

Package Leaflet: Information for the user

PenMix[®] 30 100 IU/ml suspension for injection in cartridge
PenMix[®] 40 100 IU/ml suspension for injection in cartridge
PenMix[®] 50 100 IU/ml suspension for injection in cartridge
Protaphane[®] Penfill[®] 100 IU/ml suspension for injection in cartridge
Insulin human (rDNA)

Read all of this leaflet carefully before you start using your insulin

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or your pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or your pharmacist.

1. WHAT PENMIX[®] AND PROTAPHANE[®] ARE AND WHAT THEY ARE USED FOR

PenMix[®] and Protaphane[®] are human insulins used to treat diabetes. Diabetes mellitus is a disease where your body does not produce enough insulin to control the level of your blood sugar. PenMix[®] is a mixture of fast-acting insulin and long-acting insulin. This means that it will start to lower your blood sugar about ½ hour after you take it, and the effect will last for approximately 24 hours. Protaphane[®] is a long-acting insulin. This means that it will start to lower your blood sugar about 1½ hours after you take it, and the effect will last for approximately 24 hours. Protaphane[®] is often given in combination with fast-acting insulin products.

2. BEFORE YOU USE PENMIX[®] OR PROTAPHANE[®]

Do not use PenMix[®] or Protaphane[®]:

- ▶ **In insulin infusion pumps.**
- ▶ **If you are allergic (hypersensitive)** to human insulin or any of the other ingredients in PenMix[®] or Protaphane[®] (see 7. FURTHER INFORMATION)
- ▶ **If you suspect hypoglycemia** (low blood sugar) is starting (see 4. WHAT TO DO IN AN EMERGENCY).
- ▶ **If the cartridge or the device containing the cartridge is dropped, damaged or crushed.**
- ▶ **If it has not been stored correctly** or been frozen (see 6. HOW TO STORE PENMIX[®] OR PROTAPHANE[®]).
- ▶ If the resuspended insulin does not appear uniformly white and cloudy.

Before using PenMix[®] or Protaphane[®]:

- ▶ **Check the label to make sure** it is the right type of insulin.
- ▶ **Always check** the cartridge, including the rubber stopper. Do not use it if any damage is seen or if there is a gap between the rubber stopper and the white label band. Take it back to your supplier. See your delivery system manual for further instructions.
- ▶ **Always use a new needle** for each injection to prevent contamination.
- ▶ **Needles and PenMix[®] and Protaphane[®] Penfill[®] must not be shared.**

Take special care with PenMix[®] and Protaphane[®]:

- ▶ **If you have trouble** with your kidneys or liver, or with your adrenal, pituitary or thyroid glands.
- ▶ **If you drink alcohol**, watch for signs of a hypo and never drink alcohol on an empty stomach.
- ▶ **If you exercise** more than usual or if you want to change your usual diet, as this may affect your blood sugar level.
- ▶ **If you are ill**, carry on taking your insulin and consult your doctor.
- ▶ **If you are going abroad**: travelling over time zones may affect your insulin needs and the timing of your injections. Consult your doctor if you are planning such travelling.

Using other medicines

Some medicines affect the way glucose works in your body and this may influence your insulin dose. Listed below are the most common medicines which may affect your insulin treatment. Tell your doctor, nurse or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. In particular, you should tell your doctor if you are using any medicine mentioned below that may affect your blood sugar level.

Your need for insulin may change if you also take other medicines for treatment of diabetes; monoamine oxidase inhibitors (MAOI); beta-blockers; ACE-inhibitors; acetylsalicylic acid; anabolic steroids; sulphonamides; oral contraceptives; thiazides; glucocorticoids; thyroid hormone therapy; sympathomimetics; growth hormone; danazol; octreotide or lanreotide.

Thiazolidinediones (class of oral antidiabetic medicines used for the treatment of type 2 diabetes mellitus)

Some patients with long-standing type 2 diabetes mellitus and heart disease or previous stroke who are treated with thiazolidinediones in combination with insulin may develop 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 localised swelling (oedema).

Pregnancy and breast-feeding

If you are pregnant, planning a pregnancy or breast-feeding, please contact your doctor for advice.

Driving and using machines

If you drive or use tools or machines, watch out for signs of a hypo. Your ability to concentrate or to react will be less during a hypo. Never drive or use machinery if you feel a hypo coming on. Discuss with your doctor whether you can drive or use machines at all, if you have a lot of hypos or if you find it hard to recognise hypos.

3. HOW TO USE PENMIX[®] OR PROTAPHANE[®]

Talk about your insulin needs with your doctor and nurse. Make sure you get PenMix[®] or Protaphane[®] Penfill[®] as your doctor and nurse have told you to use and follow their advice carefully.

If your doctor has switched you from one type or brand of insulin to another, your dose may have to be adjusted by your doctor.

Eat a meal or snack containing carbohydrates within 30 minutes of the injection.

It is recommended that you measure your blood sugar regularly.

How to use this insulin

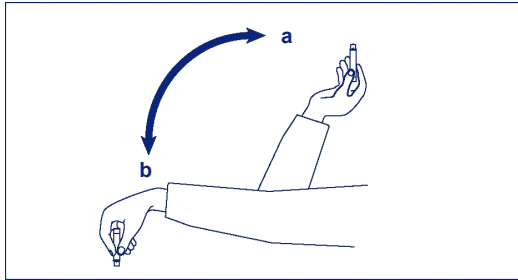
PenMix[®] and Protaphane[®] are for injection under the skin (subcutaneously). Never inject your insulin directly into a vein or muscle. Always vary the sites you inject within the same region, to reduce the risk of developing lumps or skin pitting (see 5. POSSIBLE SIDE EFFECTS). The best places to give yourself an injection are: the front of your waist

(abdomen); your buttocks; the front of your thighs or upper arms. Your insulin will work more quickly if you inject it around the waist.

Resuspending the insulin

Resuspending is easier when the insulin has reached room temperature.

Before you put the PenMix[®] or Protaphane[®] Penfill[®] cartridge into the insulin delivery system, move it up and down between positions **a** and **b** and back (see the picture) so that the glass ball moves from one end of the cartridge to the other at least 20 times. Repeat this movement at least 10 times before each injection. The movement must always be repeated until the liquid appears uniformly white and cloudy. Complete the other stages of injection without delay.



Check there are at least 12 units of insulin left in the cartridge to allow even resuspending. If there are less than 12 units left, use a new one.

How to inject this insulin

- ▶ **Inject the insulin** under the skin. Use the injection technique advised by your doctor or nurse and as described in your delivery system manual.
- ▶ **Keep the needle under your skin** for at least 6 seconds. Keep the push button fully depressed until the needle has been withdrawn. This will ensure correct delivery and limit possible flow of blood into the needle or insulin reservoir.
- ▶ **After each injection** be sure to remove and discard the needle and store PenMix[®] or Protaphane[®] Penfill[®] without the needle attached. Otherwise the liquid may leak out which can cause inaccurate dosing.

Do not refill PenMix[®] or Protaphane[®] Penfill[®].

PenMix[®] and Protaphane[®] Penfill[®] cartridges are designed to be used with Novo Nordisk insulin delivery systems and NovoFine[®] or NovoTwist[®] needles.

If you are treated with PenMix[®] or Protaphane[®] Penfill[®], and another insulin PenMix[®] or Penfill[®] cartridge, you should use two insulin delivery systems, one for each type of insulin.

As a precautionary measure, always carry a spare insulin delivery device in case your PenMix[®] or Protaphane[®] Penfill[®] cartridge is lost or damaged.

4. WHAT TO DO IN AN EMERGENCY

If you get a hypo

A hypo means your blood sugar level is too low.

The warning signs of a hypo may come on suddenly and can include: cold sweat; cool pale skin; headache; rapid heart beat; feeling sick; feeling very hungry; temporary changes in vision; drowsiness; unusual tiredness and weakness; nervousness or tremor; feeling anxious; feeling confused; difficulty in concentrating.

If you get any of these signs, eat glucose tablets or a high sugar snack (sweets, biscuits, fruit juice), then rest.

Do not take any insulin if you feel a hypo coming on.

Carry glucose tablets, sweets, biscuits or fruit juice with you, just in case.

Tell your relatives, friends and close colleagues that if you pass out (become unconscious), they must turn you on your side and seek medical advice straight away. They must not give you any food or drink as it could choke you.

- ▶ **If severe hypoglycaemia** is not treated, it can cause brain damage (temporary or permanent) and even death.
- ▶ **If you have a hypo** that makes you pass out, or a lot of hypos, talk to your doctor. The amount or timing of insulin, food or exercise may need to be adjusted.

Using glucagon

You may recover more quickly from unconsciousness with an injection of the hormone glucagon by someone who knows how to use it. If you are given glucagon, you will need glucose or a sugary snack as soon as you are conscious. If you do not respond to glucagon treatment, you will have to be treated in a hospital. Seek medical advice after an injection of glucagon; you need to find the reason for your hypo to avoid getting more.

Causes of a hypo

You get a hypo if your blood sugar gets too low. This might happen:

- If you take too much insulin
- If you eat too little or miss a meal
- If you exercise more than usual

If your blood sugar gets too high

Your blood sugar may get too high (this is called hyperglycaemia).

The warning signs appear gradually. They include: increased urination; feeling thirsty; losing your appetite; feeling sick (nausea or vomiting); feeling drowsy or tired; flushed, dry skin; dry mouth and a fruity (acetone) smell of the breath.

If you get any of these signs, test your blood sugar level and test your urine for ketones if you can. Then seek medical advice straight away.

These may be signs of a very serious condition called diabetic ketoacidosis. If you do not treat it, this could lead to diabetic coma and eventually death.

Causes of hyperglycaemia

- Having forgotten to take your insulin
- Repeatedly taking less insulin than you need
- An infection or a fever
- Eating more than usual
- Less exercise than usual

5. POSSIBLE SIDE EFFECTS

Like all medicines, PenMix[®] or Protaphane[®] can cause side effects, although not everybody gets them.

Side effects reported very commonly (in more than 1 patient in 10)

Low blood sugar (hypoglycaemia). See the advice in 4 WHAT TO DO IN AN EMERGENCY.

Side effects reported uncommonly (in less than 1 patient in 100)

Changes at the injection site (lipodystrophy). The fatty tissue under the skin at the injection site may shrink (lipoatrophy) or thicken (lipohypertrophy). Changing the site with each injection may help to reduce the risk of developing such skin changes. If you notice your skin pitting or thickening at the injection site, tell your doctor or nurse. These reactions can become more severe, or they may change the absorption of your insulin if you inject in such a site.

Signs of allergy. Reactions (redness, swelling, itching) at the injection site may occur (local allergic reactions). These usually disappear after a few weeks of taking your insulin. If they do not disappear, see your doctor.

Seek medical advice immediately:

- If signs of allergy spread to other parts of the body, or
- If you suddenly feel unwell, and you: start sweating; start being sick (vomiting); have difficulty in breathing; have a rapid heart beat; feel dizzy.

Diabetic retinopathy (eye disease related to diabetes which can lead to loss of vision). If you have diabetic retinopathy and your blood sugar level improves very fast, the retinopathy may get worse. Ask your doctor about this.

Swollen joints. When you start taking insulin, water retention may cause swelling around your ankles and other joints. Normally this soon disappears.

(PenMix[®]) Painful neuropathy (pain due to nerve damage). If your blood sugar level improves very fast, you may get nerve related pain, this is called acute painful neuropathy and is usually transient.

Side effects reported very rarely (in less than 1 patient in 10,000)

Vision problems. When you first start your insulin treatment, it may disturb your vision, but the disturbance is usually temporary.

(Protaphane[®]) Painful neuropathy (pain due to nerve damage). If your blood sugar level improves very fast, you may get nerve related pain, this is called acute painful neuropathy and is usually transient.

Serious allergic reaction to PenMix[®] or Protaphane[®] or one of their ingredients (called a systemic allergic reaction). See also the warning in 4. WHAT TO DO IN AN EMERGENCY.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist.

6. HOW TO STORE PENMIX[®] OR PROTAPHANE[®]

Keep out of the reach and sight of children.

Do not use PenMix[®] or Protaphane[®] Penfill[®] after the expiry date which is stated on the label and the carton after 'Expiry.' The expiry date refers to the last day of that month.

PenMix[®] or Protaphane[®] Penfill[®] that is not being used is to be stored in the refrigerator at 2°C - 8°C, away from the cooling element. Do not freeze.

PenMix® or Protaphane® Penfill® that is being used or carried as a spare is not to be kept in a refrigerator. After removing the PenMix® or Protaphane® Penfill® from the refrigerator, it is recommended to let it reach room temperature before resuspending the insulin as instructed for the first time use. See 3. HOW TO USE PENMIX® OR PROTAPHANE®.

You can carry it with you and keep it at room temperature (below 25°C) for up to 6 weeks.

Always keep the cartridge in the outer carton when you are not using it in order to protect it from light.

PenMix® and Protaphane® must be protected from excessive heat and light.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

7. FURTHER INFORMATION

What PenMix® contains

- **The active substance** is insulin human made by recombinant biotechnology as: PenMix® 30 - 30% as soluble insulin and 70% as isophane insulin; PenMix® 40 - 40% as soluble insulin and 60% as isophane insulin; PenMix® 50 - 50% as soluble insulin and 50% as isophane insulin. 1 ml contains 100 IU of insulin human. 1 cartridge contains 3 ml equivalent to 300 IU.

- **The other ingredients** are zinc chloride, glycerol, metacresol, phenol, disodium phosphate dihydrate, sodium hydroxide, hydrochloric acid, protamine sulphate and water for injections.

What Protaphane® contains

- **The active substance** is insulin human made by recombinant biotechnology. Protaphane® is an isophane insulin suspension (NPH). 1 ml contains 100 IU of insulin human. 1 cartridge contains 3 ml equivalent to 300 IU.

- **The other ingredients** are zinc chloride, glycerol, metacresol, phenol, disodium phosphate dihydrate, sodium hydroxide, hydrochloric acid, protamine sulphate and water for injections.

What PenMix® or Protaphane® looks like and contents of the pack

The suspension for injection comes as a cloudy, white, aqueous suspension.

It is supplied in packs of 5 cartridges of 3 ml.

Not all packs may be marketed.

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