

<b>Prescribing Protocol</b>	
<b>Title</b>	Linagliptin for Type 2 Diabetes (Trajenta®)
<b>Areas where Protocol/Guideline applicable</b>	District
<b>Areas where Protocol/Guideline not applicable</b>	Paediatrics
<b>Authorised Prescribers</b>	All authorised prescribers
<b>Indication for use</b>	<p>Approved for use in line with PBS criteria</p> <p>Type 2 diabetes mellitus, to improve glycaemic control in conjunction with diet and exercise, as add on therapy in combination with:</p> <ul style="list-style-type: none"> <li>• Metformin, or</li> <li>• Metformin and a sulfonylurea, or</li> <li>• A sulfonylurea, or</li> <li>• Metformin and a sodium-glucose co-transporter 2 (SGLT2) inhibitor, or</li> <li>• Insulin (with or without metformin)</li> </ul>
<b>Clinical condition</b>	<p>Type 2 diabetes mellitus, with a HbA1c &gt;7% despite prior treatment with any of the following antidiabetic therapies:</p> <ul style="list-style-type: none"> <li>• Metformin</li> <li>• A sulfonylurea</li> <li>• Dual therapy with metformin and a sulfonylurea</li> <li>• Dual therapy with metformin and a SGLT2 inhibitor</li> <li>• Insulin alone or insulin with oral antidiabetic agents</li> </ul>
<b>Contra-indications</b>	Hypersensitivity to linagliptin or to any of the excipients.
<b>Precautions</b>	<p>Linagliptin should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.</p> <ul style="list-style-type: none"> <li>• <i>Treatment with a sulfonylurea or insulin</i> – increases risk of hypoglycaemia</li> <li>• <i>Pancreatitis</i> – Acute pancreatitis is a rare side effect of dipeptidyl peptidase-4 inhibitors. Linagliptin should not be used in a setting of previous pancreatitis, and should be ceased if pancreatitis occurs</li> <li>• <i>Bullous pemphigoid</i> – postmarketing reports; linagliptin should be ceased if bullous pemphigoid is suspected</li> <li>• <i>Arthralgia</i> – Pain may be severe and symptom onset may be rapid or occur after longer periods. Consider cessation if patients present with or experience increased joint pain symptoms during linagliptin therapy</li> <li>• <i>Combination with glucagon like peptide (GLP-1) analogues</i> – avoid use, no studies available</li> <li>• <i>Pregnancy &amp; lactation</i> – avoid use, no human data</li> <li>• <i>Children</i> – not recommended for use in children under 18 years, lack of safety and efficacy data</li> </ul>

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<p><b>Place in Therapy</b></p>	<p>Second or third line treatment of type 2 diabetes, in combination with other oral antidiabetic agents or insulin.          Proposed place of linagliptin is based on the PBS listings detailed above.</p>
<p>If part of combination therapy, list other drugs</p>	<p>Add on therapy to metformin, sulfonylurea, or metformin plus sulfonylureas, or to insulin (with or without metformin), or to metformin plus a SGLT2 inhibitor.</p>
<p><b>Dosage</b>          (Include dosage adjustment for specific patient groups)</p>	<p>Oral 5mg once daily.          Nil dosage adjustment is required for patients with renal or hepatic impairment, or the elderly.</p>
<p><b>Duration of therapy</b></p>	<p>According to the clinical requirements and patient response.</p>
<p><b>Important Drug Interactions</b></p>	<ul style="list-style-type: none"> <li>• <i>Concurrent treatment with a sulfonylurea or insulin</i> – increases risk of hypoglycaemia</li> <li>• <i>Strong P-glycoprotein inducers &amp; CYP3A4 inducers (e.g. rifampicin)</i> – may decrease linagliptin concentration and decrease its efficacy</li> <li>• <i>Treatment with an ACE inhibitor</i> – vildagliptin has been associated with an increased risk of ACE inhibitor-induced angioedema; other DPP-4 inhibitors may also have this effect</li> </ul>
<p><b>Administration instructions</b></p>	<p>Administer orally once a day.          Linagliptin can be taken with or without a meal at any time of the day. If dose is missed, it should be taken as soon as identified. A double dose should not be taken on the same day.</p>
<p><b>Monitoring requirements</b></p>	<p>HbA1c (%) – predominant measure of drug effectiveness          BGLs</p>
<p><b>Management of complications</b></p>	<p>As per standard medical care</p>
<p><b>Basis of Protocol/Guideline</b>          (including sources of evidence, references)</p>	<p>Barnett, A. H., Huisman, H., Jones, R., von Eynatten, M., Patel, S., &amp; Woerle, H. J. (2013). Linagliptin for patients aged 70 years or older with type 2 diabetes inadequately controlled with common antidiabetes treatments: a randomised, double-blind, placebo-controlled trial. <i>The Lancet</i>, 382(9902), 1413-1423.</p> <p>Gallwitz, B., Rosenstock, J., Rauch, T., Bhattacharya, S., Patel, S., von Eynatten, M., ... &amp; Woerle, H. J. (2012). 2-year efficacy and safety of linagliptin compared with glimepiride in patients with type 2 diabetes inadequately controlled on metformin: a randomised, double-blind, non-inferiority trial. <i>The Lancet</i>, 380(9840), 475-483.</p> <p>McGill, J. B., Sloan, L., Newman, J., Patel, S., Sauce, C., von Eynatten, M., &amp; Woerle, H. J. (2013). Long-term efficacy and safety of linagliptin in patients with type 2 diabetes and severe renal impairment: a 1-year, randomized, double-blind, placebo-controlled study. <i>Diabetes Care</i>, 36(2), 237-244.</p> <p>Taskinen, M. R., Rosenstock, J., Tamminen, I., Kubiak, R., Patel, S., Dugi, K. A., &amp; Woerle, H. J. (2011). Safety and efficacy of linagliptin as add-on therapy to metformin in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study. <i>Diabetes, Obesity and Metabolism</i>, 13(1), 65-74.</p> <p>MIMS, <a href="#">Trajenta@ product information</a>, last amended 06/07/17</p> <p>Australian Medicines Handbook, <a href="#">Linagliptin monograph</a>, last updated July 2018</p> <p>eTG, Endocrinology – <a href="#">Management of type 2 diabetes</a>, published November 2013</p>
<p><b>Groups consulted in development of this protocol</b></p>	<p>Endocrinology</p>

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