

INFORMATION FOR THE PATIENT
3 ML DISPOSABLE INSULIN DELIVERY DEVICE

HUMALOG[®] Mix75/25[™] Pen
75% INSULIN LISPRO PROTAMINE SUSPENSION AND
25% INSULIN LISPRO INJECTION
(rDNA ORIGIN)

WARNINGS

THIS LILLY HUMAN INSULIN ANALOG MIXTURE IS DIFFERENT FROM OTHER INSULIN MIXTURES IN THAT ITS ONSET OF ACTION IS VERY QUICK. THE QUICK ONSET OF ACTION MEANS THAT YOU SHOULD TAKE YOUR DOSE OF HUMALOG[®] Mix75/25[™] (75% INSULIN LISPRO PROTAMINE SUSPENSION AND 25% INSULIN LISPRO INJECTION, [rDNA ORIGIN]) WITHIN 15 MINUTES BEFORE YOU EAT.

ANY CHANGE OF INSULIN SHOULD BE MADE CAUTIOUSLY AND ONLY UNDER MEDICAL SUPERVISION. CHANGES IN STRENGTH, MANUFACTURER, TYPE (E.G., REGULAR, NPH, ANALOG), SPECIES (BEEF, PORK, BEEF-PORK, HUMAN), OR METHOD OF MANUFACTURE (rDNA VERSUS ANIMAL-SOURCE INSULIN) MAY RESULT IN THE NEED FOR A CHANGE IN THE TIMING OR DOSAGE OF HUMALOG Mix75/25.

PATIENTS TAKING HUMALOG Mix75/25 MAY REQUIRE A CHANGE IN DOSAGE FROM THAT USED WITH OTHER INSULINS. IF AN ADJUSTMENT IS NEEDED, IT MAY OCCUR WITH THE FIRST DOSE OR DURING THE FIRST SEVERAL WEEKS OR MONTHS.

TO OBTAIN AN ACCURATE DOSE, CAREFULLY READ AND FOLLOW THE “DISPOSABLE INSULIN DELIVERY DEVICE USER MANUAL” AND THIS “INFORMATION FOR THE PATIENT” INSERT BEFORE USING THIS PRODUCT. BEFORE EACH INJECTION, YOU SHOULD PRIME THE PEN, A NECESSARY STEP TO MAKE SURE THE PEN IS READY TO DOSE. PRIMING THE PEN IS IMPORTANT TO CONFIRM THAT INSULIN COMES OUT WHEN YOU PUSH THE INJECTION BUTTON AND TO REMOVE AIR THAT MAY COLLECT IN THE INSULIN CARTRIDGE DURING NORMAL USE. IF YOU DO NOT PRIME, YOU MAY RECEIVE TOO MUCH OR TOO LITTLE INSULIN (*see also* INSTRUCTIONS FOR PEN USE section).

DIABETES

Insulin is a hormone produced by the pancreas, a large gland that lies near the stomach. This hormone is necessary for the body's correct use of food, especially sugar. Diabetes occurs when the pancreas does not make enough insulin to meet your body's needs.

To control your diabetes, your doctor has prescribed injections of insulin products to keep your blood glucose at a near-normal level. You have been instructed to test your blood and/or urine regularly for glucose. Studies have shown that some chronic complications of diabetes such as eye disease, kidney disease, and nerve disease can be significantly reduced if the blood sugar is maintained as close to normal as possible. The American Diabetes Association recommends that if your premeal glucose levels are consistently above 140 mg/dL, bedtime glucose levels are consistently above 160 mg/dL or your hemoglobin A_{1c} (HbA_{1c}) is more than 8%, consult your doctor. A change in your diabetes therapy may be needed. If your blood tests consistently show below-targeted glucose levels, you should also let your doctor know. Proper control of your

diabetes requires close and constant cooperation with your doctor. Despite diabetes, you can lead an active and healthy life if you eat a balanced diet, exercise regularly, and take your insulin injections as prescribed.

Always keep an extra Humalog Mix75/25 Pen as well as a spare needle on hand. Always wear diabetic identification so that appropriate treatment can be given if complications occur away from home.

HUMALOG Mix75/25

Description

Humalog (insulin lispro) is made by a special non-disease-producing laboratory strain of *Escherichia coli* bacteria that has been genetically altered by the addition of the gene for this human insulin analog. Humalog Mix75/25 is a mixture of 75% insulin lispro protamine suspension and 25% insulin lispro. It is a longer-acting insulin combined with the more rapid onset of action of Humalog. The duration of activity is similar to that of Humulin[®] 70/30 and may last up to 24 hours following injection. The time course of Humalog Mix75/25 action, like that of other insulins, may vary in different individuals or at different times in the same individual, based on dose, site of injection, blood supply, temperature, and physical activity. Humalog Mix75/25 is a sterile suspension and is for subcutaneous injection. It should not be used intravenously. The concentration of Humalog Mix75/25 is 100 units/mL (U-100).

Humalog Mix75/25 starts lowering blood glucose more quickly than regular human insulin, allowing for convenient dosing immediately before a meal (within 15 minutes). In contrast, mixtures containing regular human insulin should be given 30-60 minutes before a meal.

Identification

Insulin lispro injection (rDNA origin), manufactured by Eli Lilly and Company, has the trademark Humalog. Humalog products are available in two formulations — Humalog and Humalog Mix75/25. Your doctor has prescribed the type of insulin that he/she believes is best for you.

DO NOT USE ANY OTHER INSULIN EXCEPT ON YOUR DOCTOR'S ADVICE AND DIRECTION. YOU SHOULD NOT MIX HUMALOG Mix75/25 WITH ANOTHER INSULIN.

The Humalog Mix75/25 Pen is available in boxes of 5 disposable insulin delivery devices ("insulin pens"). The Humalog Mix75/25 Pen is not designed to allow any other insulin to be mixed in its cartridge of Humalog Mix75/25, or for the cartridge to be removed.

Always examine the appearance of Humalog Mix75/25 suspension in the insulin pen before administering a dose. Roll the Pen between the palms 10 times. Holding the Pen by one end, invert it 180° slowly 10 times to allow the glass bead to travel the full length of the cartridge with each inversion. Humalog Mix75/25 should look uniformly cloudy or milky after mixing. If not, repeat the above steps until the contents are mixed. Pens containing Humalog Mix75/25 suspension should be examined frequently. Do not use if the insulin substance (the white material) remains visibly separated from the liquid after mixing. Do not use a Humalog Mix75/25 Pen if there are clumps in the insulin after mixing. Do not use a Humalog Mix75/25 Pen if solid white particles stick to the bottom or wall of the cartridge, giving a frosted appearance. Always check the appearance of the Humalog Mix75/25 suspension before using. If you note anything unusual in its appearance or notice your insulin requirements changing markedly, consult your doctor.

Storage

Humalog Mix75/25 Pens should be stored in a refrigerator but not in the freezer. Do not use an insulin pen if it has been frozen. The Humalog Mix75/25 Pen that you are currently using should not be refrigerated but should be kept as cool as possible and away from direct heat and light. When in use, unrefrigerated Humalog Mix75/25 Pens must be discarded after 10 days, even if they still contain Humalog Mix75/25. Do not use Humalog Mix75/25 Pens after the expiration date stamped on the label.

INSTRUCTIONS FOR PEN USE

It is important to read, understand, and follow the instructions in the “Disposable Insulin Delivery Device User Manual” before using. Failure to follow instructions may result in getting too much or too little insulin. The needle must be changed and the pen must be primed before each injection to make sure the pen is ready to dose. These steps are important to confirm that insulin comes out when you push the injection button, and to remove air that may collect in the insulin cartridge during normal use.

Every time you inject:

- Use a new needle
- Prime to make sure the pen is ready to dose
- Make sure you got a full dose.

NEVER SHARE INSULIN PENS OR NEEDLES.

PREPARING THE PEN FOR INJECTION

1. Inspect the appearance of Humalog Mix75/25 suspension in the Humalog Mix75/25 Pen. It should look uniformly cloudy or milky after mixing. Once the Humalog Mix75/25 Pen is in use, inspect the insulin in the Humalog Mix75/25 Pen before each injection.
2. Follow the instructions in the “Disposable Insulin Delivery Device User Manual” for these steps:
 - Preparing the Pen
 - Attaching the Needle. **Use a new needle for each injection.**
 - Priming the Pen. **The pen must be primed before each injection to make sure the pen is ready to dose.** Performing the priming step is important to confirm that insulin comes out when you push the injection button, and to remove air that may collect in the insulin cartridge during normal use.
 - Setting (Dialing) a Dose
 - Injecting the Dose. **To make sure you have received your dose, you must push the injection button all the way down until you see a diamond (◆) or an arrow (→) in the center of the dose window.**
 - Following an Injection

PREPARING FOR INJECTION

1. Wash your hands.
2. To avoid tissue damage, choose a site for each injection that is at least 1/2 inch from the previous injection site. The usual sites of injection are abdomen, thighs, and arms.
3. Cleanse the skin with alcohol where the injection is to be made.
4. With one hand, stabilize the skin by spreading it or pinching up a large area.
5. Inject the dose as instructed by your doctor. Hold the needle under the skin for at least 5 seconds.
6. After dispensing a dose, pull the needle out and apply gentle pressure over the injection site for several seconds. **Do not rub the area.**
7. Immediately after an injection, remove the needle from the Humalog Mix75/25 Pen. Doing so will guard against contamination, and prevent leakage of Humalog Mix75/25, reentry of air, and needle clogs. **Do not reuse needles. Dispose of needles in a responsible manner.**

DOSAGE

Your doctor has told you which insulin to use, how much, and when and how often to inject it. Because each patient’s case of diabetes is different, this schedule has been individualized for you. Your usual Humalog Mix75/25 dose may be affected by changes in your food, activity, or work schedule. Carefully follow your doctor’s instructions to allow for these changes. Other things that may affect your Humalog Mix75/25 dose are:

Illness

Illness, especially with nausea and vomiting, may cause your insulin requirements to change. Even if you are not eating, you will still require insulin. You and your doctor should establish a sick day plan for you to use in case of illness. When you are sick, test your blood glucose/urine ketones frequently and call your doctor as instructed.

Pregnancy

Good control of diabetes is especially important for you and your unborn baby. Pregnancy may make managing your diabetes more difficult. If you are planning to have a baby, are pregnant, or are nursing a baby, consult your doctor. Humalog Mix75/25 has not been tested in pregnant or nursing women.

Medication

Insulin requirements may be increased if you are taking other drugs with hyperglycemic activity, such as oral contraceptives, corticosteroids, or thyroid replacement therapy. Insulin requirements may be reduced in the presence of drugs with blood-glucose-lowering activity, such as oral antidiabetic agents, salicylates (for example, aspirin), sulfa antibiotics, alcohol, and certain antidepressants. Your health care professional is aware of these and other medications that may affect your diabetes control. Therefore, always discuss any medications you are taking with your doctor.

Exercise

Exercise may lower your body's need for insulin products during and for some time after the physical activity. Exercise may also speed up the effect of a Humalog Mix75/25 dose, especially if the exercise involves the area of your injection site. Discuss with your doctor how you should adjust your regimen to accommodate exercise.

Travel

Persons traveling across more than 2 time zones should consult their doctor concerning adjustments in their insulin schedule.

COMMON PROBLEMS OF DIABETES

Hypoglycemia (Insulin Reaction)

Hypoglycemia (too little glucose in the blood) is one of the most frequent adverse events experienced by insulin users. It can be brought about by:

1. **Missing or delaying meals**
2. Taking too much insulin
3. Exercising or working more than usual
4. An infection or illness (especially with diarrhea or vomiting)
5. A change in the body's need for insulin
6. Diseases of the adrenal, pituitary or thyroid gland, or progression of kidney or liver disease
7. Interactions with other drugs that lower blood glucose, such as oral antidiabetic agents, salicylates (for example, aspirin), sulfa antibiotics, and certain antidepressants
8. Consumption of alcoholic beverages

Symptoms of mild to moderate hypoglycemia may occur suddenly and can include:

- sweating
- dizziness
- palpitation
- tremor
- hunger
- restlessness
- tingling in the hands, feet, lips, or tongue
- lightheadedness
- inability to concentrate
- drowsiness
- sleep disturbances
- anxiety
- blurred vision
- slurred speech
- depressed mood
- irritability
- abnormal behavior
- unsteady movement

- headache
 - personality changes
- Signs of severe hypoglycemia can include:
- disorientation
 - seizures
 - unconsciousness
 - death

Therefore, it is important that assistance be obtained immediately.

Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as long duration of diabetes, diabetic nerve disease, use of medications such as beta-blockers, changing insulin preparations, or intensified control (3 or more injections per day) of diabetes. A few patients who have experienced hypoglycemic reactions after transfer from animal-source insulin to human insulin have reported that the early warning symptoms of hypoglycemia were less pronounced or different from those experienced with their previous insulin.

Without recognition of early warning symptoms, you may not be able to take steps to avoid more serious hypoglycemia. Be alert for all of the various types of symptoms that may indicate hypoglycemia. Patients who experience hypoglycemia without early warning symptoms should monitor their blood glucose frequently, especially prior to activities such as driving. If the blood glucose is below your normal fasting glucose, you should consider eating or drinking sugar-containing foods to treat your hypoglycemia.

Mild to moderate hypoglycemia may be treated by eating foods or drinks that contain sugar. Patients should always carry a quick source of sugar, such as candy mints or glucose tablets. More severe hypoglycemia may require the assistance of another person. Patients who are unable to take sugar orally or who are unconscious require an injection of glucagon or should be treated with intravenous administration of glucose at a medical facility.

You should learn to recognize your own symptoms of hypoglycemia. If you are uncertain about these symptoms, you should monitor your blood glucose frequently to help you learn to recognize the symptoms that you experience with hypoglycemia.

If you have frequent episodes of hypoglycemia or experience difficulty in recognizing the symptoms, you should consult your doctor to discuss possible changes in therapy, meal plans, and/or exercise programs to help you avoid hypoglycemia.

Hyperglycemia and Diabetic Ketoacidosis

Hyperglycemia (too much glucose in the blood) may develop if your body has too little insulin. Hyperglycemia can be brought about by any of the following:

1. Omitting your insulin or taking less than the doctor has prescribed
2. Eating significantly more than your meal plan suggests
3. Developing a fever, infection, or other significant stressful situation.

In patients with type 1 or insulin-dependent diabetes, prolonged hyperglycemia can result in diabetic ketoacidosis (DKA). The first symptoms of DKA usually come on gradually, over a period of hours or days, and include a drowsy feeling, flushed face, thirst, loss of appetite, and fruity odor on the breath. With DKA, urine tests show large amounts of glucose and ketones. Heavy breathing and a rapid pulse are more severe symptoms. If uncorrected, prolonged hyperglycemia or DKA can lead to nausea, vomiting, stomach pains, dehydration, loss of consciousness, or death. Therefore, it is important that you obtain medical assistance immediately.

Lipodystrophy

Rarely, administration of insulin subcutaneously can result in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue). If you notice either of these conditions, consult your doctor. A change in your injection technique may help alleviate the problem.

Allergy

Local Allergy — Patients occasionally experience redness, swelling, and itching at the site of injection. This condition, called local allergy, usually clears up 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. If you have local reactions, contact your doctor.

Systemic Allergy — Less common, but potentially more serious, is generalized allergy to insulin, which 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. If you think you are having a generalized allergic reaction, notify a doctor immediately.

ADDITIONAL INFORMATION

Additional information about diabetes may be obtained from your diabetes educator.

DIABETES FORECAST is a national magazine designed especially for patients with diabetes and their families and is available by subscription from the American Diabetes Association, National Service Center, 1660 Duke Street, Alexandria, Virginia 22314, 1-800-DIABETES (1-800-342-2383). Another publication, **DIABETES COUNTDOWN**, is available from the Juvenile Diabetes Foundation International (JDF), 120 Wall Street, 19th Floor, New York, New York 10005-4001, 1-800-JDF-CURE (1-800-533-2873).

Additional information about Humalog Mix75/25 and Humalog Mix75/25 Pen can be obtained by calling 1-888-88-LILLY (1-888-885-4559) or consult the Eli Lilly and Company Internet Web Site at <http://www.lilly.com/diabetes>.

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