AUSTRALIAN PRODUCT INFORMATION

Actrapid® insulin (rys) 100 IU/mL injection multidose vial
Actrapid® Penfill® insulin (rys) 100 IU/mL injection multidose cartridge
Mixtard® 30/70 InnoLet® insulin (rys) 100 IU/mL injection multidose cartridge
Mixtard® 30/70 Penfill® insulin (rys) 100 IU/mL injection multidose cartridge
Mixtard® 50/50 Penfill® insulin (rys) 100 IU/mL injection multidose cartridge
Protaphane® insulin (rys) 100 IU/mL injection multidose vial
Protaphane® InnoLet® insulin (rys) 100 IU/mL injection multidose cartridge
Protaphane® Penfill® insulin (rys) 100 IU/mL injection multidose cartridge

1. NAME OF THE MEDICINE

insulin (rys)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Actrapid®: 1 mL solution contains 100 international units insulin (rys). Also contains: glycerol, metacresol, zinc chloride, water for injections. Hydrochloric acid and sodium hydroxide are used to adjust the pH.

Protaphane®: 1 mL suspension contains 100 international units isophane insulin (rys). Also contains: glycerol, metacresol, phenol, dibasic sodium phosphate dihydrate, zinc chloride, protamine sulfate (a fish product), water for injections. Hydrochloric acid and sodium hydroxide are used to adjust the pH.

Mixtard® 30/70: 1 mL suspension contains 100 international units soluble insulin (rys)/isophane insulin (rys) in the ratio 30/70. Also contains: glycerol, metacresol, phenol, dibasic sodium phosphate dihydrate, zinc chloride, protamine sulfate (a fish product), water for injections. Hydrochloric acid and sodium hydroxide are used to adjust the pH.

Mixtard® 50/50: 1 mL suspension contains 100 international units soluble insulin (rys)/isophane insulin (rys) in the ratio 50/50. Also contains: glycerol, metacresol, phenol, dibasic sodium phosphate dihydrate, zinc chloride, protamine sulfate (a fish product), water for injections. Hydrochloric acid and sodium hydroxide are used to adjust the pH.

One IU (International Unit) of insulin corresponds to 0.035 mg of anhydrous insulin (rys).

Insulin (rys) is produced by recombinant DNA technology using *Saccharomyces cerevisiae.*

Actrapid, Protaphane, Mixtard 30/70 and Mixtard 50/50 contain less than 1 mmoL sodium (23 mg) per dose, i.e. these products are essentially ‘sodium-free’.

3. PHARMACEUTICAL FORM

Actrapid: Solution for injection. The solution is clear, colourless and aqueous.

Protaphane: Suspension for injection. The suspension is cloudy, white and aqueous.

Mixtard 30/70: Suspension for injection. The suspension is cloudy, white and aqueous.

Mixtard 50/50: Suspension for injection. The suspension is cloudy, white and aqueous.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

The treatment of insulin-requiring diabetes.

4.2 Dose and Method of Administration

Dosage

Dosage is individual and determined by the physician in accordance with the needs of the patient.

The average range of total daily insulin requirement for maintenance therapy in type 1 diabetes lies between 0.5 and 1.0 IU/kg/day. However, in pre-pubertal children it usually varies from 0.7 to 1.0 IU/kg/day, but can be much lower during the period of partial remission. In insulin resistance, (e.g., during puberty or due to obesity) the daily insulin requirement may be substantially higher.

Initial dosages for type 2 diabetes are often lower, e.g., 0.3 to 0.6 IU/kg/day. This should be adjusted slowly until optimum glycaemic control is reached. The total daily insulin requirement for maintenance therapy in type 2 diabetes is usually higher than the initial dose.

In people with diabetes mellitus optimised metabolic control effectively delays the onset and slows the progression of diabetic late complications. Optimised metabolic control, including glucose monitoring, is therefore recommended.

In the elderly the primary aim of treatment may be symptom relief and avoidance of hypoglycaemic events.

Method of Administration

Insulin is usually administered subcutaneously by injection in the abdominal wall, the thigh, the gluteal region or the deltoid region. Injection sites should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis (see Section 4.4 Special Warnings and Precautions for Use and 4.8 Adverse Effects (Undesirable Effects).

Subcutaneous injection into the abdominal wall ensures a faster absorption than from other injection sites. Injection into a lifted skin fold minimises the risk of intramuscular injection. Keep the needle under the skin for at least 6 seconds to make sure the entire dose is injected.

Insulin solution - Actrapid:

Actrapid is a short-acting insulin and is often used in combination with intermediate or long-acting insulins. An injection should be followed by a meal or snack containing carbohydrates

within 30 minutes. In an emergency, Actrapid is suitable for intramuscular administration under medical guidance. In an emergency, Actrapid is also suitable for intravenous administration but only if administered by a physician. For emergency use with Penfill, the insulin must first be withdrawn into a syringe. Discard Penfill cartridge after emergency use.

- Actrapid may also be administered when insulin is required in the following situations:
- Initial stabilisation of diabetes.
- Treatment of diabetic ketoacidosis and hyperosmolar non ketotic syndrome.
  Insulin given as a continuous intravenous infusion or intramuscular injection regime is part of the overall management of both diabetic ketoacidosis and hyperosmolar non ketotic syndrome.
- During stress situations such as severe infection.
  Clinical management of severe infections may require higher doses of insulin than normal, intravenous insulin or short-term insulin treatment in patients normally taking oral hypoglycaemic agents.
- Major trauma and/or surgery in people with diabetes.
  Management of the patient is determined by the nature and severity of the trauma and/or surgery, the duration of peri-operative fasting and the patient's ability to produce insulin. People normally treated with insulin will generally require insulin administration. People with poorly controlled type 2 diabetes or those undergoing major surgery will generally require insulin. Frequent blood glucose monitoring is required during and after surgery. When the patient is able to eat normally, their usual therapy can be re-instated.

Due to the risk of precipitation in pump catheters, Actrapid should not be used in insulin pumps for continuous subcutaneous insulin infusion.

For intravenous use, infusion systems with Actrapid at concentrations 0.05 IU/mL - 1.0 IU/mL insulin in the following infusion fluids; 0.9% sodium chloride, 5% dextrose and 10% dextrose inclusive 40 mmol/L potassium chloride, using polypropylene infusion bags, are stable at room temperature for 24 hours. Although stable over time, a certain amount of insulin will initially be absorbed to the material of the infusion bag. Monitoring of blood glucose is necessary during the infusion.

Pre-mixed insulin suspensions - Mixtard 30/70 and Mixtard 50/50:

Mixtard (pre-mixed) insulins are usually given once or twice daily when a rapid initial effect together with a more prolonged effect is required. Mixtard 50/50 has the strongest initial effect followed by Mixtard 30/70. An injection should be followed by a meal or snack containing carbohydrates within 30 minutes.

Insulin suspension - Protaphane:

The physician determines whether one or more daily injections are necessary. Protaphane is usually given once or twice daily. The preparation may be used alone or mixed with short-acting soluble insulin (e.g., Actrapid, NovoRapid®). In intensive insulin therapy the suspensions may be used as basal insulin (evening and/or morning injection) with soluble insulin given at meals. Protaphane may also be used in combination with oral antidiabetic drugs (OADs) when OADs alone have not given satisfactory control of blood glucose.

Protaphane, Mixtard 30/70 and Mixtard 50/50 are suitable for intramuscular administration in emergency under medical guidance only. For such use with Penfill/InnoLet, the insulin must first be withdrawn into a syringe. Discard Penfill/InnoLet cartridge/syringe after emergency

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

Preparations containing cloudy insulins should be gently agitated by rolling between the hands (10 mL vials only) or gently shaken (Penfill and InnoLet only) before use to ensure that the insulin is uniformly distributed throughout the liquid and the injection should be given immediately thereafter.

Mixing with other insulins

Insulin preparations may be admixed in the syringe. The insulin mixture should be injected immediately after preparation. When short-acting soluble insulin is mixed with longer-acting insulin, the short-acting insulin should be drawn into the syringe first to prevent contamination of the vial by the longer-acting preparation.

If an intermediate-acting or long-acting insulin is mixed with NovoRapid (insulin aspart – a short acting insulin analogue), NovoRapid should be drawn into the syringe first. The injection should be made immediately after mixing.

Instructions for use and handling

10 mL vials

Insulin vials are for use with U100 insulin syringes. A Consumer Medicine Information leaflet is available with instructions for use and handling. The insulin suspensions must be resuspended immediately before use so that they appear uniformly white and cloudy.

Penfill 3 mL cartridges

The Consumer Medicine Information leaflet is available with instructions for use and handling. The insulin suspensions must be resuspended immediately before use so that they appear uniformly white and cloudy.

Penfill preparations are for use by one person only. The cartridge must not be refilled.

Penfill cartridges are designed to be used with Novo Nordisk insulin delivery systems and NovoFine® needles. The patient should be advised to discard the needle after each injection.

InnoLet 3 mL

The carton contains a Consumer Medicine Information package leaflet with instructions for use and handling. The insulin suspensions must be resuspended immediately before use so that they appear uniformly white and cloudy.

InnoLet preparations are for use by one person only. The cartridge inside the pre-filled insulin delivery device must not be refilled. InnoLet are designed to be used with NovoFine needles. Cartridges/pre-filled delivery devices should only be used in combination with products that are compatible with them and that allow the cartridge/device to function safety and effectively.

Penfill and InnoLet are for use by one person only. The container must not be refilled.

4.3 Contraindications

- Hypoglycaemia
- Hypersensitivity to insulin or any of the excipients

- Insulin suspensions should not be administered intravenously
- Insulin suspensions are not suitable for the treatment of diabetic ketoacidotic coma.

4.4 Special Warnings and Precautions for Use

Hyperglycaemia

Inadequate dosing or discontinuation of treatment, especially in type 1 diabetes, may lead to hyperglycaemia and diabetic ketoacidosis. The first symptoms of hyperglycaemia usually come on gradually over a period of hours or days. They include nausea, vomiting, drowsiness, flushed dry skin, dry mouth, increased urination, thirst and loss of appetite as well as acetone breath. In type 1 diabetes, untreated hyperglycaemic events lead to diabetic ketoacidosis which is potentially lethal.

Hypoglycaemia

Omission of a meal or unplanned, strenuous physical exercise may lead to hypoglycaemia (see Section 4.8 Adverse Effects (Undesirable Effects) and Section 4.9 Overdose).

Concomitant illness, especially infections and conditions with fever, usually increases the patient's insulin requirements.

Under certain circumstances, e.g. insufficient food intake, increased physical activity, etc, the daily dose administered to the patient may represent an overdose leading to hypoglycaemia. A change in insulin dosage may be necessary to correct recurrent hypoglycaemia.

Patients whose blood glucose control is greatly improved, e.g. by intensified insulin therapy, may experience a change in their usual warning symptoms of hypoglycaemia, and should be advised accordingly. Usual warning symptoms may disappear in patients with longstanding diabetes.

Transfer from other insulin products

Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (rapid-acting, intermediate-acting, long-acting, etc.), and/or species (animal, insulin analogue) may result in the need for a change in dose.

If an adjustment is needed, it may occur with the first dose or during the first several weeks or months.

Patients currently stabilised on bovine insulins may require a dosage reduction, depending upon the dosage, purity and formulation of the insulin(s) currently administered. Variations in glycaemic control may occur and adjustments in therapy should be made under the guidance of a physician. Any patient receiving over 100 units per day may need to be referred to hospital for transfer. These guidelines are general indications only.

A few patients who have experienced hypoglycaemic reactions after transfer from animal source insulin have reported that early warning symptoms of hypoglycaemia were less pronounced or different from those experienced with their previous insulin.

When patients are transferred between different types of insulin products, the early warning symptoms of hypoglycaemia may change or become less pronounced than those experienced with their previous insulin.

Skin and subcutaneous tissue disorders

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 from an affected to an unaffected area, and dose adjustment of antidiabetic medications may be considered.

Travelling with insulin

Before travelling between different time zones, the patient should be advised to consult their doctor or diabetes education nurse, since this may mean that the patient has to inject their insulin and eat their meals at different times.

Combination of thiazolidinediones and insulin medicinal products

Cases of congestive heart failure have been reported when thiazolidinediones were used in combination with insulin, especially in patients with risk factors for development of congestive heart failure. This should be kept in mind if treatment with the combination of thiazolidinediones and insulin medicinal products is considered. If the combination is used, patients should be observed for signs and symptoms of congestive heart failure, weight gain and oedema. Thiazolidinediones should be discontinued if any deterioration in cardiac symptoms occurs.

Avoidance of accidental mix-ups/medication errors

Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between Actrapid/Protaphane/Mixtard 30/70/Mixtard 50/50 and other insulin products.

Use in renal and hepatic impairment

Renal or hepatic impairment may reduce the patient's insulin requirements.

Renal or hepatic impairment, or concomitant diseases in the kidney or liver or affecting the adrenal, pituitary or thyroid gland, can require changes in the insulin dose.

Use in the elderly

Data were not assessed as part of this medicine registration.

Paediatric use

Data were not assessed as part of this medicine registration.

Effects on laboratory tests

Data were not assessed as part of this medicine registration.

4.5 Interactions with Other Medicines and Other Forms of Interactions

A number of drugs are known to interact with glucose metabolism. The physician must therefore take possible interactions into account.

The following substances may reduce the patient's insulin requirements: oral hypoglycaemic agents (OHAs), octreotide, lanreotide, monoamine oxidase inhibitors (MAOIs), non-selective beta-adrenergic blocking agents, angiotensin converting enzyme (ACE) inhibitors, salicylates,

alcohol, anabolic steroids (except danazol and oxymetholone), alpha-adrenergic blocking agents, quinine, quinidine and sulphonamides.

The following substances may increase the patient's insulin requirements: oral contraceptives, thiazides, frusemide, ethacrynic acid diuretics, glucocorticoids, thyroid hormones, sympathomimetics, octreotide, lanreotide, growth hormone, diazoxide, asparaginase, nicotinic acid, oxymetholone and danazol.

Beta blocking agents may mask the symptoms of hypoglycaemia and delay recovery from hypoglycaemia.

Alcohol may intensify and prolong, or reduce, the hypoglycaemic effect of insulin.

Hypoglycaemia in the presence of concomitant use of a beta-adrenergic blocking agent may precipitate a hypertensive crisis.

4.6 Fertility, Pregnancy and Lactation

Effects on fertility
Data were not assessed as part of this medicine registration.

Use in pregnancy
Pregnancy Category: Uncategorised

It is essential to maintain continuous good control of insulin-requiring diabetes throughout pregnancy. There are no restrictions on the treatment of diabetes with insulin during pregnancy as insulin does not pass the placental barrier.

Both hypoglycaemia and hyperglycaemia, which occur with inadequately controlled diabetes therapy, increase the risk of malformations and death *in utero*.

Intensified treatment and monitoring of pregnant women with diabetes is recommended throughout pregnancy and when contemplating pregnancy. Insulin requirements usually fall in the first trimester and increase subsequently during the second and third trimesters. After delivery, insulin requirements normally return rapidly to pre-pregnancy levels, leading to the risk of hypoglycaemia if the patient's insulin dose is not adjusted. Blood glucose levels should be monitored closely during the post-partum period and the patient's insulin dose adjusted accordingly

Use in lactation
There are no restrictions on treatment of diabetes with insulin during lactation. Insulin treatment of the nursing mother should not affect the baby. However the insulin dosage, or diet, or both, may need to be reduced.

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. People should be advised to take precautions to avoid hypoglycaemia whilst driving or operating machinery. 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 or operating machinery should be considered in these circumstances.

4.8 Adverse Effects (Undesirable Effects)

Post Marketing data:
Hypoglycaemia is a frequently occurring undesirable effect of insulin therapy. It may occur if the insulin dose is too high in relation to the insulin requirement. Symptoms of hypoglycaemia usually occur suddenly. They may include cold sweats, cool pale skin, nervousness or tremor, anxious feeling, unusual tiredness or weakness, confusion, difficulty in concentration, drowsiness, excessive hunger, temporary vision changes, headache, nausea and palpitations. Severe hypoglycaemia may lead to unconsciousness and/or convulsions and may result in temporary or permanent impairment of brain function or even death.

Oedema and refraction anomalies may occur upon initiation of insulin therapy. These symptoms are usually transitory in nature.

Fast improvement in blood glucose control may be associated with acute painful neuropathy, which is usually reversible.

Intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy.

Lipodystrophy is reported as uncommon. Lipodystrophy (including lipohypertrophy, lipoatrophy) and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions (see Section 4.4 Special Warnings and Precautions for Use).

As with any insulin therapy, injection site reactions may occur and include pain, redness, itching, hives, bruising, swelling and inflammation. Continuous rotation of the injection site within a given area may help to reduce these reactions. Reactions usually resolve in a few days to a few weeks. On rare occasions, injection site reactions may require discontinuation of a particular brand or brands of insulin.

Local hypersensitivity reactions (redness, swelling and itching at the injection site) may occur during treatment with insulin. These reactions are usually transitory and normally they disappear during continued treatment.

Generalised hypersensitivity reactions may rarely occur. Generalised hypersensitivity reactions are potentially life threatening.

Hypersensitivity and Skin
Uncommon: lipodystrophy
Rare: hypersensitivity reactions
Not known: cutaneous amyloidosis (see description above).

Endocrine
Rare: insulin resistance

Reporting Suspected Adverse Effects
Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare

professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 Overdose

A specific overdose of insulin cannot be defined, however, hypoglycaemia may develop over sequential stages if doses are administered which are too high relative to the patient's requirements:

- Mild hypoglycaemic episodes can be treated by oral administration of glucose or sugary products. It is therefore recommended that the person with diabetes always carry products containing sugar with them.
- Severe hypoglycaemic episodes, where the patient has become unconscious, can be treated by glucagon (0.5 to 1 mg) given intramuscularly or subcutaneously by a trained person or glucose given intravenously by a medical professional. Glucose must also be given intravenously if the patient does not respond to glucagon within 10 to 15 minutes.

  Upon regaining consciousness, oral administration of carbohydrate is recommended for the patient in order to prevent relapse.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Mechanism of action
Insulin lowers blood glucose levels by binding to insulin receptors to increase glucose uptake and inhibit hepatic glucose output.

In clinical practice the duration of insulin action may be shorter or longer than the duration specified below. Variations between and within patients may occur depending upon injection site and technique, insulin dosage, diet and exercise.

Actrapid is a short-acting insulin preparation. Its hypoglycaemic effect after subcutaneous administration begins after approximately 0.5 hour, is maximal between 2.5 and 5 hours, and terminates after approximately 8 hours.

Protaphane is an intermediate-acting insulin preparation. Its hypoglycaemic effect after subcutaneous administration begins after approximately 1.5 hours, is maximal between 4 and 12 hours, and lasts up to approximately 24 hours.

Mixtard 30/70 is an intermediate-acting insulin preparation. Its hypoglycaemic effect after subcutaneous administration begins after approximately 0.5 hour, is maximal between 2 and 12 hours and terminates after approximately 24 hours. Mixtard 30/70 is not exactly equivalent to its component insulins.

Mixtard 50/50 is an intermediate-acting insulin preparation. Its hypoglycaemic effect after subcutaneous administration begins after approximately 0.5 hour, is maximal between 4 and 8 hours and terminates after approximately 24 hours. Mixtard 50/50 is not exactly equivalent to its component insulins.

Clinical trials
Data were not assessed as part of this medicine registration.

5.2 Pharmacokinetic Properties

Data were not assessed as part of this medicine registration.

5.3 Preclinical Safety Data

Genotoxicity
Data were not assessed as part of this medicine registration.

Carcinogenicity
Data were not assessed as part of this medicine registration.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Refer to Section 2. Qualitative and Quantitative Composition.

6.2 Incompatibilities

Insulin should only be added to compounds with which it has known compatibility. Drugs added to the insulin solution may cause degradation of the insulin, e.g. if the drugs contain thiols or sulphites. Upon mixing Actrapid with infusion fluids an unpredictable amount of insulin will be adsorbed to the infusion material. Monitoring of the patient's blood glucose during infusion is therefore recommended.

Insulin suspensions should not be added to infusion fluids.

6.3 Shelf Life

The shelf life is 30 months when stored between 2°C and 8°C.

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special Precautions for Storage

Storage Conditions

Before opening:
Insulin preparations should be stored between 2°C and 8°C (in a refrigerator), not in or near the freezing compartment. Do not freeze. Insulin preparations which have been frozen must not be used. Insulin preparations should be protected from excessive heat and light. When not in use, the product should be kept in the carton, or stored with its cap on (prefilled devices only), to protect the insulin from light.

Insulin solutions should not be used if they do not appear water-clear and colourless.Insulin suspensions should not be used if they do not appear uniformly white and cloudy after suspension.

During use or when carried as a spare:
Vial: Store at room temperature (below 25°C) for up to 4 weeks.

Penfill and InnoLet: Store at room temperature (below 25°C) for up to 4 weeks.

Insulin products should not be exposed to excessive heat or light. Keep the product in the carton (vial, Penfill) or keep the cap on (InnoLet) when not in use, to protect it from light.

6.5 Nature and Contents of Container

Insulin (rys) 100 IU/mL

Penfill 3 mL
Penfill cartridges are made of glass, contain a rubber piston and are closed with a rubber disc. The insulin suspension cartridges contain a glass ball to facilitate resuspension. Five cartridges are packed in a carton.

Actrapid Penfill 3 mL, Protaphane Penfill 3 mL, Mixtard 30/70 Penfill 3 mL, Mixtard 50/50 Penfill 3 mL.

InnoLet 3 mL
Insulin delivery device containing a 3 mL cartridge. The cartridge is made of glass, contains a rubber piston and is closed with a rubber disc. Five prefilled insulin delivery devices are packed in a carton. The device is made of plastic and is disposable.

Protaphane InnoLet 3 mL, Mixtard 30/70 InnoLet 3 mL.

10 mL Vial
The 10 mL glass vial is closed with a rubber disc. One vial is packed in a carton.

Actrapid, Protaphane 10 mL vial.

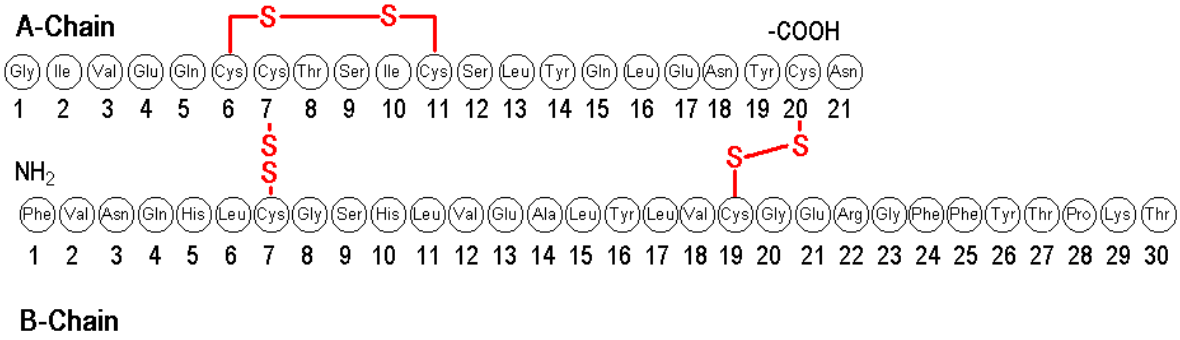
Not all presentations are marketed in Australia.

6.6 Special Precautions for Disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical Properties

Chemical structure
Insulin (rys) is characterised by being identical to natural human insulin. Insulin has the empirical formula $C_{257}H_{383}N_{65}O_{77}S_6$ and a molecular weight of 5808.



CAS number
11061-68-0

7. MEDICINE SCHEDULE (POISONS STANDARD)

S4

8. SPONSOR

Novo Nordisk Pharmaceuticals Pty Ltd
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www.novonordisk.com.au

9. DATE OF FIRST APPROVAL

28 April 2011

10. DATE OF REVISION

18 July 2023

Summary table of changes

Section Changed	Summary of new information
2	Deletion of cancelled ARTG entries (FlexPen range and Actrapid InnoLet).
4.2	Deletion of cancelled ARTG entries (FlexPen range and Actrapid InnoLet).
6.4	Deletion of cancelled ARTG entries (FlexPen range and Actrapid InnoLet).
6.5	Deletion of cancelled ARTG entries (FlexPen range and Actrapid InnoLet).
8	Update of sponsors address