NEW ZEALAND DATASHEET

1. PRODUCT NAME

HUMULIN® R (Regular), 100 IU/mL, solution for injection

HUMULIN® NPH, 100IU/mL, suspension for injection

HUMULIN® 30/70, 100 IU/mL, suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Insulin human (rbe) recombinant DNA origin solution/suspension for injection containing 100 IU/mL.

For the full list of excipients, see **6.1 List of excipients**.

3. PHARMACEUTICAL FORM

HUMULIN R (Regular)

(also called soluble insulin injection) is a sterile, clear colourless aqueous solution of human insulin (rbe) adjusted to a pH range of 7.0 to 7.8. HUMULIN R is a short-acting insulin preparation.

HUMULIN NPH

(also called isophane insulin injection) is a sterile suspension of a white, crystalline precipitate of isophane human insulin (rbe) in an isotonic phosphate buffer adjusted to a pH range of 6.9 to 7.5. HUMULIN N is an intermediate-acting insulin preparation.

HUMULIN 30/70

(also called biphasic isophane insulin injection) is a mixture of human insulin (70% isophane human insulin (rbe), 30% soluble human insulin (rbe)) adjusted to a pH range of 6.9 to 7.5. HUMULIN Mixture 70/30 is an intermediate acting insulin preparation.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

HUMULIN is indicated for the treatment of insulin-requiring diabetes mellitus.

4.2 Dose and method of administration

The dosage should be determined by the physician, according to the requirement of the patient. During changes to a patient's insulin regimen, increase the frequency of glucose monitoring.

Vials

HUMULIN R vials should be given by subcutaneous injection. They may also be administered intravenously.

HUMULIN NPH and **HUMULIN 30/70** vials should be given by subcutaneous injection. These formulations should not be administered intravenously.

Cartridges

HUMULIN R, **HUMULIN NPH**, and **HUMULIN 30/70** cartridges should only be given by subcutaneous injection using the HumaPen.

General

Subcutaneous administration should be in the upper arms, thighs, buttocks or abdomen. Use of injection sites should be rotated so that the same site is not used more than approximately once a month, in order to reduce the risk of lipodystrophy and localised cutaneous amyloidosis. Do not inject into areas of lipodystrophy or localised cutaneous amyloidosis.

Care should be taken when injecting any HUMULIN insulin preparation to ensure that a blood vessel has not been entered. After any insulin injection, the injection site should not be massaged. Patients must be educated to use proper injection techniques.

HUMULIN NPH may be administered in combination with HUMULIN R. (see **4.2 Dose and method of administration, Instructions for use, Mixing of insulins**).

HUMULIN 30/70 formulation is a ready-made defined mixture of HUMULIN R and HUMULIN NPH insulin designed to avoid the need for the patient to mix insulin preparations. A patient's treatment regimen should be based on their individual metabolic requirements.

Instructions for use

HUMULIN R

Vials and cartridges containing HUMULIN R do not require re-suspension. HUMULIN R is a clear and colourless liquid with a water-like appearance and consistency. Do not use HUMULIN R if it appears cloudy, thickened, slightly coloured, or if solid particles are visible.

HUMULIN NPH and HUMULIN 30/70

Re-suspension instructions

Vials

Carefully shake or rotate the insulin bottle several times to completely mix the insulin. Insulin should look uniformly cloudy or milky after mixing. If not, repeat the above step until contents are mixed.

Vials of insulin should be examined frequently.

Do not use if the insulin substance (the white material) remains at the bottom of the vial after mixing.

Do not use if there are clumps in the insulin after mixing.

Do not use if solid white particles stick to the bottom or wall of the vial, giving a frosted appearance.

Cartridges

Roll the cartridge between the palms 10 times. Holding the cartridge by one end, invert it 180° slowly 10 times to allow the glass bead to travel the full length of the cartridge with each inversion. Insulin should look uniformly cloudy or milky after mixing. If not, repeat the above steps until the contents are mixed.

Cartridges of insulin should be examined frequently.

Do not use if the insulin substance (the white material) remains visibly separated from the liquid after mixing.

Do not use if there are clumps in the insulin after mixing.

Do not use if solid white particles stick to the bottom or wall of the cartridge, giving a frosted appearance.

Insulin cartridges are not designed to allow any other insulin to be mixed in the cartridge.

Mixing of insulins

The shorter acting insulin (HUMULIN R) should be drawn into the syringe first, to prevent contamination of the vial by the longer acting preparation (HUMULIN NPH). It is advisable to inject directly after mixing. However, if a delay is necessary, a consistent routine must be followed.

Alternatively a separate syringe or, separate cartridges of HUMULIN R and HUMULIN NPH, can be used for administration of the correct amount of each formulation.

Administration instructions for all insulins

Vials

To administer insulin, use an insulin syringe marked for the strength of insulin being administered.

Cartridges

To load the cartridge into the device and to attach the needle prior to administration of the insulin, refer to the manufacturer's instruction for the insulin delivery device. For instructions on how to administer insulin, refer to the manufacturer's instruction for the insulin delivery device.

To prevent the possible transmission of disease, each cartridge must be used by one patient only, even if the needle is changed.

4.3 Contraindications

Hypoglycaemia.

Hypersensitivity to HUMULIN or to the formulation excipients (unless used as part of a desensitisation program).

Under no circumstances should any HUMULIN formulation other than HUMULIN R be given intravenously.

4.4 Special warnings and precautions for use

Insulin Changes

Transferring a patient to another type or brand of insulin should be done under strict medical supervision with increased frequency of glucose monitoring. Changes in strength, brand (manufacturer), type (Regular, NPH, etc.), species (animal, human, human insulin analogue), and/or method of manufacture (recombinant DNA versus animal-source insulin) may result in the need for a change in dosage.

Some patients taking human insulin may require a change in dosage from that used with animal-source insulins. If an adjustment is needed, it may occur with the first dose or during the first several weeks or months.

A few patients who experienced hypoglycaemic reactions after transfer to human insulin have reported that the early warning symptoms were less pronounced or different from those experienced with their previous animal insulin. Patients whose blood glucose is greatly improved, e.g. by intensified insulin therapy, may lose some or all of the warning symptoms of hypoglycaemia and should be advised accordingly. Other conditions which may make the early warning symptoms of hypoglycaemia different or less pronounced include long duration of diabetes, diabetic nerve disease, or medications such as beta blockers. Uncorrected hypoglycaemic and hyperglycaemic reactions can cause loss of consciousness, coma or death.

Injection technique

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis. There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites with these reactions. A sudden change in the injection site to an unaffected area has been reported to result in hypoglycaemia. Blood glucose monitoring is recommended after the change in the injection site, and dose adjustment of antidiabetic medications may be considered.

Concomitant Disease States

Insulin requirements may change significantly in diseases of the adrenal, pituitary or thyroid glands and in the presence of renal or hepatic impairment.

Illness or Emotional Disturbances

Insulin requirements may be increased during illness or emotional disturbances.

Activity or Diet Changes

Adjustment of insulin dosage may also be necessary if patients change their level of physical activity or change their usual diet.

Thiazolidinediones (TZDs) used in combination with insulin

TZDs in combination with insulin are associated with an increased risk of oedema and heart failure; especially in patients with underlying cardiac disease.

4.5 Interactions with other medicines and other forms of interactions

The patient should check with their physician when using other medicines in addition to HUMULIN (see **4.4 Special warnings and precautions for use**).

Insulin requirements may be decreased in the presence of medicines with hypoglycaemic activity e.g. anabolic steroids, guanethidine, propranolol (masking effect), oral antidiabetic agents, alcohol, sulpha-antibiotics (e.g. sulphonamides), octreotide, certain antidepressants (monoamine oxidase inhibitors), angiotensin converting enzyme inhibitors (captopril and enalapril), angiotensin II receptor blockers and beta-adrenergic blockers, or salicylates.

Insulin requirements may be increased by medicines with hyperglycaemic activity, e.g. oral contraceptives, isoniazid, corticosteroids or thyroid hormone replacement therapy.

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data available.

Use in pregnancy

It is essential to maintain good control of the insulin treated (insulin-dependent or gestational diabetes) patient throughout pregnancy. Insulin requirements usually fall during the first trimester and increase during the second and third trimesters. Patients with diabetes should be advised to inform their doctors if they are pregnant or are contemplating pregnancy.

Use in lactation

Diabetic patients who are lactating may require adjustments in insulin dose and/or diet.

4.7 Effects on ability to drive and use machines

The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. This may constitute a risk in situations where these abilities are of special importance (e.g. driving a car or operating machinery). Patients should be advised to take precautions to avoid hypoglycaemia whilst driving, this is particularly important in those who have reduced or absent awareness of the warning signs of hypoglycaemia or have frequent episodes of hypoglycaemia. The advisability of driving should be considered in these circumstances.

4.8 Undesirable effects

Body as a Whole

Allergic reaction(s)

Local allergy in patients may occur as redness, swelling, or itching at the site of injection. These minor reactions usually resolve in a few days to a few weeks. In some instances, these reactions may be related to factors other than insulin, such as irritants in the skin cleansing agent or poor injection technique.

Systemic allergy to insulin is less common but potentially more serious.

Generalised allergy to insulin may cause rash over the whole body, shortness of breath, wheezing, reduction in blood pressure, rapid pulse or sweating. Severe cases of generalised allergic reaction may be life-threatening.

Skin and appendages

Lipodystrophy

Metabolic

Hypoglycaemia; Insulin resistance

Hypoglycaemia is the most frequent undesirable effect of insulin therapy that a patient with diabetes may suffer. Severe hypoglycaemia may lead to loss of consciousness and, in extreme cases, death.

Spontaneous Data

Cases of oedema have been reported with insulin therapy, particularly if previous poor metabolic control is improved by intensified insulin therapy (see **4.4 Special warnings and precautions for use**).

Lipodystrophy and localised cutaneous amyloidosis at the injection site have occurred. Hyperglycaemia has been reported with repeated insulin injections into areas of lipodystrophy or localised cutaneous amyloidosis; hypoglycaemia has been reported with a sudden change to an unaffected injection site. (see section **4.4 Special warnings and precautions for use**).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

Overdose causes hypoglycaemia with accompanying symptoms that may include listlessness, confusion, palpitations, sweating, vomiting and headache. Hypoglycaemia may occur as a result of an excess of human insulin relative to food intake, energy expenditure or both. Mild episodes of hypoglycaemia usually can be treated with oral glucose. Adjustments in medicine dosage, meal patterns, or exercise may be needed. More severe episodes with coma, seizure, or neurologic impairment may be treated with intramuscular or subcutaneous administration of glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycaemia may recur after apparent clinical recovery.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

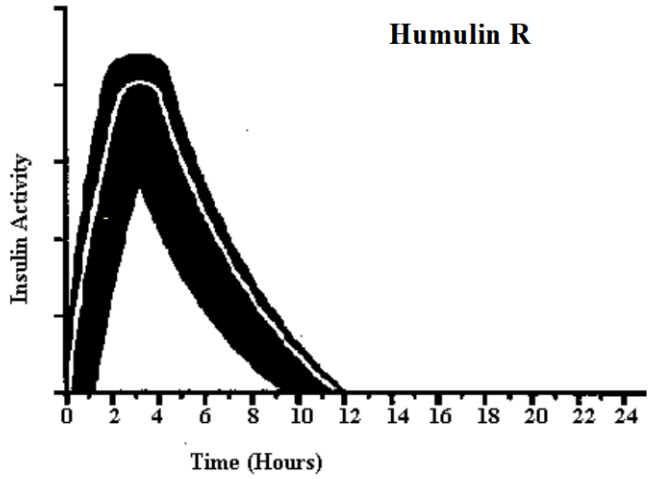
5.1 Pharmacodynamic properties

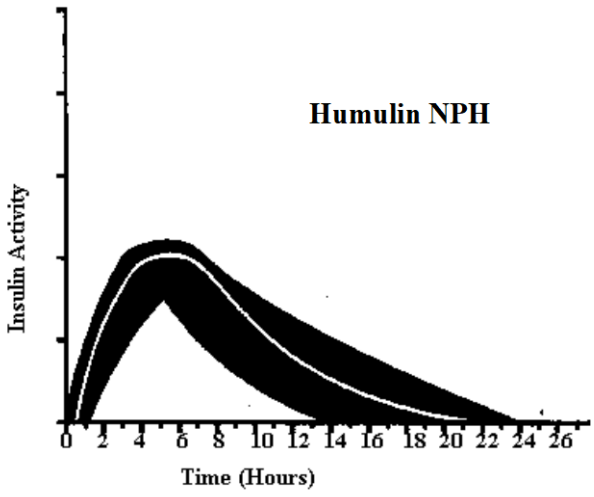
Pharmacotherapeutic group: insulin, human, ATC Code: ATC Code: HUMULIN R - A10AB01; HUMULIN NPH - A10AC01; HUMULIN 30/70 - A10AD01

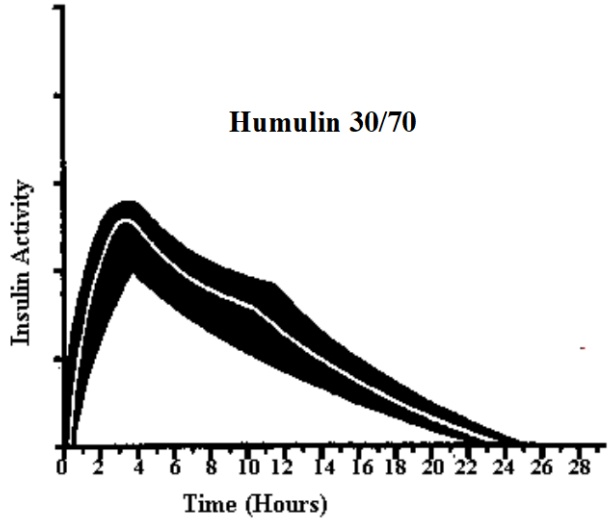
Pharmacodynamic effects

The primary activity of human insulin is the regulation of glucose metabolism. In addition, insulin has several anabolic and anti-catabolic actions on many tissues in the body. In muscle and other tissues (except the brain), insulin causes rapid transport of glucose and amino acids intracellularly, promotes anabolism, and inhibits protein catabolism. In the liver, insulin promotes the uptake and storage of glucose in the form of glycogen, inhibits gluconeogenesis, and promotes the conversion of excess glucose into fat.

The typical activity profile (glucose utilisation curves) are illustrated below by the heavy line. Variations that a patient may experience in timing and/or intensity of insulin activity are illustrated by the shaded area. Individual variability will depend on factors such as size of dose, site of injection temperature and physical activity of the patient.







5.2 Pharmacokinetic properties

The pharmacokinetics of insulin do not reflect the metabolic action of that hormone. Therefore, it is more appropriate to examine glucose utilisation curves (as discussed above) when considering the activity of insulin. Individual variation of blood glucose response profiles are dependent upon factors such as the size of dose, site of injection and physical activity of the patient.

5.3 Preclinical safety data

Human insulin is produced by recombinant technology. No serious events have been reported in subchronic toxicology studies. Human insulin was not mutagenic in a battery of in vitro and in vivo genetic toxicity assays.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

HUMULIN R

Each vial or cartridge will contain human insulin (recombinant DNA origin) and the following excipients:

- metacresol distilled 2.5 mg/mL,
- glycerol,
- water for injections.
- Hydrochloric acid and/or sodium hydroxide may have been used during manufacture.

HUMULIN NPH and HUMULIN 30/70

Each vial or cartridge will contain human insulin (recombinant DNA origin) and the following excipients:

- metacresol distilled 1.6 mg/mL,

- glycerol,
- phenol 0.65 mg/mL,
- protamine sulphate,
- dibasic sodium phosphate heptahydrate,
- zinc oxide,
- water for injections.
- Hydrochloric acid and/or sodium hydroxide may have been used during manufacture.

6.2 Incompatibilities

The effects of mixing human insulin with insulins of animal source or human insulin produced by other manufacturers have not been studied.

6.3 Shelf-life

Unopened

The shelf life for HUMULIN R, HUMULIN NPH and HUMULIN 30/70 vials and cartridges is two years when stored under appropriate conditions.

In-use

When in use, all HUMULIN 10 mL vials may be kept at room temperature (30° C) for up to 28 days.

When in use, all 3 mL cartridges may be kept at room temperature (30° C) for up to 21 days.

6.4 Special precautions for storage

HUMULIN preparations should be stored in a refrigerator between 2° and 8° C. HUMULIN preparations should not be frozen or exposed to excessive heat or sunlight.

6.5 Nature of contents of container

Vials 10 mL: HUMULIN R, NPH and HUMULIN 30/70 are available individually.

Cartridges 3.0 mL: HUMULIN R, NPH and HUMULIN 30/70 are available in packs of five.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Eli Lilly and Company (NZ) Limited

PO Box 109 197

Newmarket

Auckland 1149

Contact telephone number: 0800 500 056

9. DATE OF FIRST APPROVAL

13 March 1986

10. DATE OF REVISION OF THE TEXT

28 August 2025

11. SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
6.3	Update to unopened shelf-life for HUMULIN NPH and 30/70 cartridges. Update to in-use shelf-life for all HUMULIN R, NPH, and 30/70 cartridges.
Throughout	Editorial updates.

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