NHS Herts Valleys Clinical Commissioning Group

NHS East and North Hertfordshire Clinical Commissioning Group

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)

DULAGLUTIDE (TRULICITY®) FOR TYPE 2 DIABETES MELLITUS

RECOMMENDED FOR RESTRICTED USE

Name: generic (trade)	What it is	Indication	Date Decision last revised	Decision Status	NICE / SMC Guidance
dulaglutide (Trulicity®)	glucagon-like peptide-1 (GLP-1) receptor agonist	Type 2 diabetes mellitus (T2DM)	June 2016	Final	NICE - none SMC – approved for restricted use

Dulaglutide (Trulicity®) is RECOMMENDED FOR RESTRICTED USE as a GLP-1 receptor agonist option when a GLP-1 receptor agonist is indicated as add-on therapy in line with NICE guidelines for type 2 diabetes (see Policy Drivers overleaf)

- if a specialist service switches a patient from an alternative GLP-1 receptor agonist to dulaglutide clear information should be supplied on rationale and switch process to primary care colleagues.

EFFICACY

- From AWARD studies for change in HbA1c from baseline, weekly dulaglutide was demonstrated to be:
  - (1.5mg or 0.75mg) superior to placebo and exenatide twice daily at 26 weeks
  - (1.5mg or 0.75mg) superior to sitagliptin at 52 weeks
  - 1.5mg non-inferior to liraglutide 1.8mg daily at 26 weeks
  - (1.5mg or 0.75mg) non-inferior to insulin glargine at 52 weeks. Superiority demonstrated for 1.5mg dose.
- Open label design of some of the AWARD studies may have biased results
- No data directly compared to exenetide weekly, liraglutide 1.2mg, lixisenatide or albiglutide.

SAFETY

- According to SPC most common adverse events (≥1/10) are hypoglycaemia, particularly in combination with a sulfonylurea or insulin, and gastrointestinal (GI) disorders.
- According to the EPAR:
  - across the phase II and III integrated safety population, incidence of common events are consistent with other GLP-1 receptor agonists.
  - long-term safety concerns of pancreatitis and pancreatic and thyroid cancers are consistent with other GLP-1 receptor agonists.

COST

- Annual cost of dulaglutide 1.5mg or 0.75mg once weekly is £952:
  - Same cost as most commonly prescribed GLP-1 agonist liraglutide daily at 1.2mg dose and lower cost than 1.8mg dose.
  - Same cost as exenatide weekly.
  - Higher cost than exenatide (twice daily), lixisenatide (daily) & albiglutide (weekly).
- SMC economic analysis suggested dulaglutide was cost effective vs exenatide (twice daily) & lixisenatide (daily) & cost minimising vs liraglutide & exenatide weekly.

PATIENT FACTORS

- Weekly formulation may be preferable for patients to a daily formulation. There would be less demand on time if healthcare professionals are administering injections.
- The prefilled disposable pen device appears to be easier to use than the other weekly GLP-1 agonist devices - needle is hidden and retracts after use & dulaglutide does not require reconstitution (exenatide weekly & albiglutide do)
- Dulaglutide & albiglutide can be used in moderate renal impairment, exenatide weekly cannot.

Background Information

- Dulaglutide is licensed for use in adults with T2DM to improve glycaemic control as: Monotherapy (*NOTE: monotherapy use NOT approved by NICE or locally*) when diet and exercise alone do not provide adequate glycaemic control in patients for whom the use of metformin is considered inappropriate; Add-on therapy in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.
- Dulaglutide available as 0.75mg & 1.5mg solution for subcutaneous injection in single use pre-filled pens.
- The recommended dose is 0.75 mg once weekly (monotherapy) and 1.5 mg once weekly (add-on therapy).
- Should be stored in a refrigerator (2-8 °C) but may be stored unrefrigerated for up to 14 days at up to 30°C.

Assessment against Ethical Framework

Evidence of Clinical Effectiveness and Safety

- Refer to efficacy and safety boxes.
- European Public Assessment report (EPAR) states that the overall effect of dulaglutide on weight was modest across AWARD trials (-0.87kg to -3.03kg), & the clinical relevance of observed effect size with the 1.5 mg dose is uncertain.
- Limited data in certain populations eg people >75 years and people with renal or hepatic disease and heart failure.
- Limited long-term efficacy and safety data.
- As with other GLP-1 agonists, there are limited data from RCTs relating to patient-oriented outcomes, such as rates of macrovascular or microvascular events.
- EPAR reported that dulaglutide has not been studied with sodium-glucose co-transporter 2 inhibitors. Limited experience with basal insulin, thiazolidinediones or sulfonylureas alone, sulfonylureas + thiazolidinediones, & metformin + sulfonylureas + thiazolidinediones.

Safety

- According to the SPC injection site reactions are uncommon (more than 1/1000 to less than 1/100).
- Small mean increases in PR interval (2 to 3 milliseconds from baseline vs placebo) & a 2.4% incidence of first-degree atrioventricular block observed with dulaglutide 1.5mg in people with normal conduction. Clinical relevance uncertain.
- In common with other GLP-1 agonists dulaglutide has CV effects such as reducing blood pressure and increasing heart rate. Clinical relevance uncertain.

Cost of Treatment and Cost Effectiveness

- Refer to cost box

The needs of the population (with the condition)

- Refer to patient factors box.
- Needs of the population may be low as there are alternative GLP-1 agonist options.

The needs of the community (overall local population)

- There would currently be no increased costs if patients prescribed liraglutide 1.2mg/1.8mg or exenatide weekly were prescribed dulaglutide instead. However, dulaglutide is higher cost than other GLP-1 agonists.
- Overall, potential cost impact of the availability of dulaglutide is uncertain. Costs would be increased if it was preferentially used over lower cost alternatives.
- The 1st GLP-1 agonist to lose patent (exenatide) does not do so until the end of 2021.
- A long acting exenatide implant is in development (availability and cost uncertain).

Policy Drivers (national guidance & directions and decisions of other local CCGs)

- Dulaglutide approved as preferred GLP-1 receptor agonist by North Central London Joint Formulary Committee.
- No recommendations/not considered by any other neighbouring CCGs.
- Previous NICE TA recommendations for GLP-1 agonists (liraglutide & exenatide weekly) have been updated and replaced by NICE guideline 28 - T2DM in adults: management. NICE did not consider dulaglutide. Guideline recommendations refer to GLP-1 agonists at a class level. NICE recommends:
  - If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider combination therapy with metformin, a sulfonylurea and a glucagon-like peptide-1 (GLP-1) mimetic for adults who:
    - have a BMI of 35 kg/m^2 or higher (adjust accordingly for people from black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity or
    - have a BMI lower than 35 kg/m^2 and:
      - for whom insulin therapy would have significant occupational implications or
      - weight loss would benefit other significant obesity-related comorbidities.
  - Only continue GLP-1 mimetic therapy if the person has had a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months).
  - Only offer a GLP-1 mimetic in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team
- SMC: approved for restricted use as part of a triple therapy in patients with inadequate glycaemic control on two oral anti-diabetic drugs, as an alternative GLP-1 agonist option.

Equity: No impact anticipated **Implementability:** No issues identified.	**Selected References** (full reference list available in HMMC evaluation) • NICE Evidence summary: new medicine: T2DM:dulaglutide (ESNM59, June 2016) http://www.nice.org.uk/advice/esnm59/chapter/Key-points-from-the-evidence • SMC appraisal: dulaglutide Jan 2016 https://www.scottishmedicines.org.uk/SMC_Advice/Advice/1110_15_dulaglutide_Trulicity/dulaglutide_Trulicity