

## Enc 2 Appx 3

### Clinical Expert Summary Dulaglutide (Trulicity<sup>®</sup>▼) 1.5 mg and 0.75 mg solution for injection

Dulaglutide (Trulicity<sup>®</sup>▼) for adults with type 2 diabetes mellitus to improve glycaemic control as: monotherapy when diet and exercise alone do not provide adequate glycaemic control in people for whom the use of metformin is considered inappropriate due to intolerance or contraindications; as 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.

#### 1. Existing guidelines

Guidelines highlighted by experts include the National Institute for Health and Care Excellence (NICE) guideline on the management of type 2 diabetes in adults (NG 28; published December 2015)<sup>1</sup>, which is consistent with advice given by the Consensus Guidelines for Wales: Designed for the management of adults with diabetes mellitus across Wales (2008)<sup>2</sup>. Experts stated that local health boards in Wales would usually follow the NICE guideline, and that GLP-1 agonist treatment in Wales is often started in secondary care in some areas, but does also happen in primary care.

#### 2. Disease prevalence

Experts referred to a Welsh government source which states that around 7% of adults in Wales are being treated for diabetes and it affects 16% of people over 65 years<sup>3</sup>. The prevalence is expected to rise to 11.5% by 2030<sup>3</sup>. Experts estimated that around 5% of people with type 2 diabetes in Wales are being treated with a GLP-1 agonist, but that this includes people treated outside a triple therapy regimen.

#### 3. Current treatment options

Experts stated that four GLP-1 agonist injectable therapies for type 2 diabetes are available in Wales:

- twice-daily exenatide (Byetta<sup>®</sup>)
- once-daily lixisenatide (Lyxumia<sup>®</sup>▼)
- once-daily liraglutide (Victoza<sup>®</sup>)
- once-weekly exenatide (Bydureon<sup>®</sup>).

All are approved for use in triple therapy, typically with metformin and a sulfonylurea, as an alternative to starting insulin therapy. They note that NICE guidelines have more stringent stopping rules compared to other antidiabetic medicines: 1% reduction HbA<sub>1c</sub> over six months and a 3% reduction in body weight. The experts highlighted their benefits over insulin as: low risk of hypoglycaemia, simplicity of use, and weight loss.

Experts said that liraglutide (Victoza<sup>®</sup>) is the most frequently prescribed GLP-1 agonist in Wales. In some health boards, lixisenatide (Lyxumia<sup>®</sup>▼) is a favoured first-line treatment because it is cheaper than the other treatments and has been shown to be non-inferior to twice daily exenatide (Byetta<sup>®</sup>). Byetta<sup>®</sup> is not commonly prescribed, because it needs to be given twice daily at meal times. Experts stated that uptake of once-weekly exenatide (Bydureon<sup>®</sup>) has been limited, partly due to issues with the injection device and a need for resuspension.

#### 4. Unmet needs

Experts identified that dulaglutide may provide an option for people with reduced (but not severely impaired) renal function. Once-weekly exenatide is not recommended in people with moderate renal impairment (estimated glomerular filtration rate [eGFR] 30-50 ml/min/1.73 m<sup>2</sup>), and lixisenatide and twice-daily exenatide should be used with caution in moderate renal impairment. However, no dose changes of dulaglutide are needed for people with mild-to-moderate renal impairment (eGFR ≥ 30 ml/min/1.73 m<sup>2</sup>).

Experts suggested that once-weekly administration of a treatment is an attractive option for some people with type 2 diabetes. Experts identified that once-weekly administration would save time and cost when injection therapy needs to be given by healthcare staff. Once-weekly dosing may also allow further primary care engagement in starting people on GLP-1 agonist treatment.

### **5. Knowledge of product in given indication**

Experts commented that if approved, dulaglutide would provide an alternative GLP-1 agonist for triple therapy. It was felt that dulaglutide would probably displace Bydureon® as the preferred once-weekly option and would make once-weekly dosing available to more people because of its ease of administration, thus competing with the current once-daily GLP-1 agonists. One expert reported that a better side-effect profile meant that dulaglutide was much better tolerated than once-weekly exenatide; none of their patients had stopped dulaglutide therapy because of gastrointestinal intolerance. Experts reported that they had seen good clinical responses for HbA<sub>1c</sub> reduction and weight loss with dulaglutide. Lixisenatide, which had been used on the basis of cost, had shown good initial HbA<sub>1c</sub> reduction but the response was not sustained for long which necessitated changeover to another GLP-1 agonist.

Experts said that in comparison with Bydureon® the pen device for administering dulaglutide was easy to use: it is smaller and there is no need for resuspension. They commented that specialist diabetes nurses had found that the pen device for dulaglutide was easier to educate to patients in comparison with the once-weekly exenatide device and this had saved clinic time.

One expert felt that if approved, dulaglutide might be initiated by specialists in secondary care. Assessment after six months could be followed by repeat prescribing in primary care. An alternative view was expressed that initiation might be carried out in the primary setting, without input from the secondary sector.

It should be noted that one expert involved in compiling this response declared a personal specific interest in relation to dulaglutide for the indication under consideration; three experts declared personal non-specific interests.

### **REFERENCES**

1. National Institute for Health and Care Excellence. NICE guideline NG28. Type 2 diabetes in adults: management. Dec 2015. Available at: <https://www.nice.org.uk/guidance/ng28>. Accessed Feb 2016.
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3. Welsh Government. Together for health - a diabetes delivery plan. 2013. Available at: <http://gov.wales/docs/dhss/publications/130923diabetesen.pdf>. Accessed Mar 2016.