Package leaflet: Information for the user

Actrapid®
100 IU/ml (international units/ml) solution for injection in vial
human insulin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

1. What Actrapid® is and what it is used for

Actrapid® is human insulin with a fast-acting effect.

Actrapid® is used to **reduce the high blood sugar level** in patients with diabetes mellitus (diabetes). Diabetes is a disease where your body does not produce enough insulin to control the level of your blood sugar. Treatment with Actrapid® helps to prevent complications from your diabetes.

Actrapid® will start to lower your blood sugar about half an hour after you inject it, and the effect will last for approximately 8 hours. Actrapid® is often given in combination with intermediate-acting or long-acting insulin preparations.

2. What you need to know before you use Actrapid®

Do not use Actrapid®

- ► If you are allergic to human insulin or any of the other ingredients in this medicine, see section 6.
- ► If you suspect hypoglycaemia (low blood sugar) is starting, see *Summary of serious and very common side effects* in section 4.
- ► In insulin infusion pumps.
- ► If the protective cap is loose or missing. Each vial has a protective, tamper-proof plastic cap. If it is not in perfect condition when you get the vial, return the vial to your supplier.
- ► If it has not been stored correctly or if it has been frozen, see section 5.
- ► If the insulin does not appear clear and colourless.

If any of these apply, **do not use Actrapid®**. Talk to your doctor, pharmacist or nurse for advice.

Before using Actrapid®

- ► Check the label to make sure it is the right type of insulin.
- ► Remove the protective cap.
- ► Always use a new needle for each injection to prevent contamination.
- ► Needles and syringes must not be shared.

Warnings and precautions

Some conditions and activities can affect your need for insulin. Consult your doctor:

► If you have trouble with your kidneys or liver, or with your adrenal, pituitary or thyroid glands.
► 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 hereof.

Other medicines and Actrapid®

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.
Some medicines affect your blood sugar level, and this may mean that your insulin dose has to change. Listed below are the most common medicines which may affect your insulin treatment.

Your blood sugar level may fall (hypoglycaemia) if you take:
- Other medicines for the treatment of diabetes
- Monoamine oxidase inhibitors (MAOI) (used to treat depression)
- Beta-blockers (used to treat high blood pressure)
- Angiotensin converting enzyme (ACE) inhibitors (used to treat certain heart conditions or high blood pressure)
- Salicylates (used to relieve pain and lower fever)
- Anabolic steroids (such as testosterone)
- Sulfonamides (used to treat infections).

Your blood sugar level may rise (hyperglycaemia) if you take:
- Oral contraceptives (birth control pills)
- Thiazides (used to treat high blood pressure or excessive fluid retention)
- Glucocorticoids (such as 'cortisone' used to treat inflammation)
- Thyroid hormone (used to treat thyroid gland disorders)
- Sympathomimetics (such as epinephrine [adrenaline], salbutamol or terbutaline used to treat asthma)
- Growth hormone (medicine for stimulation of skeletal and somatic growth and pronounced influence on the body's metabolic processes)
- Danazol (medicine acting on ovulation).

Octreotide and lanreotide (used for treatment of acromegaly, a rare hormonal disorder that usually occurs in middle-aged adults, caused by the pituitary gland producing excess growth hormone) may either increase or decrease your blood sugar level.

Beta-blockers (used to treat high blood pressure) may weaken or suppress entirely the first warning symptoms which help you to recognise low blood sugar.

Pioglitazone (tablets used for the treatment of type 2 diabetes)
Some patients with long-standing type 2 diabetes and heart disease or previous stroke who were treated with pioglitazone and insulin experienced the development of heart failure. Inform your doctor as soon as possible if you experience signs of heart failure such as unusual shortness of breath or rapid increase in weight or localised swelling (oedema).

If you have taken any of the medicines listed here, **tell your doctor, pharmacist or nurse**.

Actrapid® with alcohol

► If you drink alcohol, your need for insulin may change as your blood sugar level may either rise or fall. Careful monitoring is recommended.

Pregnancy and breast-feeding

- ► If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. Actrapid® can be used during pregnancy. Your insulin dose may need to be changed during pregnancy and after delivery. Careful control of your diabetes, particularly prevention of hypoglycaemia, is important for the health of your baby.
- ► There are no restrictions on treatment with Actrapid® during breast-feeding.

Ask your doctor, pharmacist or nurse for advice before taking this medicine while pregnant or breast-feeding.

Driving and using machines

- ► Please ask your doctor whether you can drive a car or operate a machine:
- If you have frequent hypoglycaemia.
- If you find it hard to recognise hypoglycaemia.

If your blood sugar is low or high, it might affect your concentration and ability to react and therefore also your ability to drive or operate a machine. Bear in mind that you could endanger yourself or others.

Actrapid® contains sodium

Actrapid® contains less than 1 mmol sodium (23 mg) per dose, i.e. Actrapid® is essentially 'sodium-free'.

3. How to use Actrapid®

Dose and when to take your insulin

Always use your insulin and adjust your dose exactly as your doctor has told you. Check with your doctor, pharmacist or nurse if you are not sure.

Eat a meal or snack containing carbohydrates within 30 minutes of the injection to avoid low blood sugar.

Do not change your insulin unless your doctor tells you to. 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.

Use in children and adolescents

Actrapid® can be used in children and adolescents.

Use in special patient groups

If you have reduced kidney or liver function, or if you are above 65 years of age, you need to check your blood sugar more regularly and discuss changes in your insulin dose with your doctor.

How and where to inject

Actrapid® is administered **by injection under the skin** (subcutaneously). You must never inject yourself directly into a vein (intravenously) or muscle (intramuscularly). If necessary Actrapid® can be given directly into a vein, but this must only be done by healthcare professionals.

With each injection, change the injection site within the particular area of skin that you use. This may reduce the risk of developing lumps or skin pitting, see section 4. 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. The insulin will work more quickly if you inject into the waist (abdomen). You should always measure your blood sugar regularly.

How to take Actrapid®

Actrapid® vials are for use with insulin syringes with the corresponding unit scale.

If you only use one type of insulin

1. Draw into the syringe the same amount of air as the dose of insulin you are going to inject. Inject the air into the vial.
2. Turn the vial and syringe upside down and draw the correct insulin dose into the syringe. Pull the needle out of the vial. Then expel the air from the syringe and check that the dose is correct.

If you have to mix two types of insulin

1. Just before use, roll the vial of intermediate- or long-acting (cloudy) insulin between your hands until the liquid is uniformly white and cloudy.
2. Draw into the syringe the same amount of air as the dose of intermediate- or long-acting insulin. Inject the air into the vial containing intermediate- or long-acting insulin and pull out the needle.
3. Draw into the syringe the same amount of air as the dose of Actrapid®. Inject the air into the vial containing Actrapid®. Then turn the vial and syringe upside down and draw up the prescribed dose of Actrapid®. Expel any air from the syringe and check that the dose is correct.
4. Push the needle into the vial of intermediate- or long-acting insulin, turn the vial and syringe upside down and draw out the dose you have been prescribed. Expel any air from the syringe and check that the dose is correct. Inject the mixture immediately.
5. Always mix Actrapid® and intermediate- or long-acting insulin in the same sequence.

How to inject Actrapid®

- ► Inject the insulin under your skin. Use the injection technique advised by your doctor or nurse.
- ► Keep the needle under your skin for at least 6 seconds to make sure that you have injected all the insulin.
- ► Discard the needle and syringe after each injection.

If you take more insulin than you should

If you take too much insulin your blood sugar gets too low (hypoglycaemia). See *Summary of serious and very common side effects* in section 4.

If you forget to take your insulin

If you forget to take your insulin your blood sugar may get too high (hyperglycaemia). See *Effects from diabetes* in section 4.

If you stop taking your insulin

Do not stop taking your insulin without speaking with a doctor, who will tell you what needs to be done. This could lead to very high blood sugar (severe hyperglycaemia) and ketoacidosis. See *Effects from diabetes* in section 4.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Summary of serious and very common side effects

Low blood sugar (hypoglycaemia) is a very common side effect. It may affect more than 1 in 10 people.

Low blood sugar may occur if you:
- Inject too much insulin.
- Eat too little or miss a meal.
- Exercise more than usual.
- Drink alcohol, see *Actrapid® with alcohol* in section 2.

Signs of low blood sugar: Cold sweat; cool pale skin; headache; rapid heartbeat; feeling sick; feeling very hungry; temporary changes in vision; drowsiness; unusual tiredness and weakness; nervousness or tremor; feeling anxious; feeling confused; difficulty in concentrating.

Severe low blood sugar can lead to unconsciousness. If prolonged severe low blood sugar is not treated, it can cause brain damage (temporary or permanent) and even death. 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 sugar snack as soon as you are conscious. If you do not respond to glucagon treatment, you will have to be treated in a hospital.

What to do if you experience low blood sugar:
- ► If you experience low blood sugar, eat glucose tablets or another high sugar snack (e.g. sweets, biscuits, fruit juice). Measure your blood sugar if possible and rest. Always carry glucose tablets or high sugar snacks with you, just in case.
- ► When the symptoms of low blood sugar have disappeared or when your blood sugar level is stabilised, continue insulin treatment as usual.
- ► If you have such low blood sugar that it makes you pass out, if you have had the need for an injection of glucagon, or if you have experienced many incidents of low blood sugar, talk to a doctor. The amount or timing of insulin, food or exercise may need to be adjusted.

Tell relevant people that you have diabetes and what the consequences may be, including the risk of passing out (becoming unconscious) due to low blood sugar. Let them know that if you pass out, they must turn you on your side and get medical help straight away. They must not give you any food or drink, because you may choke.

Serious allergic reaction to Actrapid® or one of its ingredients (called a systemic allergic reaction) is a very rare side effect, but it can potentially be life threatening. It may affect less than 1 in 10,000 people.

Seek medical advice immediately:
- If signs of allergy spread to other parts of your body.
- If you suddenly feel unwell, and you: start sweating; start being sick (vomiting); have difficulty in breathing; have a rapid heartbeat; feel dizzy.
- ► If you notice any of these signs, seek medical advice immediately.

List of other side effects

Uncommon side effects
May affect less than 1 in 100 people.

Signs of allergy: Local allergic reactions (pain, redness, hives, inflammation, bruising, swelling and itching) at the injection site may occur. These usually disappear after a few weeks of taking your insulin. If they do not disappear, or if they spread throughout your body, talk to your doctor immediately. See also *Serious allergic reactions* above.

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

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.

Swollen joints: When you start taking insulin, water retention may cause swelling around your ankles and other joints. Normally this soon disappears. If not, talk to your doctor.

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.

Very rare side effects
May affect less than 1 in 10,000 people.

Diabetic retinopathy (an 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.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects via

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt/adrportal

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

Effects from diabetes

High blood sugar (hyperglycaemia)

High blood sugar may occur if you:
- Have not injected enough insulin.
- Forget to inject your insulin or stop taking insulin.
- Repeatedly inject less insulin than you need.
- Get an infection and/or a fever.
- Eat more than usual.
- Exercise less than usual.

Warning signs of high blood sugar:
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.

What to do if you experience high blood sugar:
- ► If you get any of the above signs: test your blood sugar level, test your urine for ketones if you can, then seek medical advice immediately.
- ► These may be signs of a very serious condition called diabetic ketoacidosis (build-up of acid in the blood because the body is breaking down fat instead of sugar). If you do not treat it, this could lead to diabetic coma and eventually death.

5. How to store Actrapid®

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date, which is stated on the vial label and carton after 'EXP'. The expiry date refers to the last day of that month.

Before opening: Store in a refrigerator at 2°C – 8°C. Keep away from the cooling element. Do not freeze.

During use or when carried as a spare: Do not refrigerate or freeze. You can carry it with you and keep it at room temperature (below 25ºC) for up to 6 weeks.

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

Discard the needle and syringe after each injection.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Actrapid® contains

- The active substance is human insulin. Each ml contains 100 IU of human insulin. Each vial contains 1,000 IU of human insulin in 10 ml solution for injection.
- The other ingredients are zinc chloride, glycerol, metacresol, sodium hydroxide, hydrochloric acid and water for injections.

What Actrapid® looks like and contents of the pack

Actrapid® is presented as a solution for injection.

Pack sizes of 1 or 5 vials of 10 ml or a multipack of 5 packs of 1 x 10 ml vial. Not all pack sizes may be marketed.

The solution is clear and colourless.

Marketing Authorisation Holder

Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark

Manufacturer
The manufacturer can be identified by the batch number printed on the slip of the carton and on the label:

– If the second and third characters are S6 or ZF, the manufacturer is Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.

– If the second and third characters are T6, the manufacturer is Novo Nordisk Production SAS, 45 Avenue d'Orléans, F-28000 Chartres, France.

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency website http://www.ema.europa.eu.