ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Humalog-HumaPen (100 U/mL, 3.0 mL)
Insulin lispro

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Humalog-HumaPen is a sterile, clear, colourless, aqueous solution of insulin lispro ([Lys (B28), Pro (B29)] human insulin analog, rDNA origin) adjusted to pH 7.0 - 7.8. The name insulin lispro is approved by INN, USAN and BAN

Active Ingredient	Quantity per mL
insulin lispro (recombinant DNA origin produced in *E. coli*)	100 U

The concentration of insulin lispro is 3.5mg insulin lispro per ml for the 100 U/ml product.

3. PHARMACEUTICAL FORM

A solution for injection, in a prefilled/disposable pen injector containing a 3.0 mL cartridge
(100 U/mL of insulin lispro) for parenteral subcutaneous administration.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of patients with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis. Humalog-HumaPen is also indicated for the initial stabilisation of diabetes mellitus. Humalog-HumaPen is a short acting insulin and may be used in conjunction with a longer acting human insulin. Humalog-HumaPen is indicated for preprandial administration.

4.2 Posology and method of administration

The dosage should be determined by the physician, according to the requirement of the patient.

Humalog-HumaPen preparations should be given by subcutaneous injection but may, although not recommended, also be given by intramuscular injection.

Subcutaneous administration should be in the upper arms, thighs, buttocks, or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month.

Care should be taken when injecting Humalog-HumaPen to ensure that a blood vessel has not been entered. After injection, the site of injection should not be massaged.

Humalog-HumaPen takes effect rapidly and has a shorter duration of activity (2 to 5 hours) as compared with regular insulin. This rapid onset of activity allows Humalog-HumaPen to be given very close to mealtime. The time course of action of any insulin may vary considerably in different individuals or at different times in the same individual. As with all insulin preparations, the duration of action of Humalog-HumaPen is dependent on dose, site of injection, blood supply, temperature, and physical activity.

Humalog-HumaPen may be administered in conjunction with a longer acting human insulin, on the advice of a physician.

4.3 Contra-indications

Hypoglycemia.

Hypersensitivity to insulin lispro or one of its excipients.

4.4 Special warnings and special precautions for use

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular, NPH, lente, etc.), species (animal, human, human insulin analog), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.

Patients taking Humalog-HumaPen may require a change in dosage from that used with their usual insulins. If an adjustment is needed, it may occur with the first dose or during the first several weeks or months.

Patients whose blood glucose is greatly improved, e.g. by intensified insulin therapy, may lose some or all of the warning symptoms of hypoglycaemia and should be advised accordingly.

A few patients who have experienced hypoglycaemic reactions after transfer from animal-source insulin to human insulin have reported that the early warning symptoms of hypoglycaemia were less pronounced or different from those experienced with their previous insulin. Uncorrected hypoglycaemic or hyperglycaemic reactions can cause loss of consciousness, coma, or death.

Insulin requirements may be reduced in the presence of renal or hepatic impairment.

Insulin requirements may be increased during illness or emotional disturbances.

Adjustment of dosage may also be necessary if patients undertake increased physical activity or change their usual diet. Exercise taken immediately after a meal may increase the risk of hypoglycemia.

There is no significant experience with Humalog-HumaPen in children below 12 years of age

4.5 Interaction with other medicinal products and other forms of interaction

Insulin requirements may be increased by drugs with hyperglycaemic activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy, danazol, beta 2 stimulants (ritodrine, salbutamol, terbutaline).

Insulin requirements may be reduced in the presence of drugs with hypoglycemic activity, such as oral hypoglycemics, salicylates (for example, aspirin), sulfa antibiotics, and certain antidepressants, certain angiotensin converting enzyme inhibitors (captopril, enalapril), beta blockers, octreotide, alcohol.

Humalog-HumaPen should not be mixed with animal insulins.

The physician should be consulted when using other medications in addition to Humalog-HumaPen.

4.6 Use during pregnancy and lactation

There is no significant experience with Humalog-HumaPen in pregnancy.

It is essential to maintain good control of the insulin-treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Patients with diabetes should be advised to inform their doctor if they are pregnant or are contemplating pregnancy. Careful monitoring of glucose control, as well as general health, is essential in pregnant patients with diabetes.

Patients with diabetes who are lactating may require adjustments in insulin dose, diet, or both.

4.7 Effects on ability to drive and use machines

Use of the correct therapeutic dose of insulins has no known effect on driving or the use of machinery.

4.8 Undesirable effects

Hypoglycemia is the most frequent undesirable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycemia may lead to loss of consciousness, and in extreme cases, death.

Local allergy in patients occasionally occurs as redness, swelling, and itching at the site of insulin injection. This condition usually resolves in a few days to a few weeks. In some instances, this condition may be related to factors other than insulin, such as irritants in the skin cleansing agent or poor injection technique. Systemic allergy, less common but potentially more serious, is a generalized allergy to insulin. It 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.

Lipodystrophy may occur at the injection site.

4.9 Overdose

Insulins have no specific overdose definitions because serum glucose concentrations are a result of complex interactions between insulin levels, glucose availability and other metabolic processes. Hypoglycaemia may occur as a result of an excess of insulin or insulin lispro relative to food intake and energy expenditure.

Hypoglycaemia may be associated with listlessness, confusion, palpitations, headache, sweating and vomiting.

Mild hypoglycaemic episodes will respond to oral administration of glucose or other sugar or saccharated products.

Correction of moderately severe hypoglycaemia can be accomplished by intramuscular or subcutaneous administration of glucagon, followed by oral carbohydrate when the patient recovers sufficiently. Patients who fail to respond to glucagon must be given glucose solution intravenously.

If the patient is comatose, glucagon should be administered intramuscularly or subcutaneously. However, glucose solution must be given intravenously if glucagon is not available or if the patient fails to respond to glucagon. The patient should be given a meal as soon as consciousness is recovered.

5. PHARMACOLOGICAL PROPERTIES

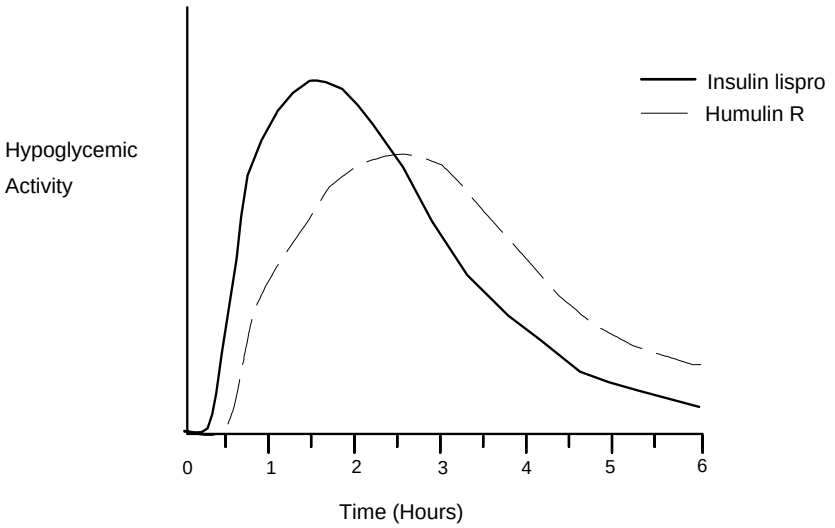
5.1 Pharmacodynamic properties

Pharmaco-therapeutic group : fast acting human insulin analogue, ATC Code A10A B04

The primary activity of insulin lispro is the regulation of glucose metabolism.

In addition, insulins have several anabolic and anti-catabolic actions on a variety of different tissues. Within muscle tissue this includes increasing glycogen, fatty acid, glycerol and protein synthesis and amino acid uptake, while decreasing glycogenolysis, glyconeogenesis, ketogenesis, lipolysis, protein catabolism and amino acid output.

Insulin lispro has a rapid onset of action (approximately 15 minutes), thus allowing it to be given closer to a meal (within zero to 15 minutes of the meal) when compared to regular insulin
(30 to 45 minutes before). Insulin lispro takes effect rapidly and has a shorter duration of activity (2 to 5 hours) when compared to regular insulin. As with all insulin preparations, the time course of insulin lispro action may vary in different individuals or at different times in the same individual and is dependent on site of injection, blood supply, temperature and physical activity. The typical activity profile following subcutaneous injection is illustrated below.



The above representation reflects the relative amount of glucose over time required to maintain subject's whole blood glucose concentrations near fasting levels and is an indicator of the effect of these insulins on glucose metabolism over time.

5.2 Pharmacokinetic properties

The pharmacokinetics of insulin lispro reflect a compound that is rapidly absorbed, and achieves peak blood levels 30 to 70 minutes following subcutaneous injection. When considering the clinical relevance of these kinetics, it is more appropriate to examine the glucose utilization curves (as discussed in 5.1).

5.3 Preclinical safety data

In *in vitro* tests, including binding to insulin receptor sites and effects on growing cells, insulin lispro behaved in a manner that closely resembled human insulin. Studies also demonstrate that the dissociation of binding to the insulin receptor of insulin lispro is equivalent to human insulin. Acute, one month, and twelve month toxicology studies produced no significant toxicity findings.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Each cartridge will contain insulin lispro and the following excipients:
(a) *m*-Cresol distilled [3.15mg/mL] (b) glycerol (c) dibasic sodium phosphate.7H2O (d) zinc oxide (e) water for injection (f) hydrochloric acid and (g) sodium hydroxide.
These are included as:
(a) preservative and stabilizer (b) tonicity modifier (c) a buffering agent (d) stabilizer (e) a vehicle (f) pH adjustment and (g) pH adjustment respectively.

6.2 Incompatibilities

Humalog-HumaPen preparations should not be mixed with animal insulin preparations.

6.3 Shelf-life

Two years when stored under appropriate conditions. The in-use shelf-life is 28 days.

6.4 Special precautions for storage

Humalog-HumaPen preparations should be stored in a refrigerator between 2° and 8°C. They should not be frozen or exposed to excessive heat or sunlight. Once in use the Humalog-HumaPen can be kept at ambient temperature (below 30˚C)for up to 28 days and should not be refrigerated.

6.5 Nature and content of container

The solution is filled aseptically into Type I flint glass cartridges. The glass conforms to Ph Eur requirements. The containers are then sealed with butyl or halobutyl disk seals and plunger heads. Dimethicone or silicone emulsion may be used to treat the cartridge plunger, and/or the glass cartridge. The closures are secured with aluminium seals. The cartridges are sealed in a disposable pen injector, the HumaPen. Needles are not included.

5 x 3ml Humalog-HumaPens

6.6 Instructions for use and handling, and disposal (if appropriate)

a) <u>Preparing a dose</u>

1. Inspect the Humalog-HumaPen.

It should be clear and colourless. Do not use Humalog-HumaPen if it appears cloudy, thickened, or slightly coloured or if solid particles are visible.

2. Put on the needle.

Wipe the rubber seal with alcohol. Remove the paper tab from the needle. Screw the capped needle onto the pen until it is tight. Hold the pen with needle pointing up and remove the outer needle cap and cover

3. Priming Pen (check insulin flow)

(a) The arrow should be visible in the dose window. If the arrow is not present, turn the dose knob clockwise until the arrow appears and notch is felt or visually aligned.

(b) Pull dose knob out (in direction of the arrow) until a "0" appears in the dose window. A dose cannot be dialled until the dose knob is pulled out.

(c) Turn dose knob clockwise until a "2" appears in the dose window.

(d) Hold the pen with needle pointing up and tap the clear cartridge holder gently with your finger so any air bubbles collect near the top. Depress the dose knob fully until you feel or hear a click. You should see a drop of insulin at the tip of the needle. If insulin does not appear, repeat the procedure until insulin appears.

(e) Always prime the pen (check the insulin flow) before each injection. Failure to prime the pen may result in an inaccurate dose.

4. Setting the Dose

(a) Turn the dose knob clockwise until the arrow appears in the dose window and a notch is felt or visually aligned.

(b) Pull the dose knob out (in the direction of the arrow) until a "0" appears in the dose window. A dose cannot be dialled until the dose knob is pulled out.

(c) Turn the dose knob clockwise until the dose appears in the dose window. If too high a dose is dialled, turn the dose knob backward (anti-clockwise) until the correct dose appears in the window. A dose greater than the number of units remaining in the cartridge cannot be dialled.

(b) <u>Injecting a Dose</u>

1. Wash your hands.

2. Choose a site for injection.

3. Clean the skin with an alcohol swab.

4. Remove outer needle cap.

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

6. Press the knob down with the thumb (until you hear or feel a click) wait 5 seconds.

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

8. Immediately after an injection, use the outer needle cap to unscrew the needle. Remove the needle from the pen. This will ensure sterility, and prevent leakage, reentry of air, and potential needle clogs. Do not reuse the needle. Dispose of the needle in a responsible manner. Needles and pens must not be shared.

   The prefilled pen can be used until it is empty. Please properly discard or recycle.

9. Replace the cap on the pen.

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

11. The dose knob should be fully depressed before using the pen again.

(c) <u>Mixing Insulins</u>

Do not mix insulin in vials with insulin in cartridges

7. MARKETING AUTHORISATION HOLDER

Eli Lilly Nederland B V., Krijtwal 17-23, 3432 ZT Nieuwegein, The Netherlands.

8. NUMBER IN THE COMMUNITY REGISTER OF MEDICINAL PRODUCTS

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF TEXT

ANNEX II
THE MANUFACTURING AUTHORISATION HOLDERS RESPONSIBLE FOR BATCH RELEASE AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

A. MANUFACTURING AUTHORISATION HOLDERS

Manufacturers responsible for batch release

Lilly France S.A., Rue du Colonel Lilly, 67640 Fegersheim, France
Manufacturing Authorisation issued on 22 May 1995 by the Agence du Médicament, France.

Lilly S.A, Avda. de la Industria 30, Polígono Industrial 28100, Alcobendas (Madrid), Spain.
Manufacturing Authorisation issued on 23 June 1994 by the Ministerio de Sanidad y Consumo, Spain.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to renewable medical prescription

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

LABEL

EU/X/9X/00X/00X HP8725

3.0 ml

Humalog-HumaPen

100 U/ml (3.5mg/ml)

Insulin lispro

Solution for injection for subcutaneous use

Exp. Date / Lot No.

CARTON

EU/X/9X/00X/00X HP8725

5 x 3ml Pens

Humalog-HumaPen

100 U/ml (3.5 mg/ ml)

insulin lispro

(rDNA origin)

Store between 2° and 8°C.

Avoid freezing.

When in use, pens may be kept at room temperature (below 30°C) for up to 28 days, but do not expose to direct sunlight or excessive heat.

Pens in use should not be refrigerated.

Keep out of reach of children.

Solution for injection for subcutaneous use

Medicinal product subject to medical prescription.

Contains glycerol, zinc oxide, dibasic sodium phosphate 7 H20 with m-cresol as a preservative in water for injection.

Sodium hydroxide and/or hydrochloric acid may be added during manufacture to adjust pH.

Eli Lilly Nederland B.V.
Krijtwal 17-23, 3432 ZT, Nieuwegein
The Netherlands

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5 x 3ml Pens

Humalog-HumaPen

100U/ml (3.5 mg/ml)

Insulin lispro

Exp date/Lot No

Humalog-HumaPen

Insulin lispro

IMPORTANT: READ ENCLOSED LITERATURE

B. PACKAGE LEAFLET

Humalog-HumaPen (100U/ml, 3.0ml)
(Insulin lispro)

What you should know about Humalog-HumaPen

Please read all this leaflet carefully before you start to use Humalog-HumaPen. This leaflet does not contain all the information about Humalog-HumaPen that you may need to know, so please ask your doctor, a pharmacist or a diabetes nurse if you have any questions. This leaflet only applies to Humalog-HumaPen.

What is in Humalog-HumaPen?

Your medicine is called Humalog-HumaPen, 100U/ml, solution for subcutaneous injection. It is used to treat diabetes. Its active ingredient is insulin lispro. This is a man-made form of human insulin. It works more quickly than normal human insulin because the insulin molecule has been changed slightly. You should normally use Humalog-HumaPen within the 15 minutes before a meal. Its strength is 100 units in each millilitre (U-100/ml) solution for injection and each Humalog-HumaPen contains 300 units (3 millilitres). The Humalog in your HumaPen is the same as the Humalog which comes in separate Humalog cartridges. The HumaPen simply has a built in cartridge. When the pen is empty you cannot use it again.

Humalog-HumaPen also contains the inactive ingredients m-cresol, glycerol, dibasic sodium phosphate. 7 H_2O, zinc oxide and water for injection. Sodium hydroxide or hydrochloric acid may have been used to adjust the acidity.

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-HumaPen that your doctor has told you to use.

Humalog-HumaPen 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. Humalog-HumaPen is closely related to human insulin which is a natural hormone made by the pancreas.

Humalog-HumaPen is made by:

- Lilly France SA, Rue du Colonel Lilly, 67640 Fegersheim, France
- Lilly S.A., Avda de la Industria 30, Polígono Industrial 28100, Alcobendas (Madrid) Spain.

The product licence is held by: Eli Lilly Nederland B.V., Krijtwal 17-23, 3432 ZT Nieuwegein, The Netherlands

Why do I need to use Humalog-HumaPen?

You get diabetes if your pancreas does not make enough insulin to control the level of glucose in your blood. Humalog-HumaPen is a substitute for your own insulin and is

used to control glucose in the long term. It works very quickly and lasts for a shorter time than soluble insulin.

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

Before you inject Humalog-HumaPen

Make sure it is safe for you to use Humalog-HumaPen

- **If you think a "hypo" (low blood sugar) is starting, do not inject Humalog-HumaPen and do not drive. Further in this leaflet it tells you how to deal with a mild 'hypo'.**

- If you have ever had an allergic reaction to a Humalog product (see section D) tell your doctor, pharmacist or diabetes nurse.

- 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 'hypos' after switching from animal insulin to human insulin have reported that the early warning symptoms were less obvious or different. If you often have 'hypos' or have difficulty recognising 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?

- Are you taking **any** other medicines? Your insulin needs may change if you are taking the contraceptive pill, steroids, thyroid hormone replacement therapy, oral hypoglycaemics, aspirin, sulfa antibiotics, octreotide, "beta-2 stimulants" (for example ritodrine, salbutamol or terbutaline) or some antidepressants.

- Do you have trouble with your kidneys or liver?

- Are you exercising more than usual?

- Are you pregnant or thinking about becoming pregnant, or are you breast-feeding? 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 breast feeding, you may need to alter your insulin intake or diet.

- Is the patient a child under 12 years old

The amount of insulin you need may also change if you drink alcohol.

You should also tell your doctor, pharmacist or diabetes nurse specialist 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.

Using Humalog-HumaPen

Dosage

- You should normally inject Humalog-HumaPen within 15 minutes before 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-HumaPen under the skin. You should only inject it into a muscle if your doctor has told you to.

Preparing Humalog-HumaPen

- Humalog-HumaPen 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 colour and no solid pieces in it. Check this each time you inject yourself.

Getting the pen 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).

- Clear the air bubbles from your pen. There may still be some small air bubbles left in the Humalog-HumaPen - these are harmless. But if the air bubbles are too large it may affect the insulin dose.

Injecting the Humalog-HumaPen

- Before you make an injection, clean your skin well with an alcohol swab. 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 half an inch (1cm) 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 pen 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 Humalog-HumaPen you must use a new needle. Before every injection, clear any air bubbles. You can see how much insulin is left by holding the pen with the needle pointing down. The scale on the cartridge shows about how many units you have left.

- Do not mix any other insulin in your disposable pen. Once the pen 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.

Emergencies and overdoses

If your blood sugar is low, eat glucose tablets or sugar followed by fruit or biscuits, and then rest. This will often get you over a mild 'hypo' or 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 hypoglycaemia. Eat glucose or sugar after the glucagon injection. If you do not respond to glucagon you will have to go to hospital. Ask your doctor to tell you about glucagon.

If 'hypos' or 'hypers' (see A and B) are not treated they can be very serious and cause headaches, nausea, vomiting, dehydration, unconsciousness, coma or even death.

Always keep spare syringes and a spare bottle 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.

While using your insulin

Common problems of diabetes

A. Hypoglycaemia

Hypoglycaemia ('hypo' - low blood sugar) means there is not enough sugar in the blood. This can be caused if:

- you take too much Humalog-HumaPen 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 kidney 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
- rapid heartbeat

- nervousness or shakiness
- headache
- feeling sick
- cold sweat

B. Hyperglycaemia and diabetic ketoacidosis

Hyperglycaemia (‘hyper’ - too much sugar in the blood) means that your body does not have enough insulin. Hyperglycaemia can be brought about by:

- not taking your Humalog-HumaPen 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.

Hyperglycaemia 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.

D. Allergy to insulin

Local allergy: 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.

Systemic allergy: This allergy to insulin is not common. The symptoms are as follows.

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

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

E. Lipodystrophy

If you notice your skin thickening or pitting at the injection site, tell your doctor.

If you have these or any other side effects, tell your doctor.

How to store Humalog-HumaPen

Keep your Humalog-HumaPen in a fridge at between 2°-8°C. Do not put it near heat or in the sun. Do not freeze Humalog-HumaPen. If you cannot keep your Humalog-HumaPen in the fridge, you can keep it for up to 28 days at room temperature (below 30°C). Do not keep the pen that you are using in the fridge. Keep your medicine where children cannot see or reach it. Do not use it after the 'Use before' date.

Remember: This medicine is for you. Never give it to others. It may harm them, even if their symptoms are the same as yours.

USER MANUAL.

Will be incorporated into patient information leaflet or as a separate card as space allows.

Lilly

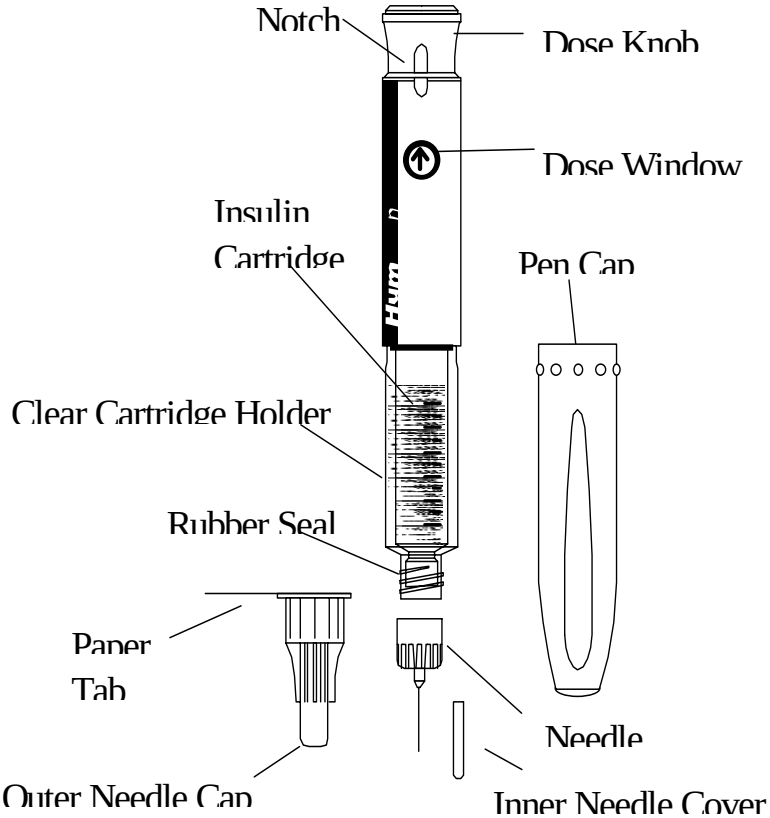
HumaPen

Instructions for Use

Read and follow these instructions carefully. Failure to follow the instructions may result in an inaccurate insulin dose.

Pen Features:

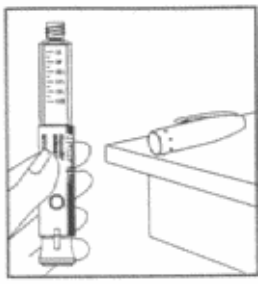
- A multiple dose, disposable prefilled pen containing 300 units of insulin
- Delivers up to 60 units per dose in single unit increments
- Easy to use; Compact size



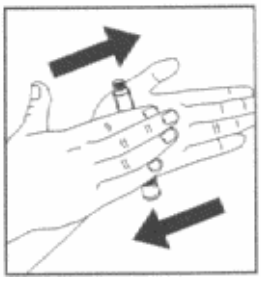
I. Preparing a Dose

1. Pull off the pen cap.

2. Check your prefilled pen to be sure it contains the correct type of insulin.

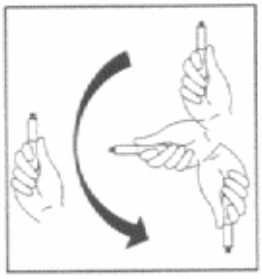


3. If using NPH or mixtures of insulin (cloudy), roll the pen back and forth 10 times.



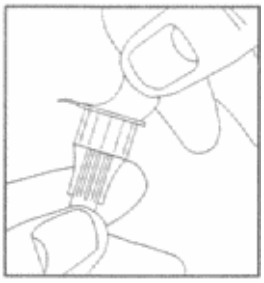
4. Then gently turn the pen up and down ten times until the insulin is evenly mixed.

Cloudy (NPH and mixtures) insulin cartridges contain a small bead to assist in mixing.

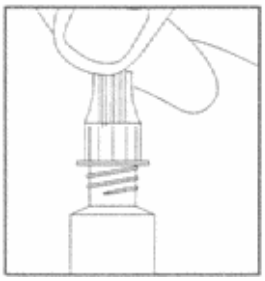


Attaching the Pen Needle

1. Remove the paper tab from the capped needle.



2. Screw the capped needle clockwise onto the end of the pen until tight.

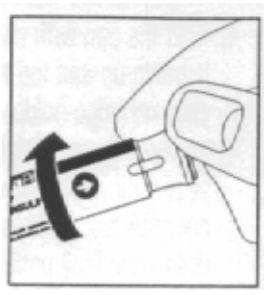


3. Hold the pen with needle pointing up and remove the outer needle cap and inner needle cover.

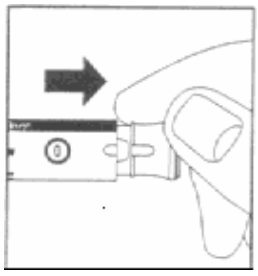
- Always attach a needle before priming, dialling and injecting your insulin dose.

Priming Pen (Check insulin flow)

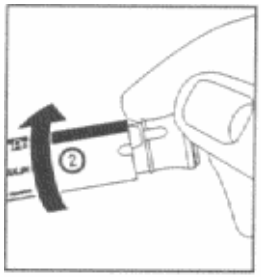
1. The arrow should be visible in the dose window. If the arrow is not present, turn the dose knob clockwise until the arrow appears and notch is felt or visually aligned.



2. Pull dose knob out (in direction of the arrow) until a "0" appears in the dose window.
   A dose cannot be dialled until the dose knob is pulled out.

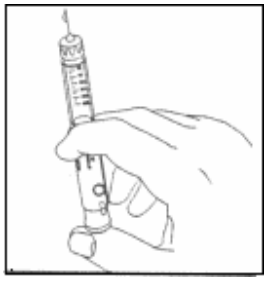


3. Turn the dose knob clockwise until a “2” appears in the dose window.



4. Hold the pen with needle pointing up and tap the clear cartridge holder gently with your finger so any air bubbles collect near the top. Depress the dose knob fully until you feel or hear a click. You should see a drop of insulin at the tip of the needle. If insulin does not appear, repeat the procedure until insulin appears.

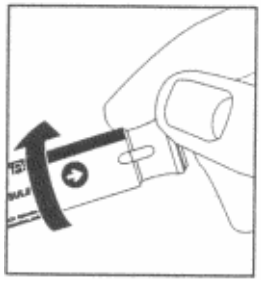
- Always prime the pen (check insulin flow) before each injection. Failure to prime the pen may result in an inaccurate dose.



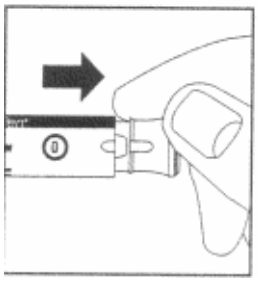
II Setting a Dose

- Always attach a needle before priming, dialling and injecting your insulin dose.

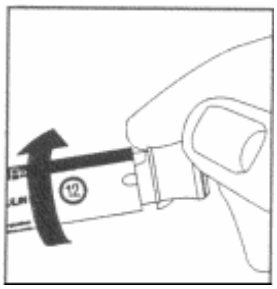
1. Turn the dose knob clockwise until the arrow appears in the dose window and a notch is felt or visually aligned.



2. Pull the dose knob out (in the direction of the arrow) until a “0” appears in the dose window. A dose cannot be dialled until the dose knob is pulled out.



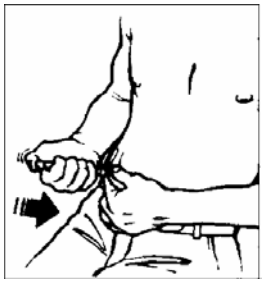
3. Turn the dose knob clockwise until your dose appears in the dose window. If too high a dose is dialled, turn the dose knob backward (anti-clockwise) until the correct dose appears in the window. A dose greater than the number of units remaining in the cartridge can not be dialled.



III Injecting a dose

- Always attach a needle before priming, dialling and injecting your insulin dose. *

1. Prepare the skin and use the injection technique recommended by your Health Care Professional. Inject the insulin by fully depressing the dose knob until you hear or feel a click. Maintain pressure for 5 seconds before removing the needle from the skin.

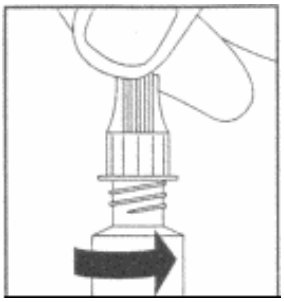


After injecting your dose a diamond ◆ or arrow ➔ will appear in the dose window.

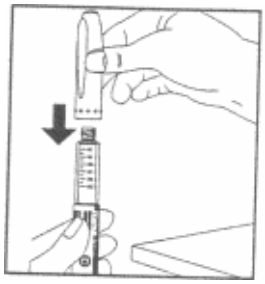
- Anytime you begin to depress the dose knob, the dose setting should not be changed until the dose knob has been fully depressed.

* If you have dialled and depressed the dose knob without a needle attached or if the needle is clogged see the Question and Answers section.

2. Replace the outer needle cap and dispose of the needle as directed by your Health Care Professional.



3. Replace the cap on the HumaPen.



4. Do not store the pen with a needle attached.

5. Subsequent Injections

Always check that the dose knob is fully depressed and the arrow is in the dose window before using the pen again. Then proceed with Preparing a Dose, Setting a Dose, and Injecting a Dose.

- Always use a new needle for each injection.

Questions and Answers

PROBLEM	ACTION
Dose dialled and dose knob depressed without a needle attached or if the needled is clogged	To obtain an accurate dose you must: - attach a new needle - fully depress the dose knob (even if a "0" appears in the window) - prime the pen
Wrong dose (too high or too low) dialled	If you have not depressed the dose knob turn the dose knob backward or forward to correct the dose. If you have depressed the dose knob the dose setting should not be changed until the dose knob has been fully depressed.
Not sure how much insulin remains in the cartridge	Hold the pen with the needle end pointing down. The scale (20 units between marks) on the insulin cartridge holder shows an estimate of the number of units remaining. These numbers should not be used for measuring an insulin dose.
Full dose cannot be dialled	The pen will prevent dialling a dose greater than the number of insulin units remaining in the cartridge. If a partial dose remains in the pen you may either: 1. Give the partial dose and then give the remaining dose using a new pen; or 2. Give the full dose with a new pen.

Important Notes

- Please read the instructions carefully before using HumaPen.
- Failure to follow the instructions may result in an inaccurate insulin dose.
- Attach the needle before priming, dialling and injecting your insulin dose.
- Do not share your HumaPen.
- The numbers on the insulin cartridge holder give an estimate of the amount of insulin remaining in the cartridge. Do not use these numbers for measuring the insulin dose.
- Keep HumaPen out of the reach of children.
- HumaPen once in use can be stored at room temperature for up to 28 days. Before use, your HumaPen should be stored in a cold place (2-8˚C), preferably in a refrigerator, but not in the freezing compartment.
- Keep the pen away from extreme hot or cold temperatures and direct sunlight. Do not use insulin that has been frozen.
- Do not store HumaPen with the pen needle attached. Doing so may cause insulin to leak, air bubbles to form, or insulin crystals to clog the needle. Use a new needle for each injection.
- Always carry an additional HumaPen in case your pen is lost or damaged.
- Any changes in insulin should be made only under medical supervision.

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