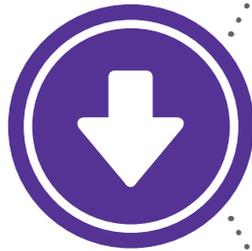


# A GLP-1 Receptor Agonist designed with the patient in mind



Significant HbA<sub>1c</sub> reduction<sup>1</sup>

Significant weight loss<sup>†1</sup>

CV benefit in a broad type 2 diabetes population<sup>2</sup>



Once-weekly dosing<sup>1</sup>



Ready-to-use pen

Pre-attached, hidden, small needle

No need for dose titration to improve GI tolerability at initiation

**Trulicity also offers 3.0 mg  
and 4.5 mg doses<sup>1</sup>**

<sup>†</sup>Trulicity is not indicated for weight loss, and weight loss was a secondary endpoint in clinical trials.<sup>1</sup>

Trulicity is designed for your patients with type 2 diabetes:



HbA<sub>1c</sub> above  
58 mmol/mol



Weight is a  
clinical concern



Cardiovascular risk is  
a clinical concern



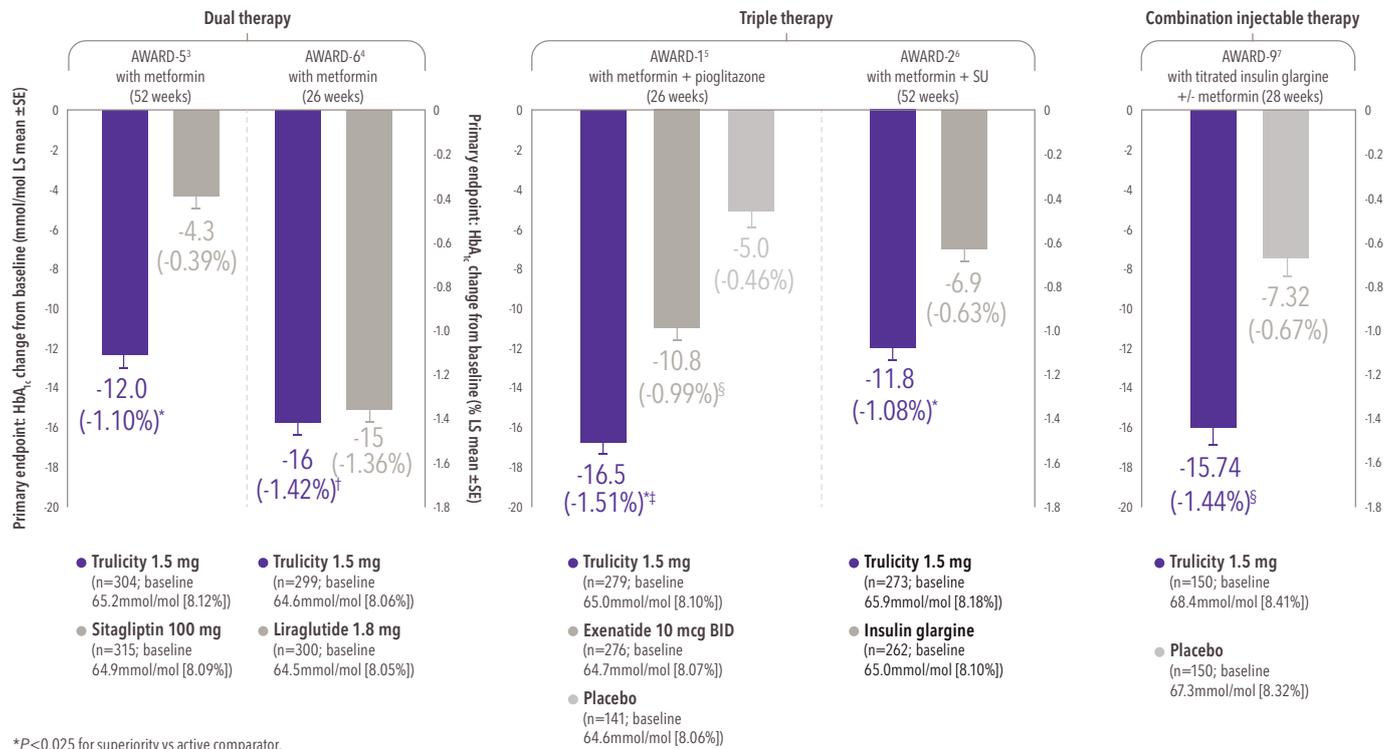
Reluctant to make the  
transition to GLP-1 RA  
therapy



Struggling to fit  
changes into a busy life

Trulicity is indicated for the treatment of adults with insufficiently controlled type 2 diabetes as an adjunct to diet and exercise as monotherapy when metformin is considered inappropriate due to intolerance or contraindications, or in addition to other medicinal products for the treatment of diabetes.<sup>1</sup>

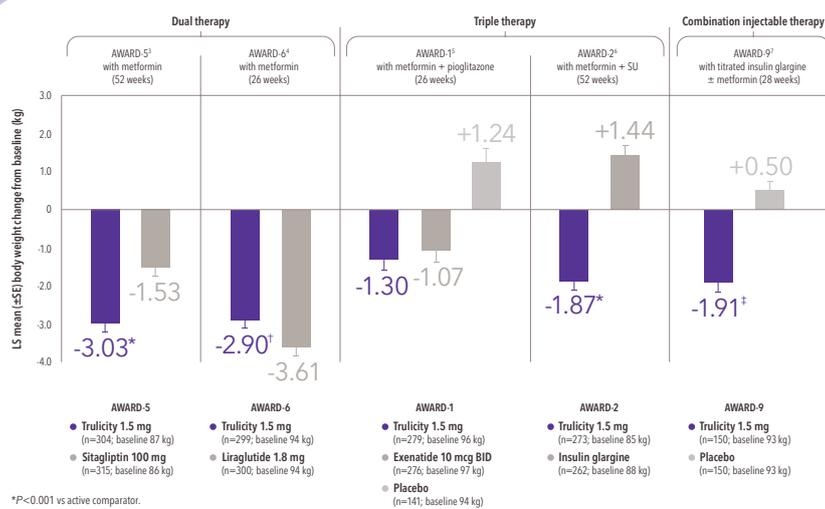
# Trulicity 1.5 mg demonstrated significant HbA<sub>1c</sub> reduction across a comprehensive phase III clinical trial programme<sup>3-7</sup>



\*P<0.025 for superiority vs active comparator.  
<sup>†</sup>P<0.0001 for noninferiority vs active comparator.  
<sup>‡</sup>P<0.001 for superiority vs placebo.  
<sup>§</sup>P<0.001 vs placebo.

No direct comparison can be made across clinical trials. All n values refer to intent-to-treat population.

## Trulicity 1.5 mg demonstrated weight reduction across a comprehensive phase III clinical trial programme<sup>1</sup>



\*P<0.001 vs active comparator.  
<sup>†</sup>P<0.05 vs active comparator.  
<sup>‡</sup>P<0.001 vs placebo.  
 No direct comparisons can be made between clinical trials.  
 Trulicity is not indicated for weight loss, and weight change was a secondary endpoint in clinical trials.<sup>1</sup>

In AWARD-1, AWARD-2 and AWARD-5, additional groups received Trulicity 0.75mg, which is the recommended dose for monotherapy. For potentially vulnerable populations 0.75 mg once weekly can be considered as a starting dose.<sup>1</sup>

# Trulicity 1.5 mg demonstrated cardiovascular benefit in a broad type 2 diabetes population in REWIND<sup>2</sup>

## Study Design

Dulaglutide 1.5 mg weekly vs placebo, both on a background of standard of care

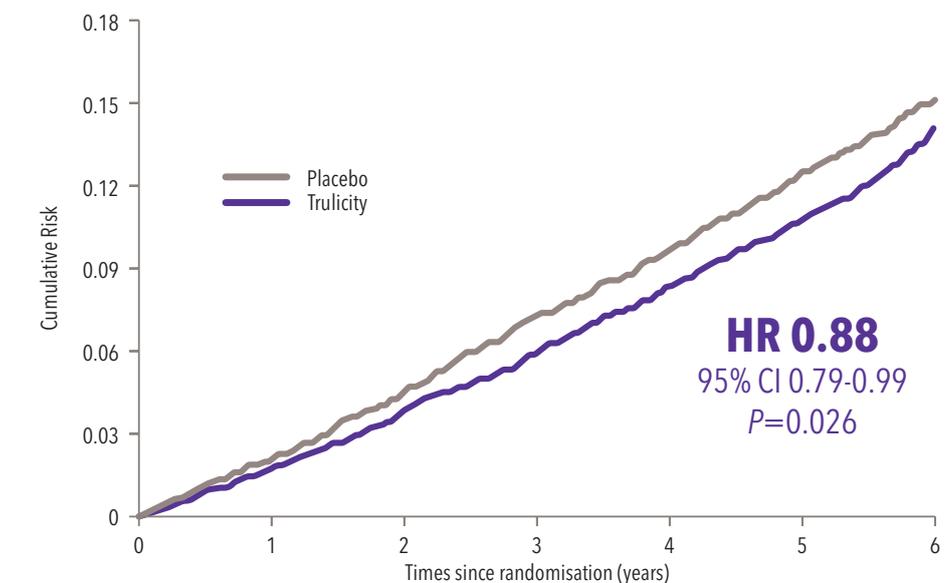
Primary endpoint was 3-point MACE:

Time to first occurrence of non-fatal MI, non-fatal stroke, CV death

## Baseline Characteristics

9901 participants	46.6% female	Median HbA <sub>1c</sub> 55 mmol/mol (7.2%)	Median duration of diabetes 9.5 years	31.5% prior CVD*	68.5% risk factors for CVD
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## Cumulative risk of 3-point MACE outcome



Trulicity 1.5 mg significantly reduced the risk for 3-component MACE by 12% compared with placebo (ARR 1.4%)

No. at Risk							
Placebo	4952	4791	4625	4437	4275	3575	742
Trulicity 1.5 mg	4949	4815	4670	4521	4369	3686	741

## ADA Standards in Medical Care for Diabetes<sup>8</sup>

"... there was consistent benefit in the dulaglutide trial in patients with and without established ASCVD."

\*Myocardial infarction, ischaemic stroke, unstable angina with ECG changes, myocardial ischaemia on imaging or stress test, or coronary, carotid, or peripheral revascularisation.

ADA = American Diabetes Association; ARR = Absolute Risk Reduction; ASCVD = Atherosclerotic Cardiovascular Disease; CI = Confidence Interval; CVD = Cardiovascular Disease; ECG = Electrocardiogram; HR = Hazard Ratio; MI = Myocardial Infarction

# 2019 update to ADA/EASD Consensus Report<sup>9</sup> includes:

"We also suggest that to reduce risk of MACE, GLP-1 receptor agonists can also be considered in patients with type 2 diabetes without established CVD with indicators of high risk, specifically, patients aged 55 years or older with coronary, carotid, or lower extremity artery stenosis >50%, left ventricular hypertrophy, an estimated glomerular filtration rate (eGFR) <60 mL min<sup>-1</sup> [1.73 m]<sup>-2</sup>, or albuminuria."

"Most other CVOTs with GLP-1 receptor agonists [other than REWIND] have included a minority of patients with risk factors only but without evidence of benefit on MACE outcomes in the lower-risk subgroups. Whether the differences in outcomes in trial subgroups without established CVD are related to study details or to the assigned therapy is uncertain."

*"To date, the level of evidence to support the use of GLP-1 receptor agonists for primary prevention is strongest for dulaglutide but lacking for other GLP-1 receptor agonists."*

## Trulicity 1.5 mg is simple to teach and simple to use

Once-weekly dosing<sup>1</sup>

Ready-to-use pen

Pre-attached, hidden, small needle

No need for dose titration to improve GI tolerability at initiation\*

### Simple 3-step injection<sup>10</sup>:



1  
Uncap



2  
Place and unlock

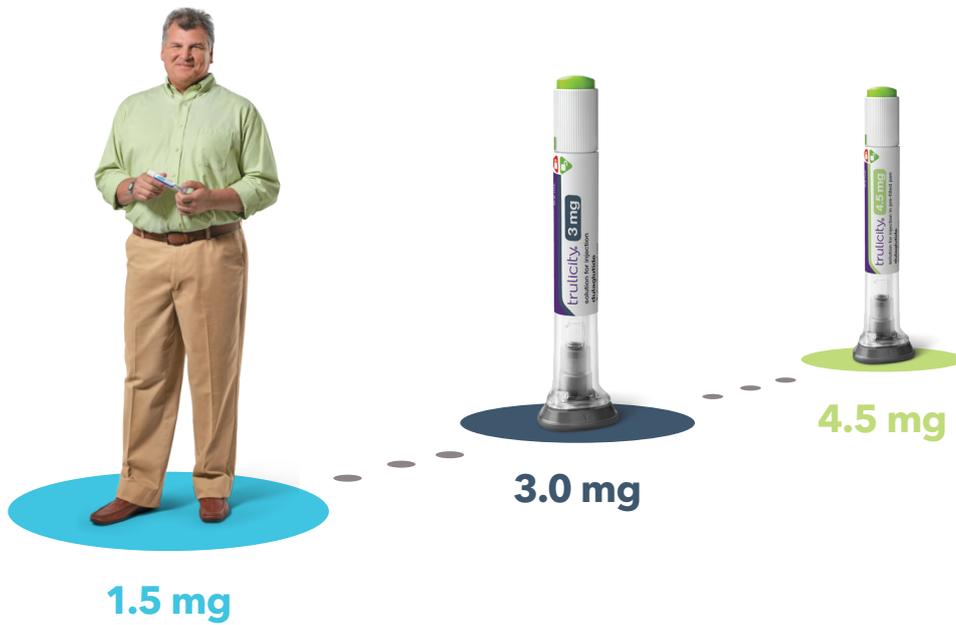


3  
Press and hold

\*For potentially vulnerable populations, 0.75 mg once weekly can be considered as a starting dose.

ADA = American Diabetes Association; CVD = Cardiovascular Disease; CVOT = Cardiovascular Outcomes Trial; EASD = European Association for the Study of Diabetes; GLP-1 = Glucagon-Like Peptide-1; MACE = Major Adverse Cardiovascular Events

# Trulicity also offers 3.0 mg and 4.5 mg doses<sup>1</sup>



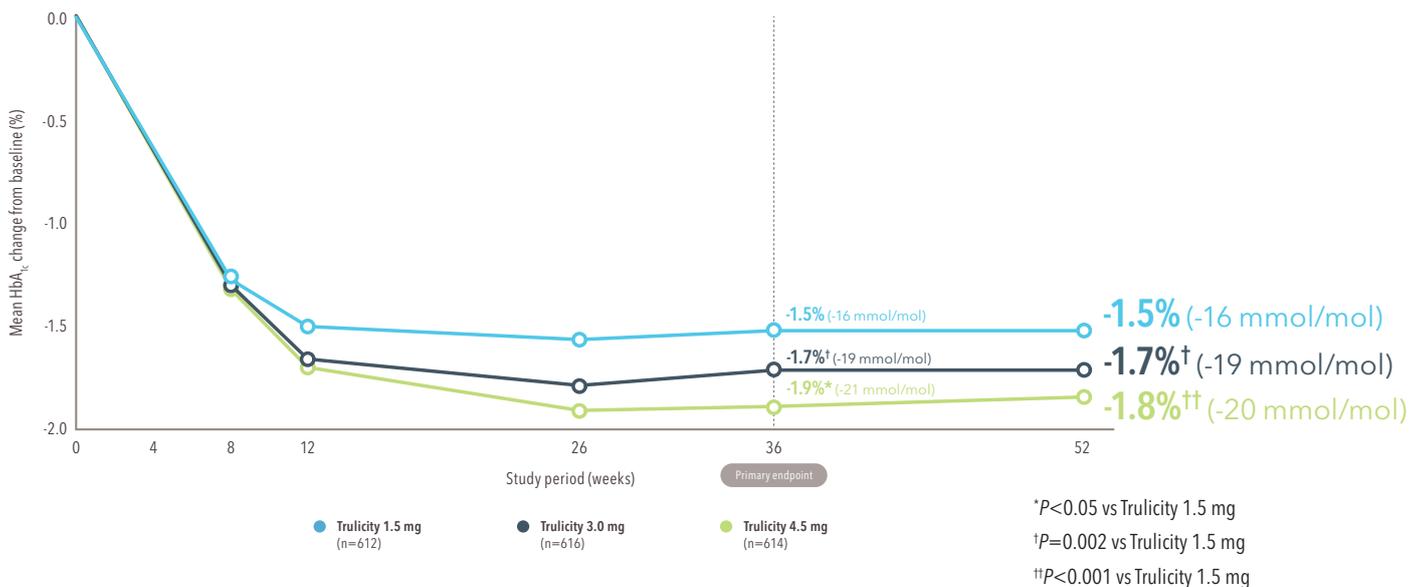
## For additional glycaemic control:<sup>1</sup>

The 1.5 mg dose may be increased after at least 4 weeks to 3.0 mg once weekly.

The 3.0 mg dose may be increased after at least 4 weeks to 4.5 mg once weekly.

## Trulicity 3.0 mg and 4.5 mg doses led to greater glucose lowering in AWARD-11<sup>11</sup>

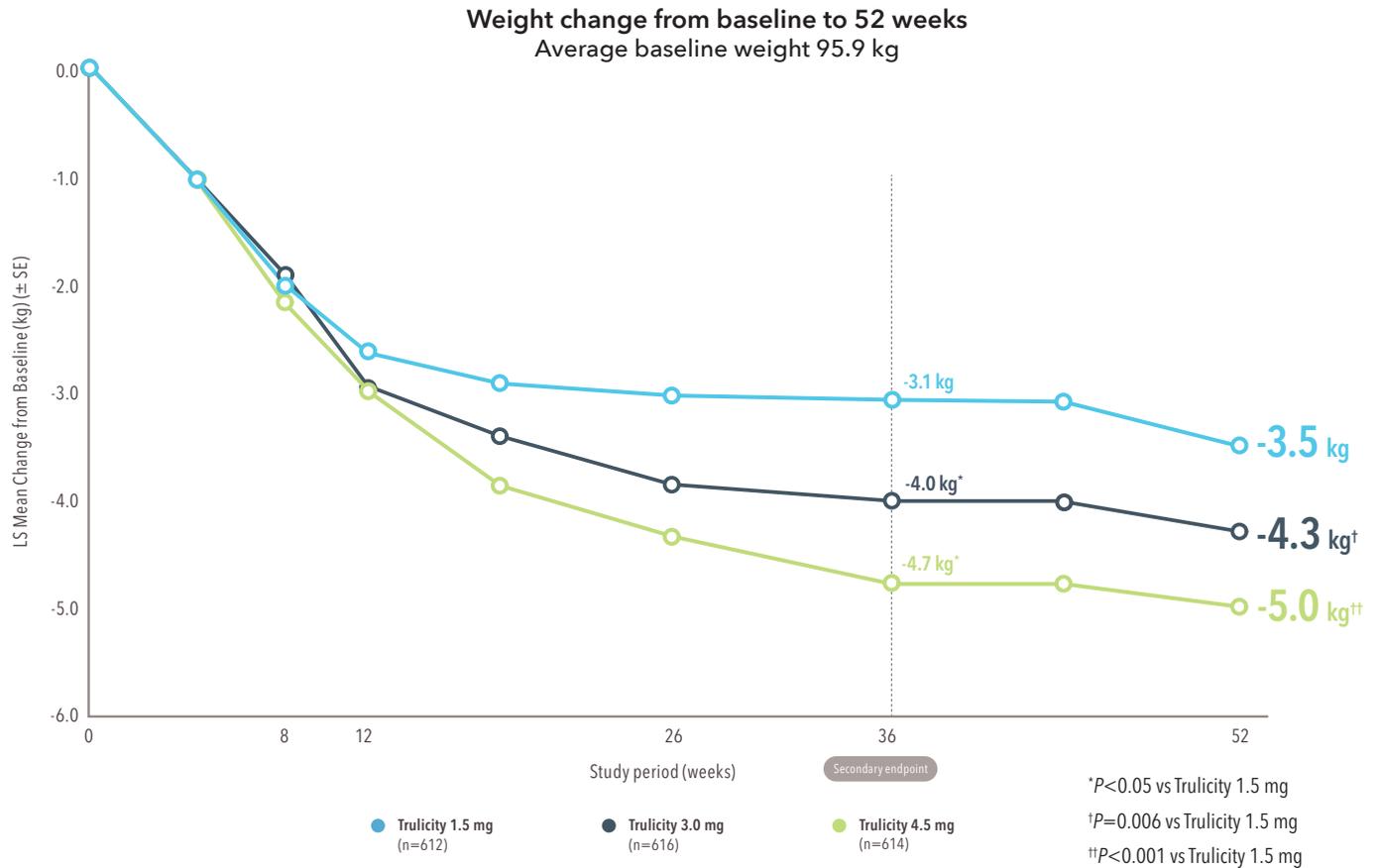
HbA<sub>1c</sub> change from baseline to 52 weeks  
Baseline HbA<sub>1c</sub>=8.6% (70 mmol/mol)



### AWARD-11 study description<sup>11</sup>

- 52-week phase III study of Trulicity 3.0 mg and 4.5 mg vs active control (Trulicity 1.5 mg)
- Treatment was added to background therapy with metformin
- Primary endpoint met: superiority of Trulicity 3.0 mg and 4.5 mg vs Trulicity 1.5 mg on HbA<sub>1c</sub> change from baseline at 36 weeks (P<0.05 vs Trulicity 1.5 mg)
- All n values refer to intent-to-treat population
- All patients initiated treatment with Trulicity 0.75 mg once weekly for 4 weeks; thereafter, the dose of Trulicity was increased every 4 weeks until the assigned dose was reached

# Trulicity 3.0 mg and 4.5 mg doses led to greater weight loss in AWARD-11<sup>11</sup>



Trulicity is not indicated for weight loss, and weight loss was a secondary endpoint in clinical trials.<sup>1</sup>

LS = Least Squares

## Side effect profiles in AWARD-11<sup>11</sup>

In the AWARD-11 trial, doses were escalated every 4 weeks

### GI side effects across doses at 52 weeks

Treatment-emergent adverse events, n (%)	Trulicity 1.5 mg (n=612)	Trulicity 3.0 mg (n=616)	Trulicity 4.5 mg (n=614)
Nausea	87 (14.2)	99 (16.1)	106 (17.3)
Vomiting	39 (6.4)	56 (9.1)	62 (10.1)
Diarrhoea	47 (7.7)	74 (12.0)	71 (11.6)

GI=gastrointestinal

### Trulicity Summary of Product Characteristics:

The safety profile in patients treated with dulaglutide 3.0 mg and 4.5 mg once weekly is consistent with that described for dulaglutide doses of 0.75 mg and 1.5 mg once weekly.<sup>1</sup>

# Trulicity: key safety data<sup>1</sup>

## Selected adverse events and precautions for use

For all information on adverse events and Adverse Event Reporting, please see Trulicity Prescribing Information

### Gastrointestinal events

The most frequently reported adverse reactions in clinical trials were gastrointestinal, including nausea, vomiting and diarrhoea. In general, these reactions were mild or moderate in severity and transient in nature.

### Dehydration

Dehydration, sometimes leading to acute renal failure or worsening renal impairment, has been reported. Patients treated with dulaglutide should be advised of the potential risk of dehydration, particularly in relation to gastrointestinal side effects, and take precautions to avoid fluid depletion.

### Addition to sulphonylurea/insulin

When it is added to existing therapy of a sulphonylurea or insulin, a reduction in the dose of sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia. Blood glucose self-monitoring is necessary to adjust the dose of sulphonylurea/insulin, particularly when dulaglutide therapy is started and insulin is reduced. Diabetic ketoacidosis has been reported in insulin-dependent patients after rapid discontinuation or dose reduction of insulin. A stepwise approach to insulin dose reduction is recommended.

To access resources to support you and your patients on Trulicity®, please visit our Lilly Diabetes Portal:

<https://www.lillydiabetes.co.uk>

**Presentation** Dulaglutide solution for injection in a pre-filled pen. Each single-use pen contains either 0.75 mg, 1.5 mg, 3 mg or 4.5 mg of dulaglutide in 0.5 ml solution. **Uses** Dulaglutide is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise, as monotherapy when metformin is inappropriate due to intolerance or contraindications, or in addition to other medicinal products for the treatment of diabetes. **Dosage and Administration** *Monotherapy:* Recommended dose 0.75 mg once weekly. *Add-on therapy:* Recommended dose 1.5 mg once weekly. For potentially vulnerable patients, 0.75 mg once weekly can be considered as a starting dose. *Additional glycaemic control:* The 1.5 mg dose may be increased after at least 4 weeks to 3 mg once weekly. The 3 mg dose may be increased after at least 4 weeks to 4.5 mg once weekly. The maximum dose is 4.5 mg once weekly. Trulicity is administered as a subcutaneous injection in the abdomen, thigh, or upper arm. It should not be administered intravenously or intramuscularly. The dose can be administered at any time of day, with or without meals. When Trulicity is added to existing metformin and/or pioglitazone therapy, the current dose of metformin and/or pioglitazone can be continued. When Trulicity is added to existing metformin and/or sodium-glucose co-transporter 2 inhibitor (SGLT2i) therapy, the current dose of metformin and/or SGLT2i can be continued. When it is added to existing sulphonylurea or insulin therapy, a reduction in the dose of sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia. Blood glucose self-monitoring is necessary to adjust the dose of sulphonylurea or insulin, particularly when Trulicity therapy is started and insulin is reduced. A stepwise approach to insulin dose reduction is recommended. *Elderly:* No dose adjustment is required based on age. *Renal impairment:* No dose adjustment is required in mild, moderate or severe renal impairment (eGFR < 90 to  $\geq 15$  mL/min/1.73 m<sup>2</sup>). Not recommended in end stage renal disease (< 15 mL/min/1.73 m<sup>2</sup>). *Hepatic impairment:* No dose adjustment is required. *Paediatric:* The safety and efficacy of dulaglutide in children < 18 years have not been established. No data are available. **Contra-indications** Hypersensitivity to the active substance or to any of the excipients. **Warnings and Special Precautions** *Traceability:* In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded. Dulaglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Dulaglutide is not a substitute for insulin. Diabetic ketoacidosis has been reported in insulin-dependent patients after rapid discontinuation or dose reduction of insulin. Not recommended in patients with severe gastrointestinal disease, including severe gastroparesis. Dehydration, sometimes leading to acute renal failure or worsening renal impairment, has been reported in patients treated with dulaglutide, especially at the initiation of treatment. Many of the reported adverse renal events occurred in patients who had experienced nausea, vomiting, diarrhoea, or dehydration. Patients treated with dulaglutide should be advised of the potential risk of dehydration, particularly in relation to gastrointestinal adverse reactions and take precautions to avoid fluid depletion. In clinical trials and the post-marketing setting, acute pancreatitis has been reported in association with dulaglutide. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, dulaglutide should be discontinued. If pancreatitis is confirmed, dulaglutide should not be restarted. Use of dulaglutide in combination with a sulphonylurea or insulin may increase the risk of hypoglycaemia. The risk of hypoglycaemia may be lowered by a reduction in the dose of sulphonylurea or insulin. Trulicity is essentially sodium-free (< 1mmol sodium (23 mg) per dose). **Interactions** Dulaglutide delays gastric emptying. For patients receiving dulaglutide in combination with oral medicinal products with rapid gastrointestinal absorption or prolonged release, there is a potential for

altered medicinal product exposure, particularly at the time of dulaglutide treatment initiation. In the clinical pharmacology studies, dulaglutide doses up to 1.5 mg did not affect the absorption of the orally administered medicinal products tested to any clinically relevant degree. No dose adjustments of paracetamol, atorvastatin, digoxin, lisinopril, metoprolol, warfarin, oral contraceptives, or metformin (immediate release formula) are required when given together with dulaglutide 1.5 mg. For the 4.5 mg dose, absence of major clinically relevant interactions was predicted by physiologically-based pharmacokinetic (PBPK) modelling simulations. For further details of these interaction studies, please see the Summary of Product Characteristics. **Fertility, pregnancy and lactation** Not recommended during pregnancy. Should not be used if breast-feeding. Effect on fertility is unknown. **Effects on ability to drive and use machines** When used in combination with a sulphonylurea or insulin, patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines. **Undesirable Effects** *Very common* ( $\geq 1/10$ ): Hypoglycaemia (when used in combination with insulin, glimepiride, metformin, or metformin plus glimepiride), nausea, diarrhoea, vomiting, abdominal pain. *Common* ( $\geq 1/100$  to < 1/10): Hypoglycaemia (when used as monotherapy, in combination with metformin plus pioglitazone, or in combination with an SGLT2 inhibitor with or without metformin), decreased appetite, dyspepsia, constipation, flatulence, abdominal distention, gastro-oesophageal reflux disease, eructation, fatigue, sinus tachycardia, first-degree atrioventricular block (AVB). *Uncommon* ( $\geq 1/1,000$  to < 1/100): Hypersensitivity, dehydration, injection site reactions, cholelithiasis, cholecystitis. *Rare* ( $\geq 1/10,000$  to < 1/1,000): Acute pancreatitis, anaphylactic reaction, angioedema. *Not Known (cannot be estimated from available data):* Non-mechanical intestinal obstruction. None of the patients with systemic hypersensitivity developed dulaglutide anti-drug antibodies. The safety profile in patients treated with dulaglutide 3 mg and 4.5 mg once weekly is consistent with that described for dulaglutide doses of 0.75 mg and 1.5 mg once weekly. *For full details of these and other side-effects, please see the Summary of Product Characteristics, which is available at : <http://www.medicines.org.uk/emc/>.* **Legal Category** POM **Marketing Authorisation Numbers and Holder** PLGB 14895/0259 PLGB 14895/0260 PLGB 14895/0261 PLGB 14895/0262. Eli Lilly Nederland B.V. Papendorpseweg 83, 3528 BJ Utrecht, The Netherlands **Cost (UK only)** £73.25 per pack of 4 single use pens (0.75 mg) £73.25 per pack of 4 single use pens (1.5 mg) £73.25 per pack of 4 single use pens (3 mg) £73.25 per pack of 4 single use pens (4.5 mg). **Date of Preparation or Last Review** October 2021 **Further Information is Available From** Eli Lilly and Company Limited, Lilly House, Basing View, Basingstoke, Hampshire, RG21 4FA. Telephone: **UK (Great Britain):** + 44-(0) 1256 315000 E-mail: ukmedinfo@lilly.com



Adverse events and product complaints should be reported.  
Reporting forms and information can be found at:  
[www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card  
in the Google Play or Apple App Store.

Adverse events and product complaints should also be reported to Lilly: Please call Lilly UK on 01256 315 000.

## References:

1. Trulicity (dulaglutide) Summary of Product Characteristics. 2. Gerstein HC et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet* 2019;394(10193):121-130. 3. Nauck M et al. Efficacy and safety of dulaglutide versus sitagliptin after 52 weeks in type 2 diabetes in a randomized controlled trial (AWARD-5). *Diabetes Care* 2014;37(8):2149-2158. 4. Dungan KM et al. Once-weekly dulaglutide versus once-daily liraglutide in metformin-treated patients with type 2 diabetes (AWARD-6): a randomised, open-label, phase 3, non-inferiority trial. *Lancet* 2014;384(9951):1349-1357. 5. Wysham C et al. Efficacy and safety of dulaglutide added onto pioglitazone and metformin versus exenatide in type 2 diabetes in a randomized controlled trial (AWARD-1). *Diabetes Care* 2014;37(8):2159-2167. 6. Giorgino F et al. Efficacy and safety of once-weekly dulaglutide versus insulin glargine in patients with type 2 diabetes on metformin and glimepiride (AWARD-2). *Diabetes Care* 2015;38(12):2241-2249. 7. Pozzilli P et al. Placebo-controlled, randomized trial of the addition of once-weekly glucagon-like peptide-1 receptor agonist dulaglutide to titrated daily insulin glargine in patients with type 2 diabetes (AWARD-9). *Diabetes Obes Metab* 2017;19(7):1024-1031. 8. American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes-2019. *Diabetes Care* 2019;42 (Suppl 1):S90-S102. 9. American Diabetes Association. 2019 Update to: Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2020;43:487-493. 10. Trulicity Instructions for Use. 11. Frias J et al. Efficacy and safety of dulaglutide 3 mg and 4.5 mg vs dulaglutide 1.5 mg: 52-week results from AWARD-11. Paper presented at: The American Diabetes Association 80th Scientific Sessions; June 12-16, 2020.