

<p><b><i>INSULIN IS A HIGH RISK MEDICINE</i></b>  <b>USE WITH CAUTION AND ENSURE THE DIRECTIONS WITHIN THIS PROTOCOL ARE FOLLOWED CAREFULLY</b></p>	
<b>Areas where applicable</b>	Adult inpatients in SESLHD facilities
<b>Areas where not applicable</b>	Paediatrics
<b>Authorised Prescribers:</b>	Initiation is restricted to Endocrine consult only All medical officers may continue existing therapy
<b>Indication for use</b>	Management of Type 1 and Type 2 Diabetes Mellitus. To improve glycaemic control in adult patients with diabetes mellitus requiring basal and prandial insulin
<b>Clinical condition</b>	Patients with type 1 diabetes Insulin-naïve patients with type 2 diabetes Patients with advanced Type 2 diabetes previously treated with insulin therapy
<b>Contraindications</b>	Hypersensitivity to insulin degludec, insulin aspart or any of the excipients
<b>Precautions</b>	<p><b>Hypoglycaemia:</b></p> <ul style="list-style-type: none"> <li>• Prolonged or severe hypoglycaemic episodes may be life threatening. Particular caution should be exercised, and intensified blood glucose monitoring is advisable in patients in whom hypoglycaemic episodes might be of particular clinical relevance and consideration of dose reduction, such as in patients:           <ul style="list-style-type: none"> <li>○ With recurrent hypoglycaemia</li> <li>○ Elderly (&gt;65 years)</li> <li>○ Low body weight</li> <li>○ Impaired renal function</li> <li>○ Impaired hepatic function</li> </ul> </li> <li>• Meal omission, dietary changes and unplanned strenuous exercise may lead to hypoglycaemia</li> <li>• Prolonged basal effect of Ryzodeg® 70/30 may delay recovery from a hypoglycaemic episode</li> </ul> <p><b>Hyperglycaemia:</b> Administration of rapid-acting insulin is recommended for treatment of severe hyperglycaemia. Ryzodeg® 70/30 is not appropriate to treat hyperglycaemia.</p> <p><b>Transfer of patients between insulin types:</b> Switching patients to Ryzodeg® 70/30 from other insulins must be completed under the supervision of the Endocrinology team, with close blood glucose monitoring and individualised dose adjustments and dose timing.</p>

**Prescribing Protocol SESLHDPR/650**  
**Insulin degludec/insulin aspart**  
**(Ryzodeg<sup>®</sup> 70/30)**



<p><b>Precautions</b></p>	<p><b>Medication error prevention:</b> Insulin labels must always be checked carefully before each injection to prevent medication errors between Ryzodeg<sup>®</sup> 70/30 and other insulins. Ryzodeg<sup>®</sup> 70/30 must not be administered IV, IM or via an infusion pump.</p> <p><b>Pregnancy (Category B3) &amp; lactation:</b> Safety and efficacy has not been established</p> <p><b>Children &lt;18 years:</b> Safety and efficacy has not been established</p>
<p><b>Place in Therapy</b></p>	<p>Ryzodeg<sup>®</sup> 70/30 is a biphasic insulin, consisting of ultra-long acting basal insulin degludec and ultra-short acting prandial insulin aspart. Ryzodeg<sup>®</sup> 70/30 provides a constant basal insulin level, with its glucose-lowering effect persisting longer than that of insulin glargine (Lantus<sup>®</sup>).</p> <p>Ryzodeg<sup>®</sup> 70/30 may be considered for patients in need of insulin:</p> <ul style="list-style-type: none"> <li>- Type 1 diabetes mellitus (1<sup>st</sup> or 2<sup>nd</sup> line)</li> <li>- Type 2 diabetes mellitus failing previous oral antidiabetic agent or insulin therapies (2<sup>nd</sup> or 3<sup>rd</sup> line)</li> </ul>
<p><b>If part of combination therapy, list other drugs</b></p>	<p>Ultra-short acting insulins (NovoRapid<sup>®</sup>, Humalog<sup>®</sup>, Apidra<sup>®</sup>)              Oral antidiabetic drugs</p>
<p><b>Important Safety Considerations</b></p>	<ul style="list-style-type: none"> <li>• Ryzodeg<sup>®</sup> 70/30 <u>must</u> be administered immediately before a carbohydrate-containing main meal</li> <li>• Not for administration via an infusion pump</li> <li>• Not for IV or IM administration</li> </ul>
<p><b>Dosage</b></p>	<p>Ryzodeg<sup>®</sup> 70/30 can be administered once- or twice-daily with carbohydrate-containing main meal(s), and should be given with the largest meal when administered once daily. Doses should be individualised in accordance with the patient's needs.</p> <p>As with all insulins, dose adjustments may be necessary during concomitant illness and if patients undertake increased physical activity or change their usual diet.</p> <p><b>Initiation</b>  <u>Type 1 diabetes</u>              The recommended starting dose is 60-70% of the total daily insulin requirements. Ryzodeg<sup>®</sup> 70/30 is to be given once daily with the largest meal, in combination with rapid-acting insulin at the remaining meals, followed by individual dose adjustments.</p> <p><u>Type 2 diabetes</u>              Initially the usual dose will be 10 units per day with the largest meal(s), followed by individual dose adjustments. However if the patient is already on larger doses of supplemental insulin, the initial dose may be higher.</p> <p><b>Switching from other insulins to Ryzodeg<sup>®</sup> 70/30</b>  <u>Type 1 diabetes</u>              The recommended starting dose is 60-70% of the total daily</p>

**Prescribing Protocol SESLHDPR/650**  
**Insulin degludec/insulin aspart**  
**(Ryzodeg® 70/30)**



	<p>insulin requirements, in combination with rapid-acting insulin at the remaining meals, followed by individual dose adjustments.</p> <p><u>Type 2 diabetes – prior basal or mixed insulin therapy</u>                  Convert insulin unit-to-unit:</p> <ul style="list-style-type: none"> <li>- Once-daily Ryzodeg® 70/30 at the same total insulin dose as the patient’s previous total daily insulin dose</li> <li>- Twice-daily Ryzodeg® 70/30 using half the total daily dose twice-daily</li> </ul> <p><u>Type 2 diabetes – prior basal-bolus insulin therapy</u>                  The dose should be converted based on individual patient needs. In general, patients are commenced on the same number of basal insulin units.</p>
<b>Duration of therapy</b>	Ongoing
<b>Important Drug Interactions</b>	<ul style="list-style-type: none"> <li>• <b>Substances that may enhance the blood glucose lowering effect and increase risk of hypoglycaemia:</b>                      Oral antidiabetic agents, Glucagon-like peptide-1 receptor agonists (e.g. exenatide), monoamine oxidase inhibitors (MAOIs), nonselective beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids (except danazol and oxymetholone), alpha-adrenergic blocking agents, quinine, quinidine and sulphonamides.</li> <li>• <b>Substances that may reduce the glucose lowering effect of insulin and increase risk of hyperglycaemia:</b>                      Corticosteroids, thiazide diuretics, oral contraceptives, thyroid hormones, sympathomimetic agents (e.g. adrenaline (epinephrine)), growth hormone, diazoxide, nicotinic acid, oxymetholone and danazol</li> <li>• <b>Thiazolidinediones:</b> Combination with insulin increases risk of heart failure. Combination with rosiglitazone is contraindicated, and use pioglitazone cautiously, observe for any signs of heart failure, oedema or weight gain. Thiazolidinedione therapy should be ceased if any cardiac deterioration occurs.</li> <li>• <b>Incompatibilities:</b> Substances added to Ryzodeg® 70/30 may cause degradation of insulin degludec and/or insulin aspart. Do not add to infusion fluids, or mix with other insulins, solutions or medicinal products.</li> </ul>
<b>Prescribing Requirements</b>	Initiation, including switching of patients from alternative insulin regimens, should only occur under the monitoring of the Endocrinology team.
<b>Administration Instructions</b>	<p>Ryzodeg® 70/30 is a biphasic insulin, consisting of ultra-long acting basal insulin degludec and ultra-short acting prandial insulin aspart.</p> <p>Ryzodeg® 70/30 can be administered once- or twice-daily, <b>immediately before carbohydrate-containing main meal(s)</b>, and should be given with the largest meal when administered once daily.</p> <p>Ryzodeg® 70/30 is for subcutaneous administration only, by injection into the abdominal wall, upper arm or thigh. Injection sites should be rotated to reduce risk of lipodystrophy.</p> <p>Available in a FlexTouch® pre-filled pen and penfill cartridges, for single patient use only. Insulin must not be administered if the</p>

**Prescribing Protocol SESLHDPR/650  
Insulin degludec/insulin aspart  
(Ryzodeg® 70/30)**



	<p>solution does not appear clear and colourless.</p> <p>An independent double check is required for every administration in accordance with NSW Health Policy.</p> <p><u>Missed dose management:</u> If a dose of Ryzodeg® 70/30 is missed, the missed dose is recommended to be administered with the next main meal of that day, and thereafter the usual dosing schedule should be resumed.</p>
<b>Monitoring Requirements</b>	<p>Blood glucose monitoring, blood ketone and HbA1c as clinically indicated. Pre-meal plasma glucose levels should be used to evaluate the adequacy of the previous dose</p> <p>Close glucose monitoring is recommended when switching between other insulins and Ryzodeg® 70/30, and in the following weeks. Doses and timing of concurrent rapid- acting insulin products or other concomitant anti-diabetic treatment may need to be adjusted.</p>
<b>Management of complications</b>	<p>Refer to local business rules for hypo- and hyperglycaemia.</p> <p>Adjustments in drug dosage, meal patterns of exercise may be required.</p>
<b>Storage requirements</b>	<p><b>Unopened/before use</b> Ryzodeg® 70/30 must be stored between +2° C and +8° C (in a refrigerator) and protected from light. Do not allow the insulin to freeze, discard if frozen. Do not put Ryzodeg® 70/30 next to the freezer compartment or a freezer pack.</p> <p><b>Opened/in use</b> Opened prefilled pens and cartridges must be discarded after 28 days (4 weeks) from first use. They should be stored at room temperature (below 30°C) and protected from light.</p>
<b>Basis of Protocol/Guideline:</b> (including sources of evidence, references)	<p><a href="#">Ryzodeg® 70/30 Product information</a> AMH Monograph – Insulins (accessed 19/02/19) Australian Diabetes Society (2018) <a href="#">Australian Blood Glucose Treatment Algorithm for Type 2 Diabetes</a> <a href="#">NSW Health PD2015_029: High-Risk Medicines Management Policy</a></p>
<b>Groups consulted in development of this guideline</b>	<p>Departments of Endocrinology at St George, Sutherland and Prince of Wales Hospitals</p> <p>Diabetes Education Centre, St George Hospital</p> <p>Chi Tran, Senior Pharmacist, POWH</p> <p>Amy Minett, Acting SESLHD Quality Use of Medicines Lead Pharmacist</p>

**Prescribing Protocol SESLHDPR/650  
 Insulin degludec/insulin aspart  
 (Ryzodeg® 70/30)**



<b>AUTHORISATION</b>	
Author (Name)	Professor Anthony (Tony) O'Sullivan
Position	Head of Department
Department	Endocrinology, St George Hospital
Department Contact	<a href="mailto:a.osullivan@unsw.edu.au">a.osullivan@unsw.edu.au</a> or <a href="mailto:Anthony.OSullivan@health.nsw.gov.au">Anthony.OSullivan@health.nsw.gov.au</a>
<b>GOVERNANCE</b>	
Enactment date	2 May 2019
<b>Expiry date:</b>	<b>May 2021</b>
Ratification date by SESLHD Drug and QUM Committee	2 May 2019
Chairperson, QUM Committee	Prof George Rubin
Approved Protocol/Guideline distributed	May 2019
Version Number	1.0