ill or are exercising more than usual, your dose may need to be adjusted.
- If you are taking pioglitazone (also used to treat diabetes) together with HUMALOG MIX 25 or HUMALOG MIX 50, it may increase the risk of oedema (e.g., swelling in arms, ankles, fluid retention) and heart failure, especially in patients with existing heart disease.
- Your insulin needs may change if you are taking other medicines e.g., the contraceptive pill, corticosteroids, thyroid replacement therapy, oral anti-diabetic medicines, salicylates, sulpha antibiotics, certain anti-depressants, and certain anti-hypertensive (blood pressure medication). Speak to your doctor when using other medication in addition to HUMALOG MIX 25 or HUMALOG MIX 50.
- 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.
- HUMALOG MIX 25 and HUMALOG MIX 50 suspension should look uniformly cloudy or milky. If the insulin lispro substance (the cloudy material) settles at the bottom of the container, it must be rotated or carefully shaken before injection so that the contents are

uniformly mixed. Do not use HUMALOG MIX 25 or HUMALOG MIX 50 if a deposit of solid particles remains on the bottom or on the sides of the container, giving it a frosted appearance or if there are clumps floating in the insulin after the container has been rotated or carefully shaken. Also, HUMALOG MIX 25 or HUMALOG MIX 50 suspension should not be used if it is clear and remains clear after the container is rotated or shaken.

- After you prepare your dose, you should administer it promptly to avoid clogging of the needle.
- The safety and effectiveness of HUMALOG MIX 25 and HUMALOG MIX 50 in patients less than 18 years of age has not been established.

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 25 and Humalog MIX 50). 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.

Other medicines and HUMALOG MIX 25 or HUMALOG MIX 50

Always tell your healthcare professional if you are taking any other medicines. (This includes complementary or traditional medicines.)

- You may require more insulin when using medicines with hyperglycaemic (high blood sugar) activity, such as the contraceptive pill, corticosteroids, or thyroid replacement therapy.

- Your insulin requirements may be decreased in the presence of certain medicines such as oral anti-diabetic agents, salicylates, sulpha antibiotics, certain anti-depressants, and certain anti-hypertensive (low blood pressure) medicines.

  Please consult a healthcare professional when using other medication in addition to HUMALOG MIX 25 or HUMALOG MIX 50.

HUMALOG MIX 25 and HUMALOG MIX 50 with food and drink

Carefully follow your doctor's instructions regarding food intake with the use of HUMALOG MIX 25 or HUMALOG MIX 50.

Pregnancy and, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist, or other health care provider for advice before taking this medicine.

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 or diet.

Driving and using machines

Your ability to concentrate and react may be reduced if you have hypoglycaemia. Please keep this 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 hypoglycaemia
- reduced or absent warning signs of hypoglycaemia.

HUMALOG MIX 25 and HUMALOG MIX 50 contain sodium

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

3. How to use HUMALOG MIX 25 and HUMALOG MIX 50

Do not share medicines prescribed for you with any other person.

Always take HUMALOG MIX 25 or HUMALOG MIX 50 exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are not sure.

Your doctor will tell you how long your treatment with HUMALOG MIX 25 or HUMALOG MIX 50 will last. Do not stop treatment early. If you have the impression that the effect of HUMALOG MIX 25 or HUMALOG MIX 50 is too strong or too weak, tell your doctor or pharmacist.

General directions for use:

- You should normally inject HUMALOG MIX 25 or HUMALOG MIX 50 within 15 minutes of a meal. If you need to, you can inject soon after a meal. Your doctor will tell you exactly how much to use, when to use it and how often. These instructions are only for you. Follow them exactly.
- If you change the type of insulin you use (for example from a human or animal to HUMALOG MIX 25 or HUMALOG MIX 50), 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 MIX 25 or HUMALOG MIX 50 subcutaneously (under the skin). You should inject either the upper arms, thighs, buttocks, or abdomen. The injection sites must be rotated so that the same site is not used more than once a month.
- Care should be taken to ensure that you do not inject directly into a vein.
- After injection, do not massage the site of injection.

To prevent the possible transmission of disease, each pen and cartridge must be used by you only.

Before starting therapy, you should read the "User Manual" that accompanies the delivery device, to ensure the correct use thereof.

Preparing a dose

Vials containing HUMALOG MIX 25 should be rotated in the palms of the hands before use to resuspend the insulin until it appears uniformly cloudy or milky.

Cartridges and KwikPens containing HUMALOG MIX 25 or HUMALOG MIX 50 should be rotated in the palms of the hands ten times and inverted 180 ° ten times immediately before use to resuspend the 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.

Vial

The vial is to be used in conjunction with an appropriate syringe (100-unit markings).

1. Wash your hands.
2. If using a new vial, flip off the plastic protective cap, but **do not** remove the stopper.
3. Draw air into the syringe equal to the prescribed HUMALOG MIX 25 dose. Wipe the

top of the vial with a swab. Put the needle through rubber top of the HUMALOG MIX 25 vial and inject the air into the vial.

4. Turn the vial and syringe upside down. Hold the vial and syringe firmly in one hand.
5. Making sure the tip of the needle is in the HUMALOG MIX 25, withdraw the correct dose into the syringe.
6. Before removing the needle from the vial, check the syringe for air bubbles that reduce the amount of HUMALOG MIX 25 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.

Remove the needle from the vial and lay the syringe down so that the needle does not touch anything.

Cartridge

HUMALOG MIX 25 and HUMALOG MIX 50 cartridges are to be used with a Lilly reusable insulin pen and should not be used with any other reusable pen as the dosing accuracy has not been established with other pens.

The instructions with each individual pen must be followed for loading the cartridge, attaching the needle, and administering the insulin injection.

KwikPen

Before using the KwikPen the user manual included in the pack must be read carefully. The KwikPen has to be used as recommended in the user manual.

Pens should not be used if any part looks broken or damaged.

Injecting a dose

If using a pre-filled or reusable pen refer to the detailed instructions for preparing the pen and injecting the dose, the following is a general description.

1. Wash your hands.

2. Choose a site for injection.

3. Clean the skin as instructed.

4. Stabilise the skin by spreading it or pinching up a large area. Insert the needle and inject as instructed.

5. Pull the needle out and apply gentle pressure over the injection site for several seconds. Do not rub the area.

6. Using the outer needle cap, unscrew the needle and dispose of it safely.

7. Use of injection sites should be rotated so that the same site is not used more than approximately once a month.

If you take more HUMALOG MIX 25 or HUMALOG MIX 50 than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, seek help at the nearest hospital or poison centre.

- Overdosage causes hypoglycaemia (low blood sugar) with accompanying symptoms that include listlessness (lack of interest and energy), confusion, palpitations (rapid irregular action of the heart), headache, sweating and vomiting.
- If your blood sugar is low (mild hypoglycaemia), eat glucose tablets, sugar, or drink something sweet (sugary). Then eat fruit, biscuits, or a sandwich, as your doctor has advised you and rest.
- 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 hypoglycaemia. Eat glucose or sugar

after the glucagon injection. If you do not respond to glucagon, you will have to go to hospital.

If you forget to use HUMALOG MIX 25 or HUMALOG MIX 50

- If you take less HUMALOG MIX 25 or HUMALOG MIX 50 than you need, your blood sugar levels may increase. Check your blood sugar and consult your doctor, pharmacist, or other healthcare professional.
- Do not take a double dose to make up for forgotten individual doses.
- If hypoglycaemia (low blood sugar) or hyperglycaemia (high blood sugar) is not treated, they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death.

If you stop using HUMALOG MIX 25 or HUMALOG MIX 50

- If you take less HUMALOG MIX 25 or HUMALOG MIX 50 than you need, your blood sugar levels may increase. Check your blood sugar and consult your doctor, pharmacist, or other healthcare professional.
- Do not change your insulin unless your doctor tells you to.

4. Possible side effects

- HUMALOG MIX 25 and HUMALOG MIX 50 can have side effects.
- Not all side effects reported for HUMALOG MIX 25 and HUMALOG MIX 50 are included in this leaflet.
- Should your general health worsen or if you experience any untoward effects while taking HUMALOG MIX 25 or HUMALOG MIX 50, please consult your health care provider for advice.

If any of the following happens, stop using HUMALOG MIX 25 or HUMALOG MIX 50 and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Rash over the whole body
- Shortness of breath, wheezing
- Reduction in blood pressure
- Fast pulse
- Sweating

These are all serious side effects. If you have them, you may have a serious reaction to HUMALOG MIX 25 or HUMALOG MIX 50. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

- Hypoglycaemia (low blood sugar). This is the most frequent side effect.
- Allergic reaction (local allergy). Redness, swelling and itching can occur at the site of insulin injection.
- Lipodystrophy (thickening or pitting of the skin) is less frequent. 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.
- Oedema (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.

If you notice any side effects not listed in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. Alternatively, report side effects to the company at ade_za@lilly.com. By reporting side effects, you can help provide more information on the safety of HUMALOG MIX 25 and HUMALOG MIX 50.

5. How to store HUMALOG MIX 25 and HUMALOG MIX 50

Do not freeze. Do not expose to excessive heat or direct sunlight.

HUMALOG MIX 25

Before use:

Store in a refrigerator at 2 to 8 ºC until time of use.

After first use/after cartridge insertion:

Vial

Store in use vial (after the stopper has been punctured) refrigerated for up to 28 days.

If refrigeration is not possible, the vial in use can be stored unrefrigerated at or below 30 °C for up to 28 days.

Cartridge

Store in use cartridge (after the disc seal has been punctured) unrefrigerated at or below 30 °C for up to 28 days. The pen with the inserted cartridge should not be stored with the needle attached.

KwikPen

Store in use pen (after the disc seal has been punctured) unrefrigerated at or below 30 °C for up to 28 days. The pre-filled pen should not be stored with the needle attached.

HUMALOG MIX 50

Before use:

Store in a refrigerator at 2 to 8 ºC until time of use.

After first use/after cartridge insertion:

Cartridge

Store in use cartridge (after the disc seal has been punctured) unrefrigerated at or below 30 °C for up to 28 days. The pen with the inserted cartridge should not be stored with the needle attached.

KwikPen

Store in use pen (after the disc seal has been punctured) unrefrigerated at or below 30 °C for up to 28 days. The pre-filled pen should not be stored with the needle attached.

Do not use product after the expiry date which is stated on the label and carton. The expiry date refers to the last day of the month.

Store all medicines out of reach of children.

Return all unused medicine to your pharmacist.

6. Contents of the pack and other information

What HUMALOG MIX 25 and HUMALOG MIX 50 contain

HUMALOG MIX 25

The active ingredient is 25 % insulin lispro and 75 % insulin lispro protamine.

HUMALOG MIX 50

The active ingredient is 50 % insulin lispro and 50 % insulin lispro protamine.

The other ingredients are protamine sulphate, metacresol, phenol, glycerol, dibasic sodium phosphate (heptahydrate), zinc oxide and water for injections. Hydrochloric acid and sodium hydroxide may be used to adjust pH.

What HUMALOG MIX 25 and HUMALOG MIX 50 looks like and contents of the pack

HUMALOG MIX 25

HUMALOG MIX 25 vials, cartridges and disposable pens contain a sterile, white suspension.

Vials: A 10 ml, clear, transparent, colourless flint-glass vial, sealed with a rubber stopper with a red aluminium seal, packed into an outer cardboard carton. Available in packs of 1.

Cartridges: A 3,0 ml, clear, transparent, colourless flint-glass cartridge sealed with a red rubber plunger head at the bottom of the cartridge and a rubber disc with an outer red aluminium seal at the top of the cartridge. The cartridges should be used in reusable pen injectors. Cartridges are packed into plastic blisters. Blisters are packed into an outer cardboard carton. Available in packs of 5.

Disposable pens: Prefilled, disposable pen injectors containing 3,0 ml cartridges are packed into an outer cardboard carton. The disposable pen injector consists of a glass cartridge, permanently sealed inside the pen’s clear protective housing. The pen components consist of a pen cap, cartridge holder, pen body and dose knob. Available in packs of 5.

HUMALOG MIX 50

HUMALOG MIX 50 cartridges and disposable pens contain a sterile, white suspension.

Cartridges: A 3,0 ml, clear, transparent, colourless flint-glass cartridge sealed with a red rubber plunger head at the bottom of the cartridge and a rubber disc with an outer red aluminium seal at the top of the cartridge. The cartridges should be used in reusable pen

injectors. Cartridges are packed into plastic blisters. Blisters are packed into an outer cardboard carton. Available in packs of 5.

Disposable pens: Prefilled, disposable pen injectors containing 3,0 ml cartridges are packed into an outer cardboard carton. The disposable pen injector consists of a glass cartridge, permanently sealed inside the pen's clear protective housing. The pen components consist of a pen cap, cartridge holder, pen body and dose knob. Available in packs of 5.

Holder of the Certificate of Registration

Eli Lilly (S.A.) (Pty) Ltd

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Registration number

HUMALOG MIX 25: 33/21.1/0073

HUMALOG MIX 50: 33/21.1/0074

Registration Details for Botswana		
Humalog Mix 25 Vial	Reg. No.: BOT0200501	Schedule 2

Humalog Mix 25 Prefilled Pens (KwikPens)	Reg. No.: BOT0200501A	Schedule 2
Humalog Mix 25 Cartridges	Reg. No.: BOT0200501B	Schedule 2
Humalog Mix 50 Prefilled Pens (KwikPens)	Reg. No.: BOT0700979	Schedule 2
Humalog Mix 50 Cartridges	Reg. No.: BOT0700979A	Schedule 2
Please report any suspected ADRs to BoMRA through e-reporting https://primaryreporting.who-umc.org/BW and e-mail reportadr@bomra.co.bw.		

Registration Details for Namibia		
Humalog Mix 25 Vial	Reg. No.: 04/21.1/0645	Schedule NS2
Humalog Mix 25 Prefilled Pens (KwikPens)	Reg. No.: 04/21.1/0645	Schedule NS2
Humalog Mix 25 Cartridges	Reg. No.: 04/21.1/0645	Schedule NS2
Humalog Mix 50 Prefilled Pens (KwikPens)	Reg. No.: 06/21.1/0254	Schedule NS2
Humalog Mix 50 Cartridges	Reg. No.: 06/21.1/0254	Schedule NS2