

Novolin[®]ge [Penfill[®]/ FlexPen[®]/ InnoLet[®]]

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. 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, diabetes nurse or your pharmacist.

ABOUT THIS MEDICATION

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

What the medication is used for:

Novolin[®]ge [Penfill[®]/ FlexPen[®]/ InnoLet[®]] premixed is human insulin used to treat diabetes. It comes in a [10 mL vial that you use to fill a syringe] [3 mL cartridge call Penfill[®] which fits into a Novo Nordisk Insulin Delivery Device] [Novolin[®]ge FlexPen[®] prefilled insulin delivery device] [Novolin[®]ge InnoLet[®] compact prefilled insulin delivery device].

Novolin[®]ge premixed insulin is indicated for:

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

What it does:

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.

When it should not be used:

Do not use Novolin[®]ge premixed insulin:

- ▶ **If you are allergic (hypersensitive)** to this insulin product, metacresol or any of the other ingredients (see 'What the important nonmedicinal ingredients are' listed below). Look out for the signs of allergy in 'Possible side effects'.
- ▶ **If you feel a hypo** coming on (a hypo is short for a hypoglycemic reaction and is a symptom of low blood sugar). See 'What to do in an emergency', for more about hypos.

What do you have to consider during pregnancy or while breastfeeding?

If you are pregnant or planning to become pregnant you should see your doctor immediately to discuss your need for and type of insulin in order to control your diabetes and avoid hyperglycaemia (too high blood sugar) and hypoglycaemia (too low blood sugar) as these conditions could harm your baby.

Breastfeeding while you are taking insulin does not put your baby at risk. Your insulin dosage and diet may, however, need to be adjusted.

Alcohol use

Alcohol (including beer and wine) may lead to hypoglycaemia (too low blood sugar). Therefore, be careful when you drink alcohol and never drink alcohol on an empty stomach. Follow your physician's advice regarding diet and alcohol consumption.

What should be done during an illness?

Never stop taking insulin if you are ill. Your need for insulin may, however, be changed.

If you have an infection, fever or an operation you may need to have more insulin than usual.

If you suffer from diarrhoea, vomiting or eat less than usual you may also need less insulin than usual.

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 important nonmedicinal ingredients are:

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

What dosage forms it comes in:

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 30/70 FlexPen[®] 3 mL

Novolin[®]ge 40/60 FlexPen[®] 3 mL

Novolin[®]ge 50/50 FlexPen[®] 3 mL

Novolin[®]ge 30/70 InnoLet[®] 3 mL

Novolin[®]ge 40/60 InnoLet[®] 3 mL

Novolin[®]ge 50/50 InnoLet[®] 3 mL

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

Novolin[®]ge premixed [FlexPen[®]] [InnoLet[®]] is designed for use with NovoFine[®] needles.

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

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Insulin suspensions are never to be administered intravenously.
- Insulin suspensions are not to be used in insulin infusion pumps.

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

- ▶ **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.
- ▶ **If you are ill:** continue taking your insulin.
- ▶ **If you go abroad:** travelling over time zones may affect your insulin needs and the timing of your injections.

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.

Pregnancy and breastfeeding

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

Driving and using machines

- ▶ **If you drive or use tools or machines:** watch 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 should drive or use machines at all, if you have a lot of hypos or if you find it hard to recognize hypos.

INTERACTIONS WITH THIS MEDICATION

When you use other medicines

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

Your need for insulin may change if you also take: oral antidiabetic products; monoamine oxidase inhibitors; (MAOI); beta-blockers; ACE-inhibitors; acetylsalicylic acid (aspirin); anabolic steroids; sulphonamides; oral contraceptives; thiazides; glucocorticoids; thyroid hormone therapy; beta-sympathomimetics; growth hormone; danazol; octreotide and lanreotide.

PROPER USE OF THIS MEDICATION

How to use

Novolin[®]ge [Penfill[®]/ FlexPen[®]/ InnoLet[®]] premixed

Talk about your insulin needs with your doctor and Diabetes Nurse Educator. 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.

It is recommended that you measure your blood glucose regularly.

Before using Novolin[®]ge premixed:

- ▶ **Check the label** to make sure you have the right type of insulin.
- ▶ **Disinfect the rubber membrane** with an alcohol swab.
- ▶ **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.

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

- ▶ **Always use a new needle** for each injection to prevent contamination

Do not use Novolin[®]ge premixed:

- ▶ **In insulin infusion pumps.**
- ▶ **If the insulin has not been stored correctly** or if it has been frozen (see 'How to Store Novolin[®]ge premixed').
- ▶ **If the insulin does not appear uniformly white and cloudy** when it is resuspended.
- ▶ **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.
- ▶ **If the [Penfill[®] cartridge or Novo Nordisk Insulin Delivery Device containing the cartridge] [FlexPen[®]] [InnoLet[®]] is dropped, damaged or crushed;** there is a risk of leakage of insulin.

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 and NovoFine[®] 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.

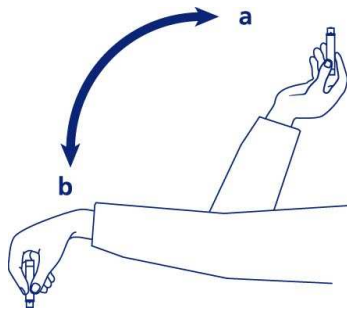
Resuspending the insulin

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.
- ▶ **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.

Usual dose:

Follow carefully the instructions given by your doctor concerning type of insulin, dose, and time of injection. Any change in insulin should be made cautiously and only under medical supervision. Your insulin requirements may change due to a number of factors (illness, stress, medications, changes in diet or exercise routines, etc.). Follow your doctor's instructions to allow for these changes. The following can be considered as general guidelines only and you should consult your doctor for information, which is specific to your diabetes.

What about travelling?

The time difference between countries may mean that you have to take your insulin and meals at different times than usual. You should therefore consult your doctor if you are planning to go abroad or travel across time zones.

Overdose:

What factors may result in hypoglycaemia (low blood sugar)?

If you take too much insulin, miss a meal or exercise more than usual your blood sugar may become too low (i.e. hypoglycaemia).

The first **symptoms of hypoglycaemia** may come on suddenly. They may include: cold sweat, cool pale skin, fatigue, drowsiness, nervousness or tremor, feelings of anxiety, unusual tiredness and weakness, confusion, difficulty concentrating, excessive hunger, changes in vision, headache and nausea and palpitation.

What to do in case of hypoglycaemia?

If you experience any of the symptoms mentioned above, you should immediately take sugar or a sugar-containing product. Therefore, always carry a few lumps of sugar, candies, biscuits or fruit juice with you.

Your relatives, friends and close work-mates should know that you have diabetes and how they can help you if you get a severe hypoglycaemic reaction. They must be aware that an unconscious person should not be given anything to eat or drink (as choking is possible), but should be turned on their side and medical assistance sought immediately.

You may recover from unconsciousness more quickly if you are given an injection of the hormone glucagon by a person who has been instructed in how to use it. If glucagon is injected, you should also be given sugar, a product containing sugar or glucose by mouth as soon as you are conscious again.

If you do not respond to glucagon treatment, you will have to be treated in a hospital. See your doctor if you have had repeated hypoglycaemic reactions, or one leading to unconsciousness, as your insulin dose may need to be adjusted.

If severe hypoglycaemia is not treated, it can cause temporary or permanent brain damage or death.

What factors may result in hyperglycaemia (high blood sugar)?

If you are ill with fever or if you eat much more than usual and repeatedly take less insulin than you need, your blood sugar may become unusually high (i.e. result in hyperglycaemia).

The **symptoms of unusually high blood sugar levels** will appear gradually. They include: increased urination, thirst, loss of appetite, nausea, vomiting, drowsiness (fatigue), flushed dry skin, dry mouth, and acetone breath.

What to do in case of hyperglycaemia?

If you recognize any of the symptoms mentioned above, you should test your blood sugar level and your urine for ketones as soon as possible as the symptoms may indicate that you have a condition called ketoacidosis. If hyperglycaemia is not treated it can cause diabetic coma or death. You should therefore seek medical advice immediately and possibly take some extra insulin.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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; 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 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 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 hypo that makes you pass out**, or if you get a lot of hypos, 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. Seek medical advice after an injection of glucagon; you need to find the reason for your hypo in order 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 hyperglycemia).

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.

If you get any of these signs, test your blood sugar level; test your urine for ketones if you can; then seek medical advice right 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.

Causes of hyperglycemia

- Forgetting to take your insulin.
- Repeatedly taking less insulin than you need.
- An infection or fever.
- Eating more than usual.
- Exercising less than usual.

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 '*What to do in an emergency*'.

Less commonly reported side effects

(less than 1 in 100)

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.

Signs of allergy Reactions (redness, swelling, itching) at the injection site may occur (local allergic reactions). These reactions 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 breathing; have a rapid heart beat; feel dizzy; feel like fainting.

You may have a very rare serious allergic reaction to Novolin[®] **ge** premixed insulin or one of its ingredients (called a systemic allergic reaction). See also the warning in '*Before you use Novolin[®] ge premixed*'.

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 reaction usually disappears.

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

How to store

Novolin[®] ge [Penfill[®] / FlexPen[®] / InnoLet[®]] premixed

Keep out of the reach and sight of children.

Novolin[®] ge premixed insulin [vial] [in Penfill[®] cartridge] [FlexPen[®]] [InnoLet[®]] 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] [FlexPen[®]] [InnoLet[®]] 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] [FlexPen[®]] [InnoLet[®]] from the refrigerator let the [vial] [cartridge] [insulin delivery device] reach room temperature before resuspending the insulin as instructed for first time use. See '*How to use Novolin[®] ge premixed*'.

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[®] /FlexPen[®] /InnoLet[®]:

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] [FlexPen[®]] [InnoLet[®]] in the outer carton when you are not using it, in order to protect it from light.

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

Do not use Novolin[®] ge premixed insulin [vial] [Penfill[®] cartridge] [FlexPen[®]] [InnoLet[®]] after the expiry date which is printed on the label and the carton. The expiry date refers to the last day of that month.

Novolin[®] ge premixed insulin [vial] [Penfill[®] cartridge] [FlexPen[®]] [InnoLet[®]] 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

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance by:

By toll-free telephone: 866-234-2345
By toll -free fax: 866-678-6789
Online: www.healthcanada.gc.ca/medeffect
By email: CanadaVigilance@hc-sc.gc.ca

By regular mail:
Canada Vigilance National Office
Marketed Health Products Safety and Effectiveness
Information Bureau
Marketed Health Products Directorate
Health Products and Food Branch
Health Canada
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Should you require information related to the management of the side effect, please contact your health care provider before notifying Canada Vigilance. 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 x 3 mL FlexPen[®] insulin delivery device
- 1 x 3 mL InnoLet[®] insulin delivery device

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

1 vial contains 10 mL equivalent to 1000 IU.

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

For further information, please refer to the '*Information for Health Care Professionals*'.

This summary does not contain all the known information about Novolin[®]ge premixed insulin. Talk to your doctor if you have any questions

This document plus the full product monograph, prepared for health professionals can be found at:
www.novonordisk.ca
or by contacting the sponsor, **Novo Nordisk Canada Inc.**, at
1-800-465-4334

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