

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

NovoMix® 30

**30% soluble insulin aspart and
70% insulin aspart protamine crystals**

Suspension for Injection

Penfill®

Read this carefully before you start taking **NovoMix® 30** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **NovoMix® 30**.

Serious Warnings and Precautions

- Hypoglycemia is the most common adverse effect of insulin, including NovoMix® 30.
- If hypoglycemia or hyperglycemic reactions are not treated they can result in the loss of consciousness, coma or death.
- Glucose monitoring is recommended for all patients with diabetes.
- Any change of insulin should be made cautiously and only under medical supervision. This may result in dosage adjustment.
- NovoMix® 30 should be given immediately before a meal because of the fast onset of action (start of the meal should be not more than 5-10 minutes after injection) or should be given immediately after the meal. (see 'How to take NovoMix® 30')
- Never inject your insulin directly into a vein.
- Do not use NovoMix® 30 in insulin pumps.
- NovoMix® 30 should not be used if it is not uniformly white and cloudy after re-suspension.

What is NovoMix® 30 used for?

The treatment of adult patients with diabetes mellitus who require insulin for the control of hyperglycemia.

How does NovoMix® 30 work?

NovoMix® 30 (30% soluble insulin aspart and 70% insulin aspart protamine crystals) is an insulin analogue used to treat diabetes.

NovoMix® 30 is long-acting insulin analogue (70%) combined with fast-acting insulin analogue (30%). This means that it will start to lower your blood sugar 10-20 minutes after you take it, has a maximum effect of between 1 and 4 hours and the effect lasts for up to 24 hours.

What are the ingredients in NovoMix® 30?

Medicinal ingredients: The active ingredient in NovoMix® 30 is a mixture of insulin (30% insulin aspart in a soluble fraction and 70% insulin aspart crystallized with protamine).

Non-medicinal ingredients: Glycerol, phenol, metacresol, zinc (as chloride), sodium chloride, disodium phosphate dihydrate, protamine sulphate, sodium hydroxide, hydrochloric acid, water

for injections

NovoMix® 30 comes in the following dosage forms:

NovoMix® 30 is available from Novo Nordisk Canada in the following formats:

- NovoMix® 30 Penfill® 3 mL cartridge (designed for use with Novo Nordisk Insulin Delivery Devices)

NovoMix® 30 Penfill® is designed for use with Novo Nordisk Insulin Delivery Devices, NovoFine®, NovoFine® Plus and/or NovoTwist® needles. Novo Nordisk cannot be held responsible for malfunctions occurring as a consequence of using NovoMix® 30 in combination with products that do not meet the same specifications or quality standards as NovoFine®, NovoFine® Plus and/or NovoTwist® needles

Do not use NovoMix® 30 if:

- You feel a hypoglycemic reaction (low blood sugar) coming on. (see '*What are possible side effects from using NovoMix® 30?*' for more about hypoglycemia).
- You are allergic (hypersensitive) to soluble insulin aspart, insulin aspart protamine crystals, metacresol or any of the other ingredients in this insulin. Look out for the signs of an allergic reaction. (see '*What are possible side effects from using NovoMix® 30?*').
- In insulin infusion pumps.
- If the Penfill® cartridge in a Novo Nordisk Insulin Delivery Device containing the insulin is dropped, damaged or crushed; there is a risk of leakage of insulin.
- The insulin has not been stored correctly or if it has been frozen. (see '*How to store NovoMix® 30*').
- The insulin is not uniformly white and cloudy when it is mixed.
- Clumps of material are present or if solid white particles stick to the bottom or the wall of the cartridge giving a frosted appearance.

Do not refill a NovoMix® 30 Penfill® cartridge.

NovoMix® 30 Penfill® cartridges are designed to be used with Novo Nordisk Insulin Delivery Devices and NovoFine®, NovoFine® Plus and NovoTwist® needles as part of **The All In-One System®**.

If you are treated with NovoMix® 30 Penfill® and another insulin in Penfill® cartridge, you should use two Novo Nordisk Insulin Delivery Devices, one for each type of insulin.

As a precautionary measure, always carry a spare insulin cartridge/delivery system in case your Penfill® is lost or damaged.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take NovoMix® 30. Talk about any health conditions or problems you may have, including if you:

- Have trouble with your kidneys or liver, or with your adrenal, pituitary or thyroid glands, your doctor may decide to alter your insulin dose.
- Drink alcohol (including wine and beer) your need for insulin may change as your blood sugar level may either rise or fall.
- Have an infection, fever or have had an operation you may need more insulin than usual.
- Suffer from diarrhea, vomiting or eat less than usual you may need less insulin than usual.

- Exercise more than usual or if you want to change your usual diet.
- Are ill: continue taking your insulin. Your need for insulin may change.
- Go abroad: travelling over time zones may affect your insulin needs and the timing of your injections. Consult your doctor if you are planning such travel.
- Are pregnant or planning a pregnancy or are breastfeeding please contact your doctor for advice.
- Drive or use tools or machines: watch for signs of a hypoglycemia. Your ability to concentrate or to react will be less during a hypoglycemic reaction. Please keep this in mind in all situations where you might put yourself and others at risk (e.g. driving a car or operating machinery). Never drive or use machinery if you feel a hypoglycemic reaction coming on.

Discuss with your doctor whether you should drive or use machines at all, if you have a lot of hypoglycemic reactions or if you find it hard to recognize hypoglycemia.

Before you travel, check with your physician or pharmacist on the availability of NovoMix® 30 in other countries. If possible, bring enough NovoMix® 30 with you on your trip.

Thiazolidinediones (class of oral antidiabetic drugs) used together with insulin may increase risk of oedema and heart failure. Inform your doctor as soon as possible if you experience localised swelling (oedema) or signs of heart failure such as unusual shortness of breath.

Other warnings you should know about:

Skin changes at the injection site

The injection site should be rotated to help prevent changes to the fatty tissue under the skin, such as skin thickening, skin shrinking or lumps under the skin. The insulin may not work very well if you inject into a lumpy, pitted, or thickened area (see 'How to take NovoMix® 30'). Tell your healthcare professional if you notice any skin changes at the injection site. Tell your healthcare professional if you are currently injecting into these affected areas before you start injecting in a different area. A sudden change of site may result in hypoglycemia. Your healthcare professional may tell you to check your blood sugar more closely, and to adjust your insulin or your other antidiabetic medications dose.

The following may interact with NovoMix® 30:

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. Tell your doctor, Diabetes Nurse Educator 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 as mentioned below that affects your blood sugar level.

If you take any of the medicines below, your blood sugar level may fall (hypoglycemia):

- 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) Sulphonamides (used to treat infections)

If you take any of the medicines below, your blood sugar level may rise (hyperglycemia):

- 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 hormones (used to treat thyroid gland disorders)
- Sympathomimetics (such as epinephrine [adrenaline], or salbutamol, 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 a hypoglycemia.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take NovoMix® 30:

NovoMix® 30 is for injection under the skin (subcutaneously). Never inject your insulin directly into a vein or muscle.

Always vary the site you inject within the same region, to avoid lumps (see '*What are possible side effects from using NovoMix® 30?*'). The best places to give yourself an injection are: the front of your thighs; the front of your waist (abdomen); the upper arm. Your insulin will work more quickly if you inject into the front of your waist.

You should always measure your blood glucose regularly.

Talk about your insulin needs with your doctor and Diabetes Nurse Educator. Do not change your insulin unless your doctor tells you to. Follow their advice carefully. This leaflet is a general guide only.

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.

NovoMix® 30 should be given immediately before a meal. When necessary, NovoMix® 30 may also be given soon after the meal.

Before using NovoMix® 30:

- Check the label to make sure you have the right type of insulin.
- Always check the Penfill® cartridge, including the rubber stopper (plunger). Don't use it if any damage is seen or if there is a gap between the rubber stopper and the white

barcode label. Take it back to your supplier or call Novo Nordisk Canada at 1 800 465-4334 for assistance. See your Novo Nordisk Insulin Delivery Device manual for further instructions.

- Always use a new needle for each injection to prevent contamination.
- Do not share your NovoMix® 30 Penfill® in a Novo Nordisk Insulin Delivery Device with another person, even if the needle is changed. Do not reuse or share needles with another person including family members. You may give another person an infection or get an infection from them.

Resuspending the insulin

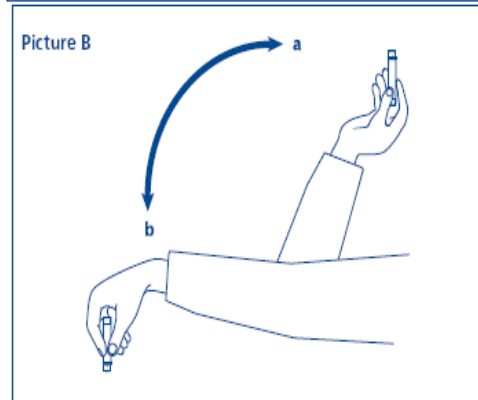
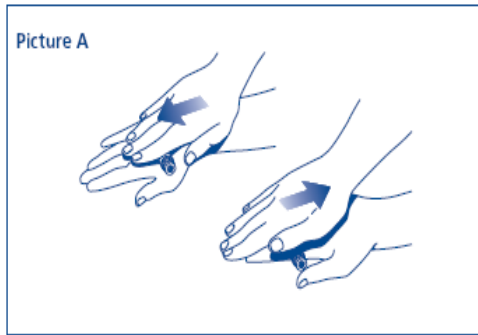
Check that there are at least 12 units of insulin left in the cartridge to allow even resuspension. If there are less than 12 units left, use a new cartridge.

Every time you use a new NovoMix® 30 Penfill® (before you put the cartridge into the insulin delivery system):

- Let the insulin reach room temperature before you use it. This makes it easier to resuspend. Roll the cartridge between your palms ten times – it is important that the cartridge is kept horizontal (see picture **A**).
- Move the cartridge up and down between positions **a** and **b** (see picture **B**) 10 times so that the glass ball moves from one end of the cartridge to the other.
- Repeat the rolling and moving procedures (see picture **A** and **B**) until the liquid appears uniformly white and cloudy. Do not use the cartridge if the resuspended insulin does not look uniformly white and cloudy.
- Complete the other stages of injection without delay.

For all subsequent injections:

- Move the insulin delivery system with the cartridge inside it, up and down between **a** and **b** (see picture **B**) at least ten times until the liquid appears uniformly white and cloudy.
- Complete the other stages of injection without delay.



How to inject this insulin

- Inject the insulin under the skin. Use the injection technique advised by your doctor or Diabetes Nurse Educator and as described in your Novo Nordisk Insulin Delivery Device 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 NovoMix® 30 without the needle attached. Otherwise, insulin may leak out which can cause inaccurate dosing.

Overdose:

You get a hypoglycemia 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.

The warning signs of a hypoglycemia 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; and difficulty 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 hypoglycemia 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 get medical help right away. They must not give you anything to eat or drink as it could choke you.

- If severe hypoglycemia is not treated, it can cause brain damage (temporary or permanent) and even death.
- If you have a hypoglycemia that makes you pass out, or if you get a lot of hypoglycemias, talk to your doctor. The amount or timing of your insulin dose, the amount of food you eat or the amount of exercise you do, may need to be adjusted.

Using glucagon

You may recover more quickly from unconsciousness with an injection of the hormone glucagon given by someone who knows how to use it. If you are given glucagon you will need to eat 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. Contact your doctor or hospital emergency after an injection of glucagon: you need to find the reason for your hypoglycemia in order to avoid getting more.

Causes of a hyperglycemia:

You get a hyperglycemia if your blood sugar gets too high.

This might happen:

- If you forget to take insulin.
- If you repeatedly take less insulin than you need.
- If you eat more than usual.
- If you exercise less 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; a dry mouth and a fruity (acetone) smelling breath.

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.

If you think you, or a person you are caring for, have taken too much NovoMix® 30, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using NovoMix® 30?

These are not all the possible side effects you may feel when taking NovoMix® 30. If you experience any side effects not listed here, contact your healthcare professional.

The most common side effect is low blood sugar (hypoglycemia). See the advice in '*How to take NovoMix® 30*'.

Less common (1 to 10 users in 1000):

Signs of allergy

Hives and rash may occur.

Seek medical advice immediately:

- If the above signs of allergy appear or
- If you suddenly feel unwell, and you: start sweating; start being sick (vomiting); have difficulty breathing; have a rapid heart beat; feel dizzy.

You may have a very rare serious allergic reaction to NovoMix® 30 or one of its ingredients (called a generalized allergic reaction). See also the warning in '*Do not use NovoMix® 30 if*'.

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)

If you inject yourself too often in the same site, fatty tissue under the skin at this injection 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 or Diabetes Nurse Educator because these reactions can become more severe, or they may change the absorption of your insulin at this site.

Swollen joints

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

Diabetic retinopathy

If you have diabetic retinopathy and your blood glucose levels improve very fast, the retinopathy may get worse. Ask your doctor about this.

Rare (less than 1 user in 10,000)

Painful neuropathy (pain due to nerve damage)

If your blood glucose levels improve very fast, you may get nerve related pain – This is called acute painful neuropathy and is usually transient.

If any of the side effects get serious, or if you notice any side effects, including those not mentioned in this leaflet, please inform your doctor, Diabetes Nurse Educator or pharmacist.

Frequency Not known

Lumps under the skin may also be caused by build-up of a protein called amyloid (cutaneous amyloidosis). See "*Other warnings you should know about*".

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
LESS COMMON (1 to 10 users in 1000)			
Signs of allergy: hives and rash		√	√
Vision problems	√		√
Skin changes where you inject your insulin injection (lipodystrophy)		√	√
Swelling around your joints	√		√
Blood glucose levels improve very fast and worsening of diabetic retinopathy		√	√
RARELY REPORTED (less than 1 user in 10,000)			
Blood glucose levels improve very fast and nerve related pain (painful neuropathy)		√	√
UNKNOWN			
Cutaneous Amyloidosis: lumps under skin		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

NovoMix® 30 Penfill® that is not being used must be stored in the fridge between 2°C to 10°C, in the original package, not in or near the freezer section or cooling element. Do not freeze.

NovoMix® 30 that is being used or is about to be should not be kept in the refrigerator. You can

carry it with you and keep it at room temperature (not above 30°C) for up to 4 weeks.

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

NovoMix® 30 should be protected from excessive heat and sunlight.

Do not use NovoMix® 30 after the expiry date printed on the label and carton.

NovoMix® 30 should not be disposed of in wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help protect the environment.

Keep out of reach and sight of children.

What NovoMix® 30 looks like and package content

NovoMix® 30 Penfill® comes as a white suspension in packages of 5 cartridges of 3 mL per carton.

1 Penfill® cartridge contains 3 mL of insulin aspart equivalent to 300 U.

If you want more information about NovoMix® 30:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.novonordisk.ca, or by calling 1-800-465-4334.

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