



### Minimising hypoglycaemia risk in type 2 diabetes

Achieving optimal glycaemic control is fundamental to the effective management of type 2 diabetes (T2D). Hypoglycaemia is one of the major limiting factors to achieving T2D control.

Hypoglycaemia due to glucose-lowering treatments for T2D can adversely affect a person's quality of life, medication adherence and treatment satisfaction, but there are steps healthcare professionals can take to minimise risk and positively impact the patient's health.

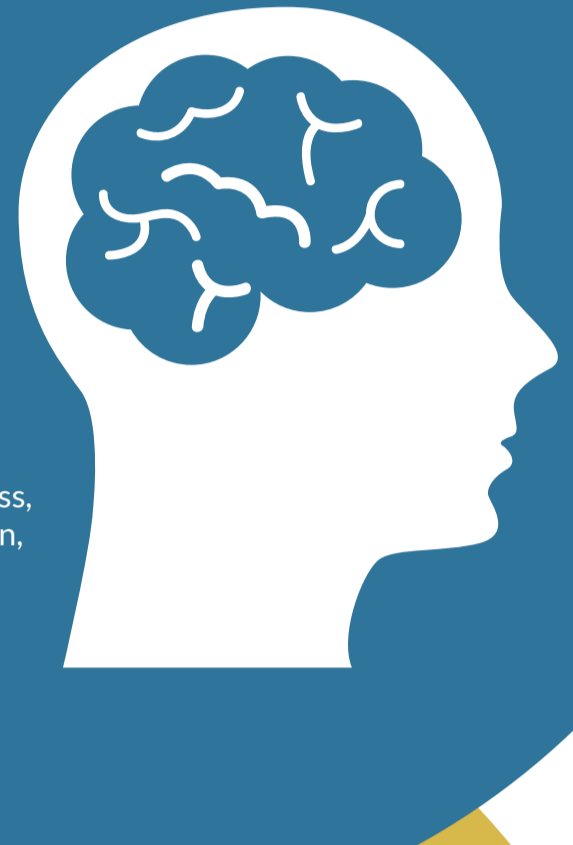
### Risk factors for hypoglycaemia



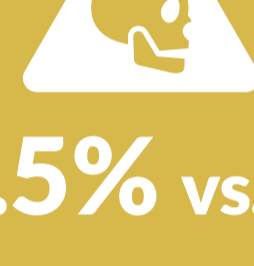
Amongst people with T2D, the prevalence of mild/moderate hypoglycaemia can be as high as **45%**<sup>4</sup>

### Negative effects of hypoglycaemia

- Quality of life<sup>1</sup> and health status<sup>5</sup>
- Cognitive<sup>2</sup> function and mood<sup>1</sup>
- Physical symptoms include:<sup>6</sup> headaches, sweating, shakiness, weakness, lack of coordination, fainting and dizziness



### Severe hypoglycaemia in T2D: hospitalisation and mortality



**0.3 per 100 patient-years**

**5.04 days**

**19.5% vs. 9%**

Rate of hospitalisation for hypoglycaemia in T2D<sup>7</sup>

Average length of stay for people with T2D admitted for hypoglycaemia (95% CI: 4.46–5.71)<sup>8</sup>

All-cause mortality rate over 5 years in people with T2D who had experienced ≥1 episode of severe hypoglycaemia and those who had not respectively (HR: 3.27, 95% CI: 2.29–4.65)<sup>9</sup>

### Steps to minimise the risk of hypoglycaemia in your patients

- Select an appropriate diet, lifestyle and therapy regimen to treat T2D:**
  - Balance the glucose-lowering efficacy of therapy with its risk of causing hypoglycaemia<sup>10</sup>
  - Support the person to aim for an HbA<sub>1c</sub> level of 53 mmol/mol (7.0%) or an alternative individualised HbA<sub>1c</sub> target<sup>10</sup>
- Assess patients for hypoglycaemia at every appointment, particularly those taking medication that increases risk, e.g. insulin or a sulphonylurea<sup>1</sup>**
- Consider each risk factor for hypoglycaemia and whether it can be modified<sup>1</sup>**
- Educate patients about the signs of hypoglycaemia<sup>1</sup>**
- Simplify complex treatment regimens<sup>1</sup>**
- Monitor hospitalised T2D patients for hypoglycaemia<sup>11</sup>**

**Low risk**  
GLP-1 receptor agonists

**High Risk**  
Insulin

**Low risk**  
Pioglitazone

### Medication considerations

Level of risk for hypoglycaemia when used as add-on to metformin:<sup>12</sup>

**Low risk**  
DPP-4 inhibitors

**Moderate risk**  
Sulphonylureas

**Low risk**  
SGLT2 inhibitors

#### References

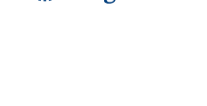
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#### Abbreviations

CI, confidence interval; DPP-4, dipeptidyl peptidase-4; HR, hazard ratio; SGLT2, sodium-glucose cotransporter 2; GLP-1, glucagon-like peptide-1



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#### Prescribing Information (UK)

#### TRAJENTA® Film-coated tablets containing 5 mg linagliptin

**Indication:** Trajenta is indicated in adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control as monotherapy when metformin is inappropriate due to intolerance, or contraindicated due to renal impairment; combination therapy in combination with other medicinal products for the treatment of diabetes, including insulin, when these do not provide adequate glycaemic control.

**Dose and Administration:** 5 mg once daily. If added to metformin, the dose of metformin should be reduced and linagliptin administered concomitantly. When used in combination with a sulphonylurea or with insulin, a lower dose of the sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia. Renal impairment: no dose adjustment required. Hepatic impairment: pharmacokinetic studies suggest that no dose adjustment is required for patients with hepatic impairment but clinical experience in such patients is lacking. Elderly: no dose adjustment is necessary based on age however, clinical experience in patients > 80 years of age is limited and caution should be exercised when treating this population. Paediatric population: the safety and efficacy of linagliptin in children and adolescents has not yet been established. No data are available. Take the tablets with or without a meal at any time of the day. If a dose is missed, it should be taken as soon as possible but a double dose should not be taken on the same day. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients.

**Warnings and Precautions:** Linagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Caution is advised when linagliptin is used in combination with sulphonylurea and/or insulin; a dose reduction of the sulphonylurea or insulin may be considered. Acute pancreatitis: In post-marketing experience of linagliptin there have been spontaneously reported adverse reactions of acute pancreatitis. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, Trajenta should be discontinued; if acute pancreatitis is confirmed, Trajenta should not be restarted. Caution should be exercised in patients with a history of pancreatitis. Bullous pemphigoid: If bullous pemphigoid is suspected, Trajenta should be discontinued.

**Interactions:** Linagliptin is a weak to moderate mechanism-based inhibitor of CYP isozyme CYP3A4, but does not inhibit other CYP isozymes. It is not an inducer of CYP isozymes. Linagliptin is a P-glycoprotein substrate and inhibits P-glycoprotein mediated transport of digoxin with low potency. Based on these results and in vivo interaction studies, linagliptin is considered unlikely to cause interactions with other P-gp substrates. The risk for clinically meaningful interactions with other medicinal products on linagliptin is low and in clinical studies linagliptin had no clinically relevant effect on the pharmacokinetics of metformin, glibenclamide, simvastatin, warfarin, digoxin or oral contraceptives (please refer to Summary of Product Characteristics for interaction on clinical data). **Fertility, pregnancy and lactation:** Avoid use during pregnancy. A risk to the breast-fed child cannot be excluded. A decision must be made whether to discontinue breast feeding or to discontinue/abstain from linagliptin therapy taking into account the benefit of breast-feeding for the human fertility have been conducted for linagliptin. **Undesirable effects:** Adverse reactions reported in patients who received linagliptin 5 mg daily as monotherapy

or as add-on therapies (frequencies identified from pooled analysis of placebo-controlled studies) in clinical trial and from post-marketing experience. The adverse reactions are listed by absolute frequency. Frequencies are defined as 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) or not known (cannot be estimated from the available data). Very common: hypoglycaemia (combination with add-on to metformin and sulphonylurea). Common: lipase increased (monotherapy; combination with add-on to metformin; combination with add-on to metformin and sulphonylurea; combination with add-on to metformin and sulphonylurea; combination with add-on to insulin; combination with add-on to metformin and empagliflozin). Uncommon: nasopharyngitis (monotherapy; combination with add-on to metformin; combination with add-on to insulin); hypersensitivity e.g. bronchial hyperreactivity (monotherapy; combination with add-on to metformin; combination with add-on to metformin and sulphonylurea; combination with add-on to metformin and sulphonylurea; combination with add-on to insulin); cough (monotherapy; combination with add-on to metformin and empagliflozin); amylase increased (combination with add-on to metformin; combination with add-on to metformin and sulphonylurea; combination with add-on to metformin and empagliflozin). Rare: angioedema (monotherapy; combination with add-on to metformin; combination with add-on to metformin and sulphonylurea; combination with add-on to metformin and sulphonylurea; combination with add-on to insulin); urticaria (monotherapy; combination with add-on to metformin and sulphonylurea; combination with add-on to metformin and empagliflozin); hypersensitivity e.g. bronchial hyperreactivity (combination with add-on to metformin and sulphonylurea; combination with add-on to metformin and empagliflozin); cough (combination with add-on to metformin and sulphonylurea; combination with add-on to metformin and empagliflozin); pancreatitis (combination with add-on to metformin and sulphonylurea; combination with add-on to metformin and sulphonylurea; combination with add-on to insulin); amylase increased (combination with add-on to metformin and sulphonylurea; combination with add-on to insulin). Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** 28 tablets £33.26. **Legal category:** POM. **MA number:** EU/1/11/707/003. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in** April 2017.