

INSUGEN[®]-N

Human Insulin of Recombinant DNA origin, 100 IU/mL

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1) What INSUGEN[®]-N is and what it is used for?

INSUGEN[®]-N contains the active substance human insulin, which is used to treat diabetes. Diabetes mellitus is a condition in which a person has high blood sugar, either because the pancreas does not produce enough insulin or the cells do not respond to the insulin that is produced; therefore, extra insulin is needed to lower your blood sugar levels. INSUGEN[®]-N is an intermediate-acting insulin.

2) How INSUGEN[®]-N works?

After administration of INSUGEN[®]-N, it will start to lower your blood sugar in about one and half hour, and the effect will last for approximately 24 hours. INSUGEN[®]-N can be prescribed along with fast-acting insulin to control your blood sugar.

3) Before you use INSUGEN[®]-N

When you must not use it

- If you are allergic (hypersensitive) to any of the ingredients in INSUGEN[®]-N (see section 9 for list of ingredients). Watch out for the signs of allergy in section 6 (*Possible side effects*) or ask your doctor for clarification.
- If you experience symptoms of low blood sugar levels (hypoglycaemia), or a hypoglycaemic attack (symptom of low blood sugar). See section 7 (*What to do in an emergency*) to know more about hypoglycaemia.

Before you start to use it

Inform your doctor if:

- You have any other medical conditions, such as infection, fever, kidney or liver problems. Some medical conditions can

alter your insulin requirements and your doctor will suggest a change in dose.

- You are pregnant, planning a pregnancy or 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.

Taking other medicines

Many medicines affect the way glucose works in your body and they may influence your insulin dose.

Talk to your doctor or pharmacist if you take or have recently taken any other medicines, even those not prescribed.

Listed below are the most common medicines which may affect your insulin treatment.

monoamine oxidase inhibitors (MAOI); beta-blockers; ACE-inhibitors; acetylsalicylic acid; anabolic steroids; sulphonamides; oral contraceptives; thiazides; glucocorticoids; thyroid hormone therapy; beta-sympathomimetic; growth hormones; danazol; octreotide or lanreotide.

Pioglitazone (oral antidiabetic medicine 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 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 localise swelling (oedema).

4) How to use INSUGEN[®]-N?

General instructions

Follow your doctor's advice about how to use, when to use and how long to use.

This leaflet is only a general guide. If your doctor has switched you from other type or brand of insulin, or if you are suffering from a medical condition, your dose may have to be adjusted by your doctor.

Site of injection

INSUGEN[®]-N is for injection under the skin (subcutaneously). Never inject your insulin directly into a vein or muscle. Always vary the sites you inject, to avoid lumps (see 6, *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.

How to use Vial

Things to be checked before using

Always check the pack and the vial label for the name and type of the insulin when you get it from your pharmacy.

- The insulin vials have a protective colour-coded, tamper-proof plastic cap, which must be removed before insulin can be withdrawn. The patient should not use the vial if the plastic cap is loose or missing, and instead return to the pharmacy.
- Never use INSUGEN[®]-N vials, if the liquid is not uniformly white and cloudy when its re suspended.
- Never use insulin after the expiry date printed on the pack or if it hasn't been stored correctly (see section 8, *Storage and Disposal of INSUGEN[®]-N*).

Instructions for Use

- First wash your hands.
- Before you make an injection, clean your skin. Clean the rubber stopper on the vial, but do not remove the stopper.
- Just before injecting this insulin, roll the vial between your hands until the liquid is uniformly white and cloudy. Re-suspending is easier, if the insulin has reached room temperature. (Do not shake vigorously as this may cause frothing which may interfere with the correct measurement of the dose).
- Draw air into the syringe equal to the dose of insulin you wish to take.
- Inject the air into the vial: Pierce the rubber stopper of the insulin vial in the middle at a 90° angle and push the air in by pressing the plunger.
- Turn the vial and syringe upside down.
- Steadily draw the right dose of insulin into the syringe.
- Pull the needle out of the vial.
- Make sure there is no air left in the syringe: point the needle upwards and push the air out.
- Check you have the right dose.
- Inject the insulin under the skin. Use the injection technique advised by your doctor or nurse.
- Keep the needle under your skin for at

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least 6 seconds to make sure that the full dose has been delivered.

To mix INSUGEN[®]-N with fast-acting insulin

- First wash your hands.
- Before you make an injection, clean your skin. Clean the rubber stopper on the vial, but do not remove the stopper.
- Roll the vial of INSUGEN[®]-N between your hands. Do this until the liquid is uniformly white and cloudy. Never shake a bottle of insulin.
- Disinfect the rubber membrane with a BD alcohol swab.
- Draw air into the syringe equal to the dose of INSUGEN[®]-N you need. Inject the air into the INSUGEN[®]-N vial and pull out the needle without drawing up the cloudy insulin. Pull the plunger back to the dose of fast-acting insulin desired; inject the air into the clear fast-acting insulin vial.
- This time, leave the needle in the bottle, turn the vial upside down and slowly draw the correct dose of fast-acting insulin into the syringe. Withdraw the needle and expel the air from the syringe and check that the dose is correct.
- Now push the needle into the vial of INSUGEN[®]-N. Turn the vial and syringe upside down and draw the correct insulin dose into the syringe. Withdraw the needle and expel the air from the syringe and check that the dose is correct.
- Inject the mixture straight away beneath the skin of the selected site.

How to use Cartridge

Things to be checked before using

- Check the label to make sure it is the right type of insulin.
- Always check the cartridge, including the rubber plunger (stopper).
- Don't use it if any damage is seen.
- Take it back to your supplier. See your insulin delivery device manual for further instructions.
- Disinfect the rubber membrane with a medicinal swab.
- Always use a new needle for each injection to prevent contamination.

Do not use

- In insulin infusion pumps.

- If the compatible insulin injector pen is dropped, damaged or crushed, there is a risk of leakage of insulin.
- If it hasn't been stored correctly or been frozen.
- If it's not uniformly white and cloudy when it's re-suspended.

Instruction for use

- Inject the insulin under the skin.
- Use the injection technique advised by your doctor or diabetes nurse and described in your insulin delivery device manual.
- Keep the needle under your skin for at least 10 seconds to make sure that the full dose has been delivered.
- After each injection be sure to remove and discard the needle and store INSUGEN[®]-N cartridge without the needle attached. Otherwise, the liquid may leak out which can cause inaccurate dosing.
- Do not mix any other insulin in an INSUGEN[®]-N cartridge. Once the cartridge is empty, do not use it again.

Direction of Use of INSUPen with Cartridges.

For use with INSUPen (re-usable injector) only
Please refer to User Manual for more information.

If you forget to use it

If you take less INSUGEN[®]-N than you need or if you forget to take a dose your blood sugar levels may increase. Check your blood sugar.

If you use too much (overdose)

If you take more INSUGEN[®]-N than your requirement it may cause hypoglycaemia (low blood sugar).

If you stop using

If you stop taking INSUGEN[®]-N than you need, your blood sugar levels may become too high

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

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

5) While you are using INSUGEN[®]-N

Things you must do

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

- It is recommended that you measure your blood glucose regularly and have regular check-ups.

Things you must not do

Driving and using machines: your ability to concentrate and react may be reduced if you have hypoglycaemia (low blood sugar). You should contact your doctor about the advisability of driving, if you have:

- Frequent episodes of hypoglycaemia.
- Reduced or absent warning signs of hypoglycaemia.

Things you must be careful of

- *If you have a habit of drinking:* watch for signs of hypoglycaemia and never drink alcohol on an empty stomach. The amount of insulin you need may also change if you drink alcohol.
- If you have trouble with your kidneys or liver, or with your adrenal, pituitary or thyroid glands
- If you are exercising more than usual or if you want to change your usual diet.
- *If you are going abroad:* travelling over time zones may affect your insulin needs and the timing of your injections.
- If you had hypoglycaemia (low blood sugar) after switching from animal insulin to human insulin and reported that the early warning symptoms were less obvious or different.
- If you are ill: carry on taking your insulin
- If you often have hypoglycaemia or have difficulty recognising the symptoms, please discuss this with your doctor.

6) Possible side effects

The most common side effect is hypoglycaemia.

You get a hypoglycaemic attack 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 you have an infection or illness (especially diarrhoea or vomiting);
- If you have a change in your need for insulin; or
- If you have trouble with your kidneys or liver which gets worse.

If you take less INSUGEN[®]-N than your requirement it may cause hyperglycaemia (high blood sugar).

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Common side effects

Symptoms resulting from release of adrenaline are common manifestations of mild to moderate hypoglycaemia. They include cold sweats, anxiety, shakiness, hunger, rapid heartbeat, headache, and nervousness. Weight gain is common when taking insulin.

Less common side effects

Allergic reactions and changes at the injection site (lipodystrophy) may occur at the injection site as a consequence of failure to rotate injection sites within an area. If you inject yourself too often at the same site, fatty tissue under the skin at this site may shrink (lipoatrophy) or thicken (lipohypertrophy). Changing the site with each injection may help to prevent such skin changes. If you notice your skin pitting or thickening at the injection site, tell your doctor because 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 heartbeat; feel dizzy; feel like fainting.

You may have a very rare serious allergic reaction to INSUGEN[®]-N or one of its ingredients (called a systemic allergic reaction). See also warning in section 3 (Before you use INSUGEN[®]-N)

Abnormal accumulation of fluid

(*oedema*): It may occur upon initiation of insulin therapy. These symptoms are usually of transitory nature.

Vision problems: you might experience transient visual disturbances when you initiate treatment with insulins.

Painful neuropathy (nerve related pain):

If your blood glucose levels improve very fast it may cause a burning, tingling or electric pain. This is called acute painful neuropathy and it usually disappears. If it

does not disappear, see your doctor.

Diabetic retinopathy (eye background changes): If you have diabetic retinopathy and your blood glucose levels improve very fast, the retinopathy may get worse. Ask your doctor about this. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please inform your health care provider (doctor, nurse, or pharmacist).

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835550, or visiting the website

<http://portal.bpfk.gov.my/> (Consumers →Reporting)

7) What to do in an emergency?

If you get a hypoglycaemic attack

Hypoglycaemia means your blood sugar level is too low.

Causes of hypoglycaemic attack

- If you take too much insulin.
- If you eat too little or miss a meal.
- If you exercise more than usual.
- If you have an infection or illness (especially diarrhoea or vomiting);
- If you have a change in your need for insulin; or
- If you have trouble with your kidneys or liver which gets worse.

The warning signs of a hypoglycaemic attack may come on suddenly and can include: 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.

If you get any of these signs:

- Eat glucose tablets or a high sugar snack (sweets, biscuits, fruit juice), then rest.
- Don't take any insulin if you feel a hypoglycaemic attack 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 hypoglycaemic attack that makes you pass out, or a lot of hypoglycaemic attack, 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 hypoglycaemic attack to avoid getting more.

If you get a hyperglycaemia

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

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.

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 don't treat it, this could lead to diabetic coma and death.

8) Storage and Disposal of INSUGEN[®]-N?

How to store

Store in a refrigerator at temperature between 2°C and 8°C.

Should not be allowed to freeze. Insugen products which have been frozen must not be used.

INSUGEN[®]-N which are in use can be kept at room temperature (up to 25°C) for up to 6 weeks.

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Keep protected from light.

Keep INSUGEN[®]-N out of reach of children.

How to Dispose

Any unused product or waste material should be disposed of in accordance with local requirements. Insugen formulations should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required.

9) INSUGEN[®]-N Description

What it looks like

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

INSUGEN[®]-N Vial

It is supplied in packs of 1 or 5 vials of 10 mL or in a multipack of 5 × (1 × 10 mL) vials. Not all packs may be marketed.

INSUGEN[®]-N Cartridge

It is supplied in 3 mL colourless tubular glass cartridges (USP Type I) sealed using lined seals and plugged with plunger stoppers.

Ingredients

Active Ingredients

The active substance is insulin human made by recombinant biotechnology. 1 mL contains 100 IU of insulin human.

Inactive Ingredients

The other ingredients are zinc oxide, glycerin, phenol, protamine sulfate, metacresol, dibasic sodium phosphate, sodium hydroxide, hydrochloric acid and water for injections.

MAL Number

MAL14015109A

10) Manufacturer and Product Registration Holder

Manufacturer

Biocon Limited
Biocon Special Economic Zone
Plot No. 2-4, Phase IV
Bommasandra-Jigani Link Road
Bommasandra Post, Bangalore – 560099
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Product Registration Holder

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11) Date of Revision

6 December 2013