

Novolin[®]ge [Penfill[®]/vial]
Premixed insulin preparations

Insulin Injection 30% and Insulin Isophane 70%
Insulin Injection 40% and Insulin Isophane 60%
Insulin Injection 50% and Insulin Isophane 50%

Human Biosynthetic

10 mL / 3 mL

This leaflet is Part III of a three-part 'Product Monograph' published when Novolin[®]ge premixed insulin was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Novolin[®]ge premixed insulin.

Contact your doctor or pharmacist if you have any questions about the drug.

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, Diabetes Nurse Educator or pharmacist.

This medicine has been prescribed for you personally and you should 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, diabetes nurse or your pharmacist.

If you have trouble reading this, ask a family member or a friend for help.

ABOUT THIS MEDICATION

A direction leaflet containing information for the patient is included in each package.

Novolin[®]ge[Penfill[®]/vial] premixed is human insulin used to treat diabetes.

Novolin[®]ge premix insulin is an antidiabetic agent used for the treatment of diabetes mellitus as it reduces the level of sugar in the blood and urine. To control your diabetes, your doctor has prescribed Novolin[®]ge premixed insulin injections.

Novolin[®]ge premixed is a mixture of fast-acting and intermediate-acting insulin. This means that it will start to lower your blood sugar about half an hour after you take it, and the effect will last for approximately 24 hours.

Novolin[®]ge premixed insulin is indicated for:

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

When Novolin[®]ge should not be used

- If you feel a hypoglycemic reaction (low blood sugar) coming on see '*Side Effect and What to do about them*' for more about hypoglycemia.
- If you are allergic (hypersensitive) to insulin - human biosynthetic, insulin isophane, metacresol or any of the other ingredients in this insulin. Look out for the signs of an allergic reaction. (see '*Possible Side Effects*')

What the medicinal ingredient is

The active ingredient in Novolin[®]ge premixed insulin preparations is Insulin Isophane, Human Biosynthetic with increasing proportions of Insulin Injection, Human Biosynthetic (Novolin[®]ge 30/70, Novolin[®]ge 40/60, Novolin[®]ge 50/50).

Novolin[®]ge premixed insulin is a suspension for injection containing Biosynthetic Human Insulin produced by recombinant DNA methods using *S. cerevisiae* (baker's yeast) and followed by unique purification processes. Human Insulin (biosynthetic) is structurally identical to natural human insulin.

What the nonmedicinal ingredients are

Zinc chloride, glycerol, metacresol, phenol, disodium phosphate dihydrate, sodium hydroxide, hydrochloric acid, protamine sulphate and water for injections.

Dosage forms

Novolin[®]ge premixed insulin is available from Novo Nordisk Canada in the following format:

Novolin[®]ge 30/70 10 mL vial

Novolin[®]ge 30/70 Penfill[®] 3 mL cartridge

Novolin[®]ge 40/60 Penfill[®] 3 mL cartridge

Novolin[®]ge 50/50 Penfill[®] 3 mL cartridge (designed for use with Novo Nordisk Insulin Delivery Devices)

Novolin[®]ge premixed insulin cartridges are designed for use with Novo Nordisk Insulin Delivery Devices NovoFine[®] and NovoTwist[®] needles.

Novo Nordisk cannot be held responsible for malfunctions occurring as a consequence of using Novolin[®]ge premixed Penfill[®] insulin cartridges in combination with products that do not meet the same specifications or quality standards as NovoFine[®] and NovoTwist[®] needles.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Hypoglycaemia is the most common adverse effect of insulin including Novolin[®]ge.
- If hypoglycemic 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.
- Insulin suspensions as Novolin[®]ge 30/70, Novolin[®]ge 40/60 and Novolin[®]ge 50/50 are not to be used in insulin infusion pumps.
- Insulin suspensions as Novolin[®]ge 30/70, Novolin[®]ge 40/60 and Novolin[®]ge 50/50 are never to be administered intravenously.
- Novolin[®]ge 30/70, Novolin[®]ge 40/60 and Novolin[®]ge 50/50 should not be used if it is not uniformly white and cloudy.

Before you use Novolin[®]ge [Penfill[®]/vial] premixed talk to your doctor or pharmacist:

- ▶ 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.
- ▶ If you drink alcohol (including wine and beer) watch for signs your need for insulin may change as your blood sugar level may rise or fall.
- ▶ If you have an infection, fever or have had an operation you may need more insulin than usual.
- ▶ If you suffer from diarrhea, vomiting or eat less than usual you may need less insulin than usual.
- ▶ If you exercise more than usual or if you want to change your usual diet.
- ▶ If you are ill: continue taking your insulin. Your need for insulin may change.

- ▶ If you 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.
- ▶ If you are pregnant, or planning a pregnancy or are breastfeeding please contact your doctor for advice.
- ▶ If you 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 hypoglycemia 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 hypoglycemias.

Before you travel, check with your physician or pharmacist on the availability of Novolin[®]ge premixed insulin in other countries. If possible, bring enough Novolin[®]ge premixed 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.

INTERACTIONS WITH THIS MEDICATION

Many 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 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 (hyperglycaemia):

- 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 middleaged 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 hypoglycaemia.

PROPER USE OF THIS MEDICATION

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.

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

Before using Novolin[®]ge premixed:

- ▶ 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 [Penfill[®]].
- ▶ Needles and Novolin[®]ge Penfill[®] must not be shared.

Do not use Novolin[®]ge premixed:

- ▶ If you feel a hypoglycemia coming on (low blood sugar). See *Possible side effects* for more about hypoglycemias.
- ▶ If you are allergic (hypersensitive) to human insulin, metacresol or any of the other ingredients in this insulin. Look out for the signs of an allergic reaction (see *Possible side effects*).
- ▶ In insulin infusion pumps.
- ▶ If the Penfill[®] cartridge or Novo Nordisk Insulin Delivery Device containing the insulin is dropped, damaged or crushed; there is a risk of leakage of insulin.
- ▶ If the insulin has not been stored correctly or if it has been frozen (see *'How to Store it'*).
- ▶ If the insulin does not appear water-clear and colourless.
- ▶ If the protective cap on the vial 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.

Do not refill a Novolin[®]ge Penfill[®] premixed insulin cartridge.

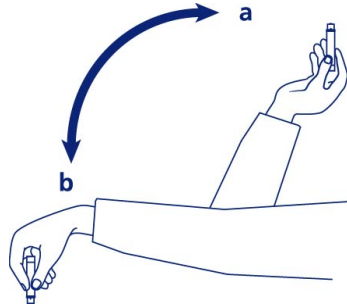
Novolin[®]ge Penfill[®] premixed cartridges are designed to be used with Novo Nordisk Insulin Delivery Devices NovoFine[®] and NovoTwist[®] needles as part of The All In-One System[®].

If you are treated with Novolin[®]ge Penfill[®] premixed insulin 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, you should carry a spare syringe and extra insulin in case the insulin delivery device is lost or damaged.

Resuspending the insulin

Resuspending is easier when the insulin has reached room temperature. Before you put the Penfill[®] cartridge into the insulin delivery device, move it up and down between positions **a** and **b** and back (see diagram) 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 Penfill®.

How to use this insulin

Novolin®ge premixed insulin is for injection under the skin (subcutaneously). Never inject your insulin directly into a vein or muscle. To avoid lumps always vary the site you inject (see *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 around the waist.

Novolin®ge 30/70 vials are for use with insulin syringes which are marked for use with IU-100 insulin. Failure to use the correct syringe can lead to dosage errors.

Before injecting Novolin®ge 30/70

1. Just before injecting this insulin, roll the vial between your hands until the liquid is uniformly white and cloudy. Resuspending is easier if the insulin has reached room temperature.
2. Draw air into the syringe, in the same amount as the dose of insulin you need.
3. Inject the air into the vial: push the needle through the rubber stopper and press the plunger.
4. Turn the vial and syringe upside down.
5. Draw the right dose of insulin into the syringe.
6. Pull the needle out of the vial.
7. Make sure there is no air left in the syringe: point the needle upwards and push the air out.
8. Check you have the right dose.
9. Inject immediately.

How to inject this insulin

- ▶ Inject the insulin under the skin. Use the injection technique advised by your doctor or Diabetes Nurse Educator [and described in your Novo Nordisk Insulin Delivery Device manual].
- ▶ Keep the needle under your skin for at least 6 seconds to make sure that the full dose has been delivered. [vial]
- ▶ 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. [Penfill]
- ▶ After each injection be sure to remove and discard the needle and store Novolin®ge Penfill® premixed insulin 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.

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.

- 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.

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.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Possible side effects

Like all medicines, Novolin[®]ge premixed insulin can cause side effects, although not everybody gets them. Novolin[®]ge premixed insulin may cause low blood sugar (hypoglycemia). See the advice in *Proper Use of this Medication*.

Less commonly reported side effects (1 to 10 users in 100)

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 Novolin[®]ge Toronto or one of its ingredients (called a generalized allergic reaction). See also the warning in *About this medication*.

Changes at the injection site (Lipodystrophy). 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 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.

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.

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

Painful neuropathy (nerve related pain) If your blood glucose levels improve very fast it may cause burning, tingling or electric pain. This is called acute painful neuropathy and it usually disappears. If it does not disappear, see your doctor.

Very rarely reported side effects (less than 1 in 10,000)

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

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

HOW TO STORE IT

Keep out of the reach and sight of children.

Novolin[®]ge premixed insulin [vial] [in Penfill[®] cartridge] that is not being used is to be stored in a refrigerator between 2°C - 10°C, not in or too near the freezer section or the cooling element and is to be kept in the original carton. Do not freeze.

Novolin[®]ge premixed insulin [vial] [in Penfill[®] cartridge] that is being used or is about to be used is not to be kept in a refrigerator. After removing Novolin[®]ge premixed [vial] [in Penfill[®] cartridge] from the refrigerator let the [vial] [cartridge] [insulin delivery device] reach room temperature before resuspending the insulin as instructed for first time use. See *Proper Use of this Medication* .

Novolin[®]ge 30/70:

You can carry the vial with you and keep it at room temperature (not above 25°C) for up to 4 weeks.

Novolin[®]ge 30/70, Novolin[®]ge 40/60, Novolin[®]ge 50/50 Penfill[®]:

You can carry the [cartridge] [insulin delivery device] with you and keep it at room temperature (not above 30°C) for up to 4 weeks.

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

Novolin[®]ge premixed insulin [vial] [Penfill[®] cartridge] must be protected from excessive heat and light.

Do not use Novolin[®]ge premixed insulin [vial] [Penfill[®] cartridge] after the expiry date which is printed on the label and the carton.

Novolin[®]ge premixed insulin [vial] [Penfill[®] cartridge] should not be disposed of in waste water or household waste. Ask your pharmacist how to dispose of medicines no longer needed. These measures will help protect the environment.

REPORTING SUSPECTED SIDE EFFECTS

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

\$ Report online at www.healthcanada.gc.ca/medeffect

\$ Call toll-free at 1-866-234-2345

\$ Complete a Canada Vigilance Reporting Form and:

- Fax toll-free to 1-866-678-6789, or

- Mail to: Canada Vigilance Program

Health Canada

Postal Locator 0701D

Ottawa, Ontario

K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect[™] Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

What Novolin[®]ge premixed insulin looks like and package content

The suspension for injection comes as a cloudy, white, aqueous suspension in packs of:

1 x 10 mL vial

1 x 5 x 3 mL Penfill[®] cartridges

1 mL contains 100 IU (International Units) of insulin human.

1 vial contains 10 mL equivalent to 1000 IU.

1 Penfill[®] cartridge contains 3 mL equivalent to 300 IU.

This document plus the full Product Monograph, prepared for health professionals can be obtained by contacting the sponsor, Novo Nordisk Canada, at 1- 800-465-4334

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