EXPERIENCE THE FREEDOM*

WITH A 2-IN-1 INSULIN CO-FORMULATION PROVIDING BASAL AND MEALTIME CONTROL[1-4]

Dosage Guide for Type 2 Diabetes

*with flexibility in dose timing when dosed with main meal(s)

This image is a model and not a real patient.

novo nordisk®

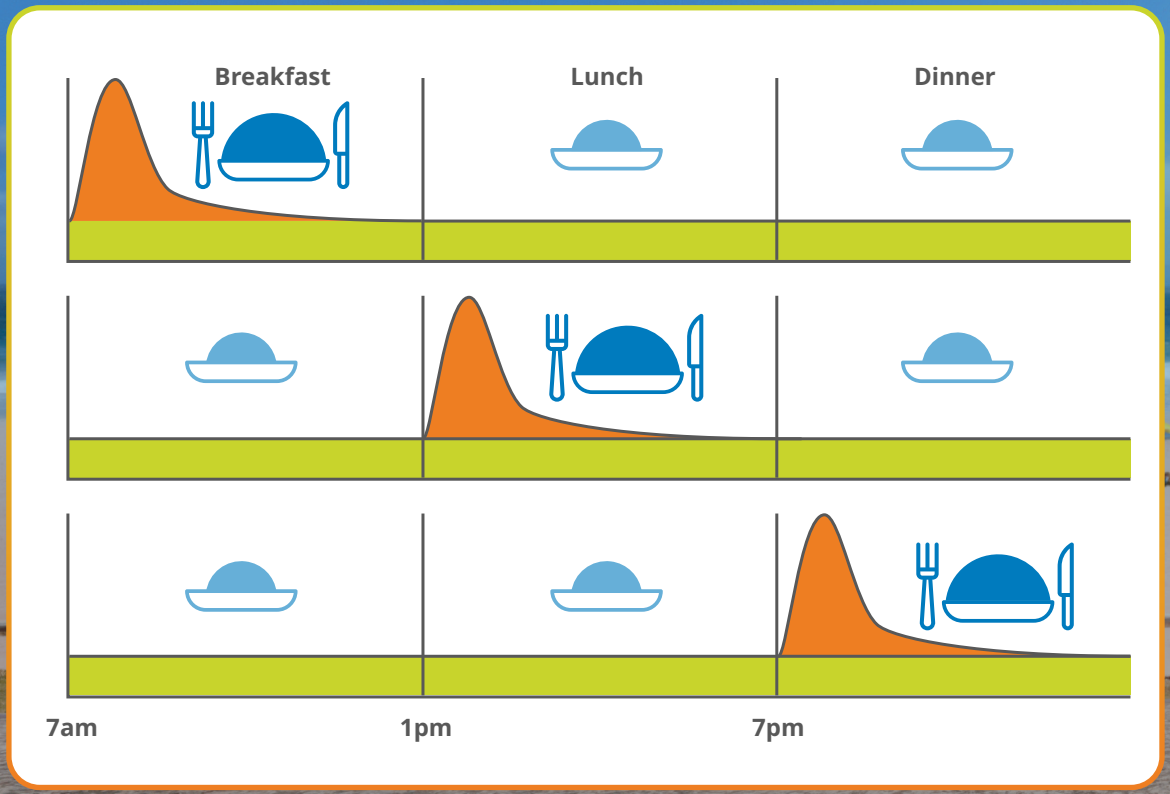
RYZODEG®

70% insulin degludec and 30% insulin aspart [rDNA origin] injection

Initiate once daily

Initiation of once-daily Ryzodeg® in Type 2 Diabetes

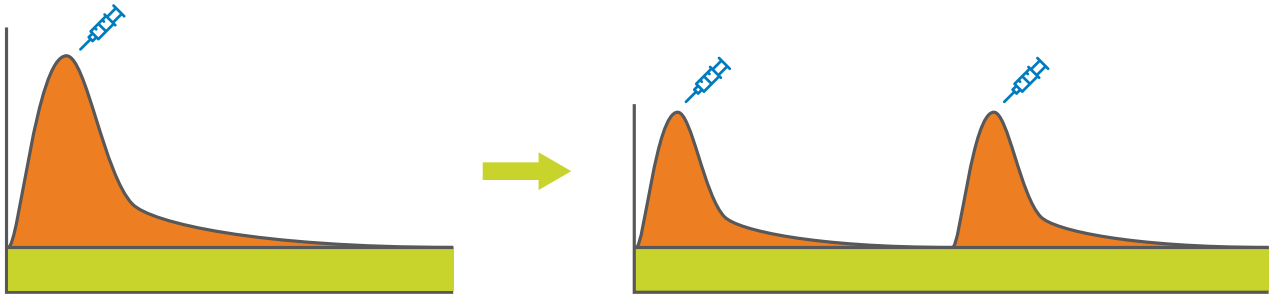
Ryzodeg® can be initiated at 10 units once daily at the time of the patient's largest carbohydrate meal[1,5]



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[1]

- **Once-daily Ryzodeg® to twice-daily Ryzodeg®[1]**

  If a patient's FPG is controlled, but HbA_{1c} is out of range (i.e. > 7%), it is recommended to split the current dose at the time of the two largest meals.[6]



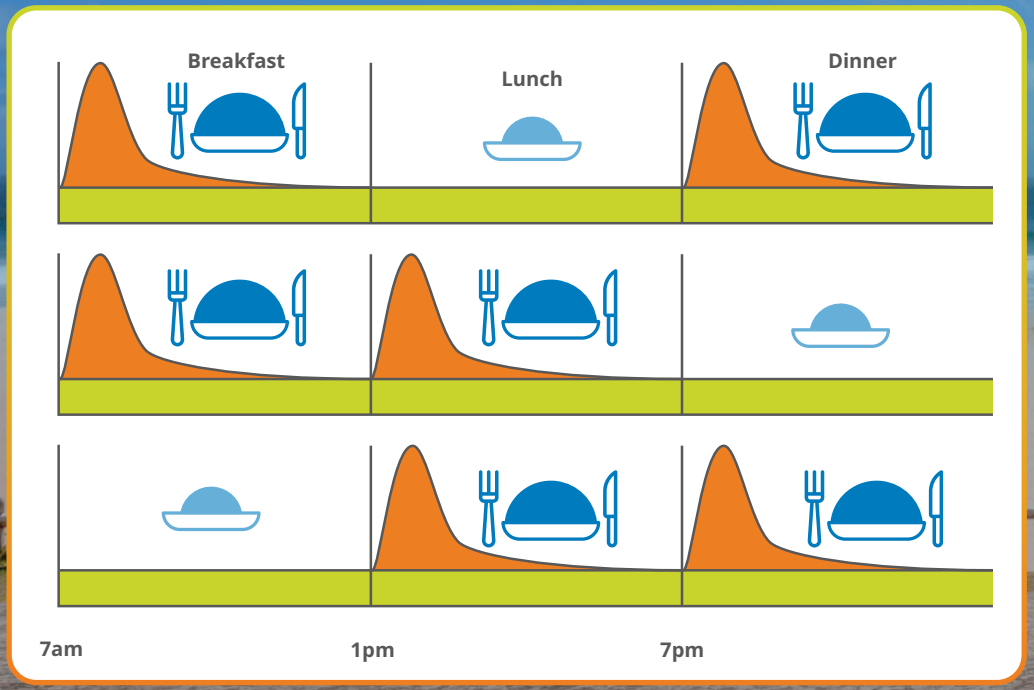
- If Ryzodeg® is administered BID, discontinue sulfonylureas.[7]

Initiate twice daily

Administration of twice-daily Ryzodeg® in Type 2 Diabetes

Should a patient not be optimally controlled on more than 2 or 3 oral agents, then proceed to initiate Ryzodeg® at a total dose of 0.3 units/kg, or per patient's individual requirements[7,8]

Consider administering Ryzodeg® twice daily at the time of the patient's two largest carbohydrate meals[1]

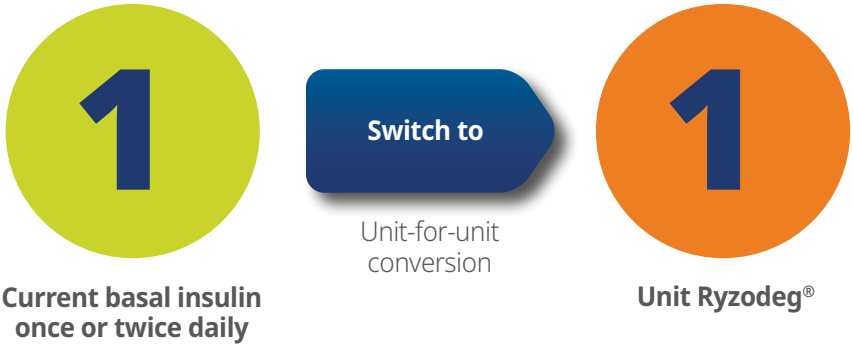


Basal Switch

It is simple to switch basal insulin patients to Ryzodeg®

Switching from basal insulin is recommended if glycaemia is insufficiently controlled, despite a threshold of 36-40 units or 0.5 units/kg/day of basal insulin.[7]

Patients switching from once-daily basal insulin therapy can be converted, unit-for-unit, to once or twice-daily Ryzodeg® at the same total insulin dose as the patient's previous total daily insulin dose.[1]

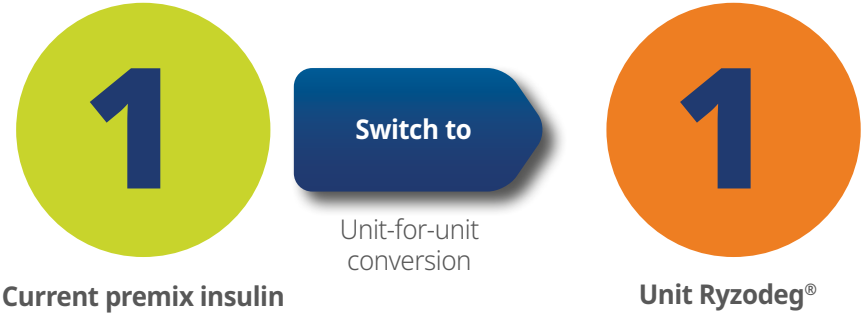


Ryzodeg® can be administered once or twice daily with main meal(s). When needed, the patient can change the time of administration, as long as Ryzodeg® is dosed with a main meal.[1]

Premix Upgrade

It is simple to switch premix insulin patients to Ryzodeg®

Patients switching from premix insulin therapy can be converted unit-for-unit to once- or twice-daily Ryzodeg® at the same total insulin dose as the patient's previous total daily insulin dose.[1]

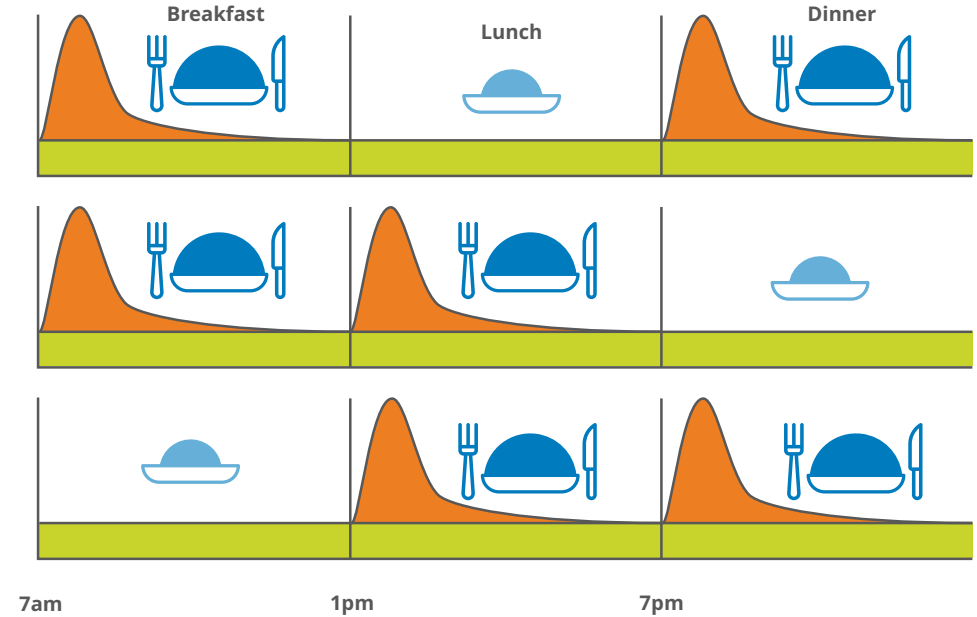


Ryzodeg® can be administered once or twice daily with main meal(s). When needed, the patient can change the time of administration, as long as Ryzodeg® is dosed with a main meal.[1]

Twice daily administration

Administration of twice-daily Ryzodeg® in Type 2 Diabetes

Consider administering Ryzodeg® twice daily at the time of the patient's two largest carbohydrate meals, if they have an HbA_{1c} > 7%[9]



Ryzodeg® can be administered once or twice daily with main meal(s). When needed, the patient can change the time of administration as long as Ryzodeg® is dosed with a main meal.[1]

Premix Upgrade

Basal-Bolus switch

Switching to Ryzodeg®

It is simple to switch from Basal-Bolus regimes

Individual patient needs will need to be taken into account when switching from Basal-Bolus insulin therapy to Ryzodeg®[10]

Use the basal insulin dose to calculate the total daily Ryzodeg® dose

When switching from Basal-Bolus therapy, split the dose in 2 and administer the doses at the two biggest carbohydrate meals of the day and not necessarily 50/50 split.

Calculation: Total daily dose of Ryzodeg® is equal to the Basal component only of the current Basal-Bolus dose.

How to titrate

Measure fasting blood glucose and titrate once weekly[8]

+2 units	Maintain	-2 units
		
Above target	At individualised target	Below target

Dose adjustments for Ryzodeg® should be based on the lowest of the 3 preceding FPG measurements
FPG targets should be individualised[7,8]

Adapted from Chan, *et al.*[8]

Considerations:

- A patient's SMBG values should be taken before breakfast on 3 consecutive days; dose adjustments for uptitration should be made on the basis of the lowest value of the three preceding FPG levels measured[8]
- For once-daily dosing, the pre-breakfast plasma glucose level is used to titrate, and for twice daily dosing, the pre-breakfast and pre-evening meal plasma glucose levels are used[8]
- Dose reduction is based on one measurement unless there is an apparent explanation for the low value, such as a missed meal[8]

SMBG - Self-monitoring of Blood Glucose; FPG - Fasting Plasma Glucose

Ryzodeg® is available in the Penfill® (cartridge) and administered with a NovoPen® 4

The benefits of the NovoPen® 4

Quick and simple to use

Easy to set, easy to read, easy to inject[1,11]

Robust design

Accurate insulin delivery and low dose force[11]

Reassuring dose delivery

Audible end-of-dose click to increase confidence[11]

Novo Nordisk® is here to support your patients throughout their Ryzodeg® journey

Scan the QR code below to access a quick guide to using the NovoPen® 4

References: 1. Ryzodeg® Professional Information. August 2022. **2.** Vijan S, *et al. J Gen Intern Med.* 2005;20(5):479–482. **3.** Fulcher G, *et al. Diabetes Care.* 2014;37(8):2084–2090. **4.** Haahr H, *et al. Clin Pharmacokinet.* 2017;56(4):339–354. **5.** Onishi Y, *et al.* Superior glycaemic control with once-daily insulin degludec/insulin aspart versus insulin glargine in Japanese adults with type 2 diabetes inadequately controlled with oral drugs: a randomized, controlled phase 3 trial. *Diabetes, Obesity and Metabolism* 2013;15:826–832. **6.** Kaneko S *et al.* Insulin degludec/insulin aspart versus biphasic insulin aspart 30 in Asian patients with type 2 diabetes inadequately controlled on basal or pre-/self-mixed insulin: A 26-week, randomised, treat-to-target trial. *Diabetes Res Clin Pract.* 2014;107(1):139-147. **7.** Mehta R, *et al.* Practical use of insulin degludec/insulin aspart in a multinational setting: beyond the guidelines. *Diabetes Obes Metab.* 2020; 22(11): 1961-1975. **8.** Chan SP, *et al*. Practical guide in using insulin degludec/insulin aspart: A multidisciplinary approach in Malaysia. *Malays Fam Physician*. 2023;18:31. **9.** Franek E, Haluzik M, Canecki Varžić S. Twice-daily insulin degludec/insulin aspart provides superior fasting plasma glucose control and a reduced rate of hypoglycaemia compared with biphasic insulin aspart 30 in insulin-na€ıve adults with Type 2 diabetes. *Diabet Med*. 2016;33(4):497-505. **10.** Glastras S.J., Cohen N, Dover T, *et al*. The Clinical Role of Insulin Degludec/Insulin Aspart in Type 2 Diabetes: An Empirical Perspective from Experience in Australia. *J Clin Med.* 2020;9:1091. **11.** Oyer D, Narendran P, Qvist M, Niemeyer M, Nadeau DA. Ease of use and preference of a new versus widely available prefilled insulin pen assessed by people with diabetes, physicians and nurses. *Expert Opinion Drug Deliv*. 2011;8(10):1259-1269.

S3 **Name of the medicine:** Ryzodeg® **Composition:** Each ml contains insulin degludec/insulin aspart (70 % soluble insulin degludec and 30 % soluble insulin aspart) 100 *units/ml*. **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 mealtimes 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. **Contra-Indications:** Hypersensitivity to the active substances or to any of the excipients. Pregnancy. **Special warnings and precautions for use:** *Hypoglycaemia:* Too high insulin dose, omission of a meal or unplanned strenuous physical exercise may lead to hypoglycaemia. Patients whose blood-glucose control is greatly improved may experience a change in their usual warning symptoms of hypoglycaemia and must be advised accordingly. Usual warning symptoms of hypoglycaemia may be altered in patients with long-standing diabetes. The patient's ability to concentrate and react may be impaired as a result of hypoglycaemia. Patients must be advised to take precautions to avoid hypoglycaemia while driving or operating machinery. *Hyperglycaemia:* Ryzodeg® should not be used to treat severe hyperglycaemia. Inadequate dosing and/or discontinuation of treatment in patients requiring insulin may lead to hyperglycaemia and potentially to diabetic ketoacidosis, which is potentially lethal. Concomitant illness, especially infections, may lead to hyperglycaemia and thereby cause an increased insulin requirement. Transferring to a new type, brand, or manufacturer of insulin must be done under strict medical supervision. **Interactions:** When using Ryzodeg® in combination with thiazolidinediones, 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 function occurs. *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. *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 to correct a tendency to hyper- or hypoglycaemia. Immediate-type allergic reactions to either insulin itself or the excipients may potentially be life threatening. *Skin and subcutaneous tissue disorders:* Injection site reactions may occur. 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. In children, extra care should be taken to match insulin doses with food intake and physical activities to minimise the risk of hypoglycaemia. Paediatric population: 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. *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. **Fertility, pregnancy and lactation:** Safety has not been established in pregnancy and lactation and Ryzodeg® should not be recommended for use during pregnancy. **Posology and administration:** Ryzodeg® can be administered once- or twice-daily with the main meal(s). When needed, the patient can change the time of administration, if 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. 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(s) followed by individual dosage adjustments. For patients with type 1 diabetes mellitus, Ryzodeg® is to be used once-daily at a 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 if 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. **Undesirable effects**: 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). Very common: Hypoglycaemia. Common: Injection site reactions. Uncommon: Peripheral oedema and rare: Hypersensitivity and urticaria. Adverse Reactions from post-marketing experience: cutaneous amyloidosis (frequency unknown). **Pharmacological classification:** A 21.1 Insulin Preparations **ATC code:** A10AD06 **Reg. No.**: 47/21.1/0165 For full prescribing details, please refer to the Professional Information approved by the Medicines Regulatory Authority.

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Novo Nordisk (Pty) Ltd. Reg. No.: 1959/000833/07. 150 Rivonia Road, 10 Marion Street Office Park, Building C1, Sandton, Johannesburg, 2196, South Africa.
Tel: (011) 202 0500. Fax: (011) 807 7989. www.novonordisk.com. 22009T. ZA23RZG00011 March 2023.

RYZODEG®

70% insulin degludec and 30% insulin aspart [rDNA origin] injection