PROFESSIONAL INFORMATION FOR RYZODEG®

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

Ryzodeg® solution for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ryzodeg®

Each mL contains:

Insulin degludec*/insulin aspart* (70 % soluble insulin degludec and 30 % soluble insulin aspart)

100 units/mL (equivalent to salt-free anhydrous insulin degludec 2,56 mg and salt-free anhydrous insulin aspart 1,05 mg).

Excipients with known effect:

Preservatives

Phenol 0,150 % *m/v*

Metacresol 0,172 % *m/v*

Ryzodeg® 100 units/mL pre-filled pen/cartridge contains 3 mL equivalent to 300 units.

*Insulin degludec and *insulin aspart are produced by recombinant DNA technology in *Saccharomyces cerevisiae.*

Sugar free.

For the full list of excipients, see section 6 .1.

3. PHARMACEUTICAL FORM

Solution for injection.

Ryzodeg® is a colourless solution, free from turbidity and particulate matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications:

- Treatment of adult diabetes mellitus patients, as basal add on to co-medication in patients who are inadequately controlled:
  - In type 1 diabetes mellitus, Ryzodeg® should be used with short-acting soluble insulin for use at the meal times when Ryzodeg® is not used.
  - In type 2 diabetes mellitus, Ryzodeg® should be used as an add on to oral antidiabetic medicines.
- Treatment of diabetes mellitus in adults, adolescents and children from the age of 2 years.

4.2 Posology and method of administration:

Ryzodeg® can be administered once- or twice-daily with the main meal(s). When needed, the patient can change the time of administration as long as Ryzodeg® is dosed with a main meal. The potency of insulin analogues, including Ryzodeg®, is expressed in units (U). 1 unit (U) Ryzodeg® corresponds to 1 international unit (IU) of human insulin and one unit of all other insulin analogues.

In patients with type 2 diabetes mellitus, Ryzodeg® can be combined with oral anti-diabetic products approved for use with insulin, with or without bolus insulin (see section 5). When using Ryzodeg® once-daily, it is recommended to consider changing to twice daily when reaching 60 units. Split the dose based on individual patient's needs and administer with main meals.
In type 1 diabetes mellitus, Ryzodeg® is combined with short-/rapid-acting insulin at the remaining meals.

Ryzodeg® is to be dosed in accordance with individual patients' needs. Dose-adjustments are recommended to be primarily based on pre-breakfast glucose measurements.

An adjustment of dose may be necessary if patients undertake increased physical activity,

change their usual diet or during concomitant illness.

Initiation

For patients with type 2 diabetes mellitus, the recommended total daily starting dose of Ryzodeg® is 10 units once daily with meal followed by individual dosage adjustments.
For patients with type 1 diabetes mellitus, Ryzodeg® is to be used once-daily at mealtime and a short-/rapid-acting insulin should be used at the remaining meals with individual dosage adjustments. The recommended starting dose of Ryzodeg® is 60 – 70 % of the total daily insulin requirements.

Transfer from other insulin medicines

Close glucose monitoring is recommended during transfer and in the following weeks.

Patients with type 2 diabetes:

Patients switching from once-daily basal or premix insulin therapy can be converted unit-to-unit to once- or twice daily Ryzodeg® at the same total insulin dose as the patient's previous total daily insulin dose.

Patients switching from more than once-daily basal or premix insulin therapy can be converted unit-to-unit to once- or twice-daily Ryzodeg® at the same total insulin dose as the patient's previous total daily insulin dose.

Patients switching from basal/bolus insulin therapy to Ryzodeg® will need to convert their dose based on individual needs. In general, patients are initiated on the same number of basal units.

Doses and timing of concomitant antidiabetic treatment may need to be adjusted.

Patients with type 1 diabetes:

For patients with type 1 diabetes mellitus, the recommended starting dose of Ryzodeg® is 60 – 70 % of the total daily insulin requirements in combination with short-/rapid-acting insulin at the remaining meals followed by individual dosage adjustments.

Doses and timing of concurrent short-/rapid-acting insulin products may need to be adjusted.

Flexibility

Ryzodeg® allows for flexibility in the timing of insulin administration as long as it is dosed with the main meal(s). If a dose of Ryzodeg® is missed, the patient can take the next dose with the next main meal of that day and thereafter resume the usual dosing schedule. Patients should not take an extra dose to make up for a missed dose.

Ryzodeg® should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Special population

Elderly

Ryzodeg® can be used in elderly patients. Glucose monitoring is to be intensified and the insulin dose adjusted on an individual basis (see section 5).

Renal and hepatic impairment

Ryzodeg® can be used in renal and hepatic impaired patients. Glucose monitoring is to be intensified and the insulin dose adjusted on an individual basis (see section 5).

Paediatric population

Ryzodeg® can be used in adolescents and children from the age of 2 years (see section 5).

When changing from another insulin regimen to Ryzodeg®, dose reduction of total insulin needs to be considered on an individual basis in order to minimise the risk of hypoglycaemia (see section 4.4).

Ryzodeg® should be used with special caution in children 2 to 5 years old because data from the clinical trial indicate that there may be a higher risk for severe hypoglycaemia in children in this age group (see section 4.4).

Method of administration

Ryzodeg® is for subcutaneous administration only.

Ryzodeg® must not be administered intravenously as it may result in severe hypoglycaemia. Ryzodeg® must not be administered intramuscularly as it may change the absorption. Ryzodeg® must not be used in insulin infusion pumps.

Ryzodeg® is administered subcutaneously by injection in the abdominal wall, the upper arm or the thigh. Injection sites are always to be rotated within the same region in order to reduce the risk of lipodystrophy.

Avoidance of accidental mix-ups

To avoid accidental mix-ups between Ryzodeg® and other insulin products, patients must be instructed to always check the label for the right type of insulin before each injection.

Patients must visually verify the dialled units on the dose counter of the pen. Therefore, the requirement for patients to self-inject is that they can read the dose counter on the pen. Patients who are blind or have poor vision must be instructed to always get help/assistance from another person who has good vision and is trained in using the insulin device.

To avoid dosing errors and potential overdose, patients and health care professionals should never use a syringe to draw the medicine from the cartridge in the pre-filled pen.

In the event of blocked needles, patients must follow the instructions described in the

instructions for use.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients. Also refer to section 4.8 and section 4.4.
- Pregnancy (see section 4.6)

4.4 Special warnings and precautions for use

Hypoglycaemia

Omission of a meal or unplanned strenuous physical exercise may lead to hypoglycaemia. Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement (see section 4.8 and section 4.9).

Severe hypoglycaemia may lead to unconsciousness and/or convulsions and may result in temporary or permanent impairment of brain function or even death. The symptoms of hypoglycaemia usually occur suddenly. They may include cold sweats, cool pale skin, fatigue, nervousness or tremor, anxiousness, unusual tiredness or weakness, confusion, difficulty in concentration, drowsiness, excessive hunger, vision changes, headache, nausea and palpitation.

In children, extra care should be taken to match insulin doses with food intake and physical activities in order to minimise the risk of hypoglycaemia.

Ryzodeg® may be associated with higher occurrence of severe hypoglycaemia compared to a basal-bolus regimen in the paediatric population, particularly in children 2 to 5 years old. For this age group, Ryzodeg® should be considered on an individual basis.

Patients whose blood glucose control is improved (e.g. by intensified insulin therapy) may experience a decreased sensitivity to usual warning symptoms of hypoglycaemia and must be advised accordingly. Usual warning symptoms may be altered in patients with long-standing

diabetes.

Concomitant illness, especially infections and fever, may increase the patient's insulin requirement. Concomitant diseases in the kidney, liver or diseases affecting the adrenal, pituitary or thyroid gland may require changes in the insulin dose.
The prolonged effect of Ryzodeg® may delay recovery from hypoglycaemia.

Hyperglycaemia
Ryzodeg® should not be used to treat severe hyperglycaemia.
Administration of rapid-acting insulin is recommended in situations with severe hyperglycaemia. Inadequate dosing and/or discontinuation of treatment in patients requiring insulin may lead to hyperglycaemia and potentially to diabetic ketoacidosis. Furthermore, concomitant illness, especially infections, may lead to hyperglycaemia and thereby cause an increased insulin requirement.
Usually, the first symptoms of hyperglycaemia develop gradually over a period of hours or days. They include thirst, increased frequency of urination, nausea, vomiting, drowsiness, flushed dry skin, dry mouth, and loss of appetite as well as acetone odour of breath. In type 1 diabetes, untreated hyperglycaemic events eventually lead to diabetic ketoacidosis, which is potentially lethal.

Transfer from other insulin products:
Transferring a patient to another type, brand, or manufacturer of insulin must be done under medical supervision and may result in the need for change in dosage.

Combination of thiazolidinediones (TZDs) and Ryzodeg®:
Cases of congestive heart failure have been reported when thiazolidinediones (also known as glitazones) 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 Ryzodeg® is considered. If the combination is used, patients should be observed for signs and symptoms of congestive heart failure, weight gain and oedema. Thiazolidinediones must be discontinued if any signs of deterioration in cardiac function occur.

Insulin antibodies

Ryzodeg® administration may cause insulin antibodies to form. In rare cases, the presence of such insulin antibodies may necessitate adjustment of the insulin dose in order to correct a tendency to hyper- or hypoglycaemia.

Immune system disorders:

With Ryzodeg® allergic reactions may occur. Immediate-type allergic reactions to either insulin itself or the excipients may potentially be life threatening.

With Ryzodeg®, hypersensitivity (manifested with swelling of tongue and lips, diarrhoea, nausea, tiredness and itching) and urticaria were reported with rare frequency.

Skin and subcutaneous tissue disorders:

Patients must be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy (including lipohypertrophy, lipoatrophy) 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.

Injection site reactions:

Injection site reactions (including injection site haematoma, pain, haemorrhage, erythema, nodules, swelling, discolouration, pruritus, warmth and injection site mass) occurred in patients

treated with Ryzodeg®.

Paediatric population:

Ryzodeg® has been administered to children and adolescents for the investigation of pharmacokinetic properties (see section 5).

Safety and efficacy have been demonstrated in a trial in children aged 2 to less than 18 years. The frequency, type and severity of adverse reactions in the paediatric population do not indicate differences to the experience in the general diabetes population with the exception of a signal of higher occurrence of severe hypoglycaemia compared to a basal-bolus regimen in the paediatric population, particularly in children 2 to 5 years old (see section 5).

Other special populations:

Based on results from clinical trials, the frequency, type and severity of adverse reactions observed in the elderly patients and in patients with renal or hepatic impairment do not indicate any differences to the broader experience in the general population.

Insulin initiation and glucose control intensification:

Intensification or rapid improvement in glucose control has been associated with transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy, and acute painful peripheral neuropathy. However, long-term glycaemic control decreases the risk of diabetic retinopathy and neuropathy.

Sodium:

Ryzodeg® contains less than 1 mmol sodium (23 mg) per dose, that is to say it is essentially sodium-free.

4.5 Interaction with other medicines and other forms of interaction

Combination with thiazolidinediones (TZDs):

Please refer to section 4.4 for the possible development of congestive heart failure.

A number of medicines are known to interact with glucose metabolism.

The following substances may reduce the insulin requirement:

Oral antidiabetic medicines, Glucagon-like peptide-1 (GLP-1) receptor agonists, monoamine oxidase inhibitors (MAOI), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids and sulphonamides.

The following substances may increase the insulin requirement:

Oral contraceptive, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormones and danazol.

Beta-blocking medicines may mask the symptoms of hypoglycaemia and may reduce the body's response to hypoglycaemia.

Octreotide and lanreotide may either increase or decrease the insulin requirement.

Alcohol may intensify or reduce the hypoglycaemic effect of insulin.

4.6 Fertility, pregnancy and lactation

Safety has not been established in pregnancy and lactation and Ryzodeg® should not be recommended for use during pregnancy (see section 4.3).

It is unknown whether insulin degludec is excreted in human milk.

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 must be advised to take precautions to avoid hypoglycaemia while 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.

4.8 Undesirable effects

Summary of the safety profile:

More than 2 000 patients have been exposed to Ryzodeg® in the clinical development programme. The most frequently reported adverse reaction during treatment is hypoglycaemia (see table below).

Tabulated list of adverse reactions

Adverse reactions listed below are based on clinical trial data. Frequency categories are defined according to the following convention: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000); not known (cannot be estimated from the available data).

System organ class	**Preferred term**	**Frequency**
Immune system disorders	Hypersensitivity	0,04 % (rare)
	Urticaria	0,04 % (rare)
Metabolism and nutrition disorders	Hypoglycaemia	95 % in subjects with type 1 diabetes 44,2 % - 57,7 % in subjects with type 2 diabetes, using Ryzodeg® o.d. 61,2 % - 73,5 % in subjects with type 2 diabetes, using Ryzodeg® b.i.d. (very common)
Skin and subcutaneous tissue disorders	Lipodystrophy	0,0 % (not known)

General disorders and administration site conditions	Injection site reactions	1,1 % (common)
	Peripheral oedema	0,4 % (uncommon)

Adverse reactions from post-marketing experience:

System organ class	Preferred term	Frequency
Skin and subcutaneous tissue disorders	Cutaneous amyloidosis	Not known.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of Ryzodeg® is important. It allows continued monitoring of the benefit/risk balance of Ryzodeg®. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

A specific overdose cannot be defined. However, hypoglycaemia may develop over sequential stages if a patient is dosed with more insulin than required. (See section 4.4).

- Mild hypoglycaemic episodes can be treated by oral administration of glucose or other products containing sugar. It is therefore recommended that the patient always carries glucose-containing products.
- Severe hypoglycaemic episodes, where the patient is not able to treat himself, can be treated with glucagon (0,5 to 1 mg) given intramuscularly or subcutaneously by a trained person or with glucose given intravenously by a healthcare professional. Glucose must be given intravenously, if the patient does not respond to glucagon within 10 to 15 minutes. Upon regaining consciousness, administration of oral carbohydrates is recommended for the patient in order to prevent a relapse.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 21.1 Insulin Preparations

Pharmacotherapeutic group: Drugs used in diabetes. Insulins and analogues for injection, intermediate or long-acting combined with fast-acting

ATC code: A10AD06

Insulin degludec/insulin aspart is a soluble insulin product consisting of insulin degludec (ultra-long-acting basal insulin) and insulin aspart (rapid-acting meal-time insulin), administered in one injection.

Insulin degludec and insulin aspart bind specifically to the human insulin receptor and result in the same pharmacological effects as human insulin.
The blood glucose-lowering effect of insulin is due to the facilitated uptake of glucose following the binding of insulin to receptors on muscle and fat cells and to the simultaneous inhibition of glucose output from the liver.

The pharmacodynamic effect of insulin degludec/insulin aspart is distinctively separated for the two components (Figure 1) and the resulting action profile reflects the individual components, the rapid-acting insulin aspart and the ultra-long-acting insulin degludec.

This effect is maintained in the co-formulation with insulin aspart and does not interfere with the rapid-acting insulin aspart monomers.
The duration of action of a single-dose of insulin degludec/insulin aspart is beyond 24 hours.

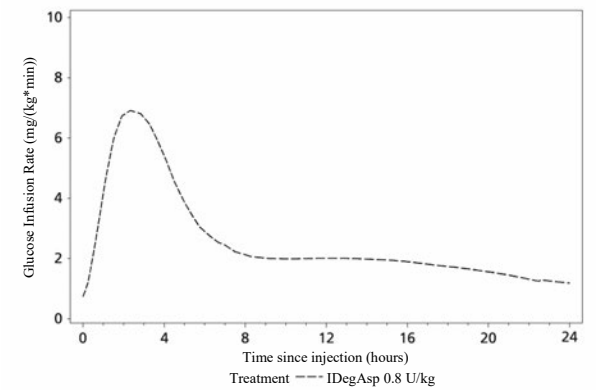


Figure 1 Glucose infusion rate mean profile of insulin degludec/insulin aspart after single dose administration of 0,8 U/kg in type 1 diabetes mellitus

The total and maximum-glucose-lowering effects of insulin degludec/insulin aspart increase linearly with increasing doses. Steady state will occur after 2 – 3 days of dose administration.

There is no difference in the pharmacodynamic effect of insulin degludec/insulin aspart between elderly and younger adult subjects.

There is no clinically relevant development of insulin antibodies after long-term treatment with insulin degludec/insulin aspart.

Paediatric population

The efficacy and safety of Insulin degludec/insulin aspart have been studied in a randomised, controlled clinical trial in children and adolescents with diabetes mellitus type 1 for a period of 16 weeks (n=362). Patients in the Insulin degludec/insulin aspart arm included 40 exposed children aged 2 – 5 years, 61 children aged 6 – 11 years and 80 adolescents aged 12 – 17 years. Insulin degludec/insulin aspart dosed once daily with the main meal plus insulin aspart for the remaining meals showed similar reduction in HbA1c at week 16 and no differences in FPG and SMPG compared to comparator insulin detemir dosed once or twice daily plus mealtime insulin aspart. At week 16, the mean total daily insulin dose was 0,88 vs 1,01 units/kg in the Insulin

degludec/insulin aspart and insulin detemir arms, respectively. The rates (events per patient-year of exposure) of confirmed hypoglycaemia (ISPAD 2009 definition: 46,23 vs 49,55) and nocturnal confirmed hypoglycaemia (5,77 vs 5,40) were comparable with Insulin degludec/insulin aspart versus insulin detemir whereas the rate of severe hypoglycaemia (0,26 vs 0,07) was higher in the Insulin degludec/insulin aspart arm although the difference was not statistically significant. Few severe hypoglycaemic episodes were reported in each group; the observed rate of severe hypoglycaemia within the Insulin degludec/insulin aspart arm was higher for subjects aged 2 – 5 years compared to subjects aged 6 – 11 years or 12 – 17 years (0,42 vs 0,21 and 0,21, respectively).

Efficacy and safety evaluation for adolescent patients with type 2 diabetes mellitus has been made using data from adolescent and adult patients with type 1 diabetes mellitus and adult patients with type 2 diabetes mellitus. This assessment supports the use of Insulin degludec/insulin aspart in adolescent patients with type 2 diabetes mellitus.

5.2 Pharmacokinetic properties

Absorption

Insulin degludec monomers gradually separate from the multi-hexamers resulting in a slow and continuous delivery of insulin degludec into the circulation. Steady state serum concentration of the ultra-long-acting component (insulin degludec) is reached after 2 – 3 days of daily insulin degludec/insulin aspart administration.

The rapid absorption characteristics of the insulin aspart are maintained by the co-formulation. The pharmacokinetic profile for insulin aspart appears 14 minutes after injection with a peak concentration after 72 minutes.

Distribution

The affinity of insulin degludec to serum albumin corresponds to a plasma protein binding of > 99 % in human plasma. Insulin aspart has a low binding to plasma proteins (< 10 %), similar to that seen with regular human insulin.

Biotransformation

Degradation of insulin degludec and insulin aspart is similar to that of human insulin; all metabolites formed are inactive.

Elimination

The half-life after subcutaneous administration of insulin degludec/insulin aspart is determined by the rate of absorption from the subcutaneous tissue. The half-life of the basal component (insulin degludec) at steady state is 25 hours independent of dose.

Linearity

Total exposure with insulin degludec/insulin aspart increases proportionally with increasing dose of the basal component (insulin degludec) and the mealtime component (insulin aspart) in type 1 and type 2 diabetes mellitus.

Elderly, renal and hepatic impairment

There are no clinical relevant differences in the pharmacokinetics of insulin degludec/insulin aspart between elderly and younger adult subjects, or between healthy subjects and patients with renal or hepatic impairment.

Paediatric population

The pharmacokinetic properties of insulin degludec/insulin aspart in type 1 diabetes mellitus were investigated in children (6 – 11 years) and adolescents (12 – 18 years) and compared to adults after single dose administration.

The steady state pharmacokinetics properties of the insulin degludec component of Insulin degludec/insulin aspart were investigated using population pharmacokinetic analysis in children down to 1 year of age.

Total exposure and peak concentration of insulin aspart were higher in children than in adults

and were similar for adolescents and adults.

The pharmacokinetic properties of insulin degludec in children (1 – 11 years) and adolescents (12 – 18 years) were at steady state comparable to those observed in adults with type 1 diabetes mellitus.

Total exposure of insulin degludec after single dose administration was higher in children and adolescents than in adults with type 1 diabetes mellitus.

5.3 Preclinical safety data

Non-clinical data reveal no safety concerns for humans based on studies of safety pharmacology, repeated dose toxicity, carcinogenic potential, and toxicity to reproduction.
The ratio of mitogenic relative to metabolic potency for insulin degludec is comparable to that of human insulin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol (E422),
hydrochloric acid (for pH adjustment) (E507),
phenol (preservative),
metacresol (preservative),
sodium chloride,
sodium hydroxide (for pH adjustment) (E524),
zinc acetate (E650), and
water for injections.

6.2 Incompatibilities

Substances added to Ryzodeg® may cause degradation of insulin degludec and/or insulin

aspart.

Ryzodeg® must not be added to infusion fluids.

Ryzodeg® must not be mixed with other medicines.

6.3 Shelf life

30 months.

In-use or carried as a spare:

Ryzodeg® FlexTouch®:

Store at or below 30 °C.

Can be stored in a refrigerator (2 °C – 8 °C).

Keep the cap on when Ryzodeg® is not in use in order to protect from light.

Ryzodeg® Penfill®:

Do not refrigerate. Store at or below 30 °C.

Keep cartridges in the outer carton in order to protect from light.

Ryzodeg® FlexTouch® and Ryzodeg® Penfill®: Ryzodeg® in-use or carried as a spare can be used for up to 4 weeks. Discard any unused portion after 4 weeks of use.

6.4 Special precautions for storage

Before use:

Store in a refrigerator (2 °C – 8 °C) but away from the freezing element. Do not freeze.

For storage conditions after first opening of Ryzodeg®, see section 6.3.

6.5 Nature and contents of container

Ryzodeg® FlexTouch®:

3 mL solution in a cartridge made of clear, colourless type 1 glass with a red plunger (halobutyl) and a cream stopper (halobutyl/polyisoprene) contained in a pre-filled multidose disposable pen

made of polypropylene. The pen(s) is/are packed in a carton box.

Pack sizes: 1 x 3 mL, 1 x 3 mL (including needle pack), 5 x 3 mL, multi-pack: 2 x (5 x 3 mL).

Ryzodeg® Penfill®:

3 mL solution in a cartridge made of clear, colourless type 1 glass with a red plunger (halobutyl) and a cream stopper (halobutyl/polyisoprene). The cartridge is packaged in press through blister pack made of aluminium foil and polyethylene terephthalate (PET). The blister is packed in a carton box.

Pack size: 5 x 3 mL.

6.6 Special precautions for disposal and other handling

Ryzodeg® must not be used if the solution does not appear clear and colourless.

Ryzodeg® which has been frozen must not be used.

Discard the needle after each injection.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Novo Nordisk (Pty) Ltd

150 Rivonia Road

10 Marion Street Office Park

Building C1

Sandton

Johannesburg 2196

8. REGISTRATION NUMBER

47/21.1/0165

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 18 February 2016

10. DATE OF REVISION OF THE TEXT

Date of revision: 10 August 2022

Instructions on how to use Ryzodeg® 100 units/mL solution for injection in pre-filled pen (FlexTouch®)

Please read these instructions carefully before using your FlexTouch® pre-filled pen. If you do not follow the instructions carefully, you may get too little or too much insulin, which can lead to too high or too low blood sugar level.

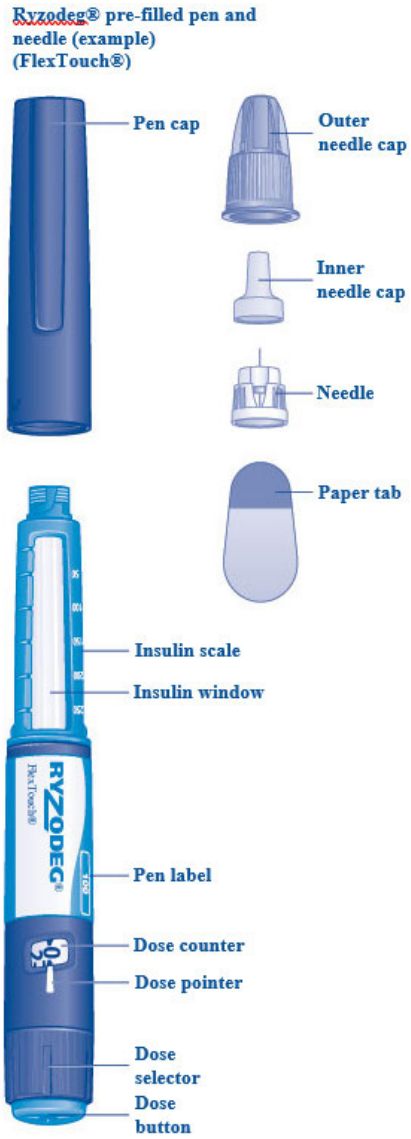
Do not use the pen without proper training from your doctor or nurse.
Start by checking your pen to **make sure that it contains Ryzodeg® 100 units/mL,** then look at the illustrations below to get to know the different parts of your pen and needle.

If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the FlexTouch® pre-filled pen.

Your pen is a pre-filled dial-a-dose insulin pen containing 300 units of insulin. You can select a **maximum of 80 units per dose, in steps of 1 unit.** Your pen is designed to be used with NovoTwist® or NovoFine® single-use disposable needles up to a length of 8 mm. Needles are not included in the pack.

⚠ Important information

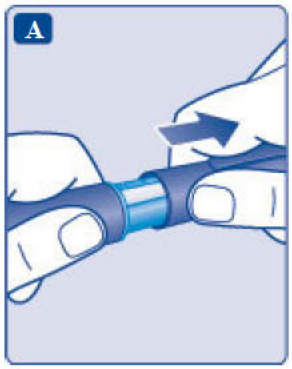
Pay special attention to these notes as they are important for correct use of the pen.



1. Prepare your pen

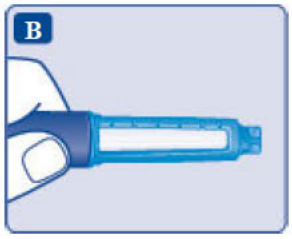
Check the name and strength on the label of your pen, to make sure that it contains Ryzodeg® 100 units/mL. This is especially important if you take more than one type of insulin. If you take a wrong type of insulin, your blood sugar level may get too high or too low.

Pull off the pen cap.

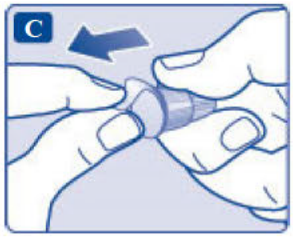


Check that the insulin in your pen is clear and colourless.

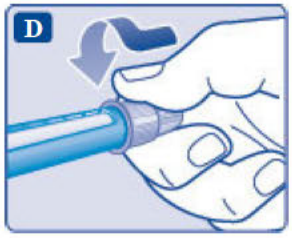
Look through the insulin window. If the insulin looks cloudy, do not use the pen.



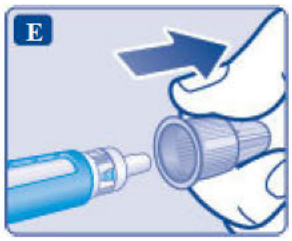
Take a new needle and tear off the paper tab.



Push the needle straight onto the pen. Turn until it is on tight.

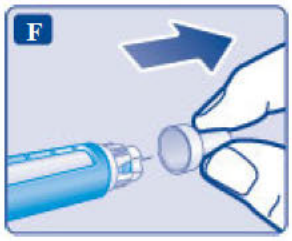


Pull off the outer needle cap and keep it for later. You will need it after the injection, to correctly remove the needle from the pen.



Pull off the inner needle cap and throw it away. If you try to put it back on, you may accidentally stick yourself with the needle.

A drop of insulin may appear at the needle tip. This is normal, but you must still check the insulin flow.



⚠ **Always use a new needle for each injection.**

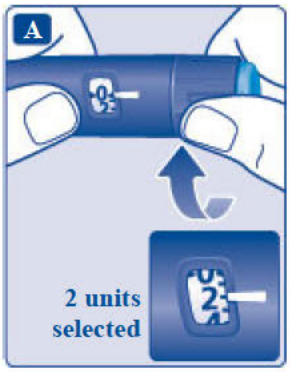
This reduces the risk of contamination, infection, leakage of insulin, blocked needles and inaccurate dosing.

⚠ **Never use a bent or damaged needle.**

2. Check the insulin flow

Always check the insulin flow before you start. This helps you to ensure that you get your full insulin dose.

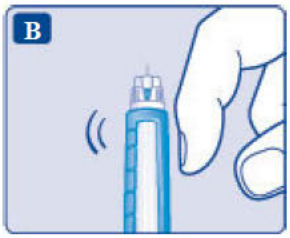
Turn the dose selector to **select 2 units. Make sure the dose counter shows 2.**



Hold the pen with the needle pointing up.

Tap the top of the pen gently a few times to let any air bubbles

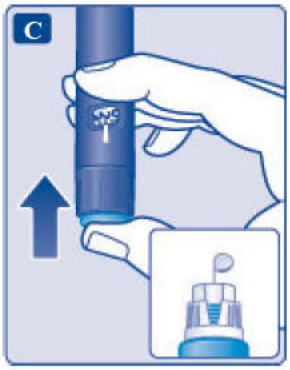
rise to the top.



Press and hold in the dose button until the dose counter returns to 0.

The 0 must line up with the dose pointer.

A drop of insulin should appear at the needle tip.



A small air bubble may remain at the needle tip, but it will not be injected.

If no drop appears, repeat steps 2**A** to 2**C** up to 6 times. If there is still no drop, change the needle and repeat steps 2**A** to 2**C** once more.

If a drop of insulin still does not appear, dispose of the pen and use a new one.

- ⚠ **Always make sure that a drop appears** at the needle tip before you inject. This makes sure that the insulin flows. If no drop appears, you will **not** inject any insulin, even though the dose counter may move.
- ⚠ **Always check the flow before you inject.** If you do not check the flow, you may get too little insulin or no insulin at all. This may lead to too high blood sugar level.

3. Select your dose

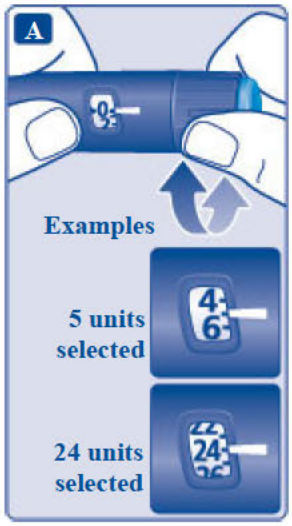
Make sure the dose counter shows 0 before you start.

The 0 must line up with the dose pointer.

Turn the dose selector to select the dose you need, as directed by your doctor or nurse.

If you select a wrong dose, you can turn the dose selector forwards or backwards to the correct dose.

The pen can dial up to a maximum of 80 units.



The dose selector changes the number of units. Only the dose counter and dose pointer will show how many units you select per dose.

You can select up to 80 units per dose. When your pen contains less than 80 units, the dose counter stops at the number of units left.

The dose selector clicks differently when turned forwards, backwards or past the number of units left. Do not count the pen clicks.

⚠ **Always use the dose counter and the dose pointer to see how many units you have selected before injecting the insulin.**

Do not count the pen clicks. If you select and inject the wrong dose, your blood sugar level may get too high or too low.

Do not use the insulin scale, it only shows approximately how much insulin is left in your pen.

4 Inject your dose Insert the needle into your skin as your doctor or nurse has shown you.

Make sure you can see the dose counter.

Do not touch the dose counter with your fingers. This could interrupt the injection.

Press and hold down the dose button until the dose counter returns to 0.

The 0 must line up with the dose pointer.

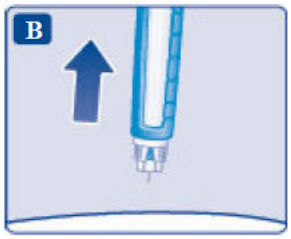
You may then hear or feel a click.

Leave the needle under the skin for at least 6 seconds to make sure you get your full dose.



Pull the needle and pen straight up from your skin.

If blood appears at the injection site, press lightly with a cotton swab. Do not rub the area.



You may see a drop of insulin at the needle tip after injecting. This is normal and does not affect your dose.

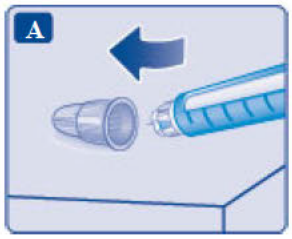
⚠ **Always watch the dose counter to know how many units you inject.**

The dose counter will show the exact number of units. Do not count the pen clicks.

Hold the dose button down until the dose counter returns to 0 after the injection. If the dose counter stops before it returns to 0, the full dose has not been delivered, which may result in too high blood sugar level.

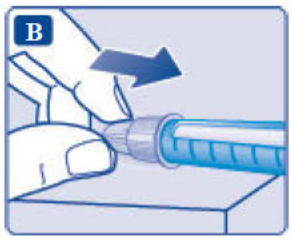
5 After your injection

Lead the needle tip into the outer needle cap on a flat surface without touching the needle or the outer cap.

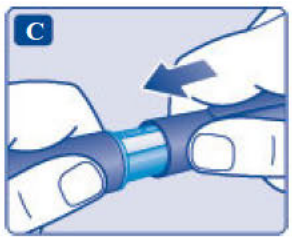


Once the needle is covered, **carefully push the outer needle cap completely on.**

Unscrew the needle and dispose of it carefully.



Put the pen cap on your pen after each use to protect the insulin from light.



Always dispose of the needle after each injection. This reduces the risk of contamination, infection, leakage of insulin, blocked needles and inaccurate dosing. If the needle is blocked, you will not inject any insulin.

When the pen is empty, throw it away **without** a needle on as instructed by your doctor, nurse, pharmacist or local authorities.

⚠ **Never try to put the inner needle cap back on the needle.**

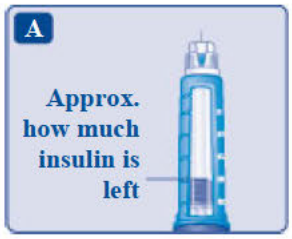
You may stick yourself with the needle.

⚠ **Always remove the needle from your pen after each injection.**

This may prevent blocked needles, contamination, infection, leakage of insulin, blocked needles and inaccurate dosing.

6. How much insulin is left?

The **insulin scale** shows you **approximately** how much insulin is left in your pen.

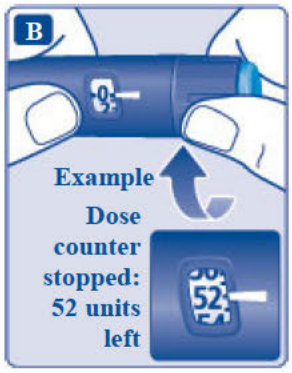


To see precisely how much insulin is left, use the dose counter:

Turn the dose selector until the **dose counter stops**.

If it shows 80, **at least 80** units are left in your pen.

If it shows **less than 80,** the number shown is the number of units left in your pen.



Turn the dose selector back until the dose counter shows 0.

If you need more insulin than the units left in your pen, you can split your dose between two pens.

⚠ Be very careful to calculate correctly if splitting your dose. If in doubt, take the full dose with a new pen. If you split the dose wrong, you will inject too little or too much insulin, which can lead to too high or too low blood sugar level.

⚠ **Further important information**

- **Always keep your pen with you.**
- **Always carry an extra pen and new needles** with you, in case of loss or damage.
- Always keep your pen and needles **out of sight and reach of others,** especially children.
- **Never share** your pen or your needles with other people. It might lead to cross-infection.
- **Never share** your pen with other people. Your medicine might be harmful to their health.
- Caregivers must **be very careful when handling used needles** – to prevent needle injury and cross-infection.

Caring for your pen

Treat your pen with care. Rough handling or misuse may cause inaccurate dosing, which can lead to too high or too low blood sugar level.

- **Do not leave the pen in a car** or other place where it can get too hot or too cold.
- **Do not expose your pen to dust, dirt or liquid.**
- **Do not wash, soak or lubricate your pen.** If necessary, clean it with mild detergent on a moistened cloth.
- **Do not drop your pen** or knock it against hard surfaces.

If you drop it or suspect a problem, attach a new needle and check the insulin flow before you inject.

- **Do not try to refill your pen.** Once empty, it must be disposed of.
- **Do not try to repair your pen** or pull it apart.