Abbreviated prescribing information:

Ryzodeg® (insulin degludec/insulin aspart) 100 units/mL solution for injection in a pre-filled pen (FlexTouch®). Ryzodeg® (insulin degludec/insulin aspart) 100 units/mL insulin solution for injection in a cartridge (Penfill®). Consult Summary of Product Characteristics before prescribing. Presentations: Ryzodeg® FlexTouch®, Ryzodeg® Penfill®. All presentations contain insulin degludec/insulin aspart. Ryzodeg® - 1 mL solution contains 100 units insulin degludec/insulin aspart in the ratio 70/30 (equivalent to 2.56 mg insulin degludec and 1.05 mg insulin aspart). One pre-filled device or one cartridge contains 300 units of degludec/insulin aspart in 3 mL solution. **Indications:** Treatment of diabetes mellitus in adults, adolescents and children from age of 2 years. **Posology and administration:** Ryzodeg® can be administered once- or twice-daily with the main meal(s). In patients with type 2 diabetes mellitus, Ryzodeg® can be administered alone, in combination with oral anti-diabetic medicinal products, and in combination with bolus insulin. In type 1 diabetes mellitus, Ryzodeg®can be administered once daily at mealtime in combination with short-/rapid-acting insulin at the remaining meals. Administration by subcutaneous injection only. Ryzodeg® should be dosed in accordance with individual patient needs. Dose adjustments are recommended to be primarily based on FPG measurements. 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 missed 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. In older patients and patients with renal and/or hepatic impairment, glucose-monitoring should be intensified and the insulin dose adjusted on an individual basis. In paediatric population, 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. 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. Ryzodeg® comes in a pre-filled pen (FlexTouch®) designed to be used with NovoFine® or NovoTwist® injection needles. The pre-filled pen delivers 1–80 units in steps of 1 unit. The dose counter shows the number of units dialled. Ryzodeg® is also available in the Penfill® cartridge designed to be used with Novo Nordisk insulin delivery systems and NovoFine® or NovoTwist® injection needles. ***Initiation:*** For patients with type 2 diabetes mellitus, the recommended daily starting dose of Ryzodeg® is 10 units with meal(s) followed by individual dosage adjustments. For patients with type 1 diabetes mellitus, the recommended daily starting dose of Ryzodeg® is 60–70% of the total daily insulin requirement, to be used once-daily at meal time, in combination with short-/rapid-acting insulin at the remaining meals, followed by individual dosage adjustments. ***Transfer:*** Close glucose monitoring is recommended during transfer and in the following weeks. Doses and timing of concurrent rapid-acting or short-acting insulin products or other concomitant anti-diabetic treatment may need to be adjusted. For patients with type 2 diabetes mellitus: those switching from once-daily basal or premix insulin can be converted unit-to-unit to once-daily or twice-daily Ryzodeg® at the same total daily insulin dose; those switching from more than once-daily basal or premix insulin can be converted unit-to-unit to once- or twice-daily Ryzodeg® at the same total daily insulin dose; those switching from basal/bolus insulin to Ryzodeg® should convert their dose based on individual needs, in general with the same number of basal units. 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. **Contraindications:** Hypersensitivity to the active substances or any of the excipients. **Special warnings and precautions:** 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 may disappear in patients with long-standing diabetes. Hyperglycaemia:Inadequate dosing and/or discontinuation of treatment in patients requiring insulin may lead to hyperglycaemia and potentially to diabetic ketoacidosis. Concomitant illness, especially infections, may lead to hyperglycaemia and thereby cause an increased insulin requirement. Transfer from other insulin medicinal products:Transferring to a new type, brand, or manufacturer of insulin must be done under strict medical supervision. Combination of pioglitazone and insulin medicinal products:When using insulin in combination with pioglitazone, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. 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.Eye disorder:Intensification of insulin therapy with abrupt improvement in glycaemic control may be associated with temporary worsening of diabetic retinopathy, while long-term improved glycaemic control decreases the risk of progression of diabetic retinopathy.Avoidance of accidental mix-ups:Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between Ryzodeg and other insulin products.Insulin antibodies: Insulin 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.Sodium:This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. it is essentially 'sodium-free'.Traceability:In

order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypoglycaemia may constitute a risk when driving or operating machinery. 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. **Pregnancy and lactation:** There is no clinical experience with use of Ryzodeg® in pregnant women or in those who are breastfeeding. **Undesirable effects:** Refer to SmPC for complete information on side 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. Not known: Lipodystrophy and cutaneous amyloidosis. Uncommon: Peripheral oedema and rare: Hypersensitivity and urticaria. With insulin preparations, allergic reactions may occur; immediate-type allergic reactions may potentially be life threatening. Injection site reactions are usually mild, transitory and normally disappear during continued treatment.

Legal category: Prescription-only medicine (POM). **Marketing authorisation holder:** Novo Nordisk A/S Novo Allé DK-2880 Bagsværd Denmark. **Date of Review of Prescribing Information:** September 2020. **Summary of Product Characteristics can be obtained from Novo Nordisk A/S.**