

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Ertugliflozin as monotherapy and in dual therapy for treating type 2 diabetes

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ertugliflozin within its marketing authorisation for treating type 2 diabetes.

Background

Diabetes mellitus is a chronic metabolic disorder characterised by elevated blood glucose levels (hyperglycaemia) resulting from a lack of the hormone insulin or resistance to its action. Type 2 diabetes results from reduced insulin secretion or reduced tissue sensitivity to insulin (known as insulin resistance). If not managed effectively, diabetes mellitus can lead to kidney failure, blindness, limb amputation, and damage to the nervous system, peripheral vasculature and skin. Cardiovascular disease is the most common complication of type 2 diabetes and is the greatest cause of morbidity and premature death. Life expectancy is reduced by up to 10 years in people with diabetes.

There were over 3 million people aged 17 and over in England with diagnosed diabetes mellitus in 2017.¹ However, many people with type 2 diabetes are undiagnosed, and so the number of people with the condition may be higher than reported. The UK prevalence of type 2 diabetes is rising because of increased prevalence of obesity, decreased physical activity and increased life expectancy after diagnosis because of better cardiovascular risk protection. Type 2 diabetes is particularly prevalent in people of African, South Asian and Caribbean family origin.

NICE guideline 28 [‘type 2 diabetes in adults: management’](#) recommends reinforcing advice on diet, lifestyle and adherence to drug treatment for all people with type 2 diabetes. If there is inadequate glycaemic control on diet and exercise alone:

- NG28 recommends standard release metformin. When metformin is contraindicated or not tolerated a dipeptidyl peptidase-4 (DPP-4) inhibitor, pioglitazone or a sulfonylurea is recommended.
- NICE [technology appraisal 390](#) recommends the selective sodium glucose-cotransporter 2 (SGLT-2) inhibitors canagliflozin, dapagliflozin and empagliflozin as options for monotherapy in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if a DPP-4 inhibitor would

otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate.

When there is inadequate glycaemic control following initial therapy, treatment is intensified:

- NICE guideline 28 recommends dual therapy with metformin plus a DPP-4, pioglitazone or a sulfonylurea. When metformin is contraindicated or not tolerated alternative dual therapies such as a DPP-4 and pioglitazone, a DPP-4 and a sulfonylurea or pioglitazone and a sulfonylurea are recommended.
- NICE [technology appraisals 315](#), [288](#) and [336](#) recommend a SGLT-2 inhibitor (canagliflozin, dapagliflozin and empagliflozin respectively) in a dual therapy regimen with metformin, only if a sulfonylurea is contraindicated or not tolerated or the person is at significant risk of hypoglycaemia or its consequences.

The technology

Ertugliflozin (Steglatro, Merck Sharp & Dohme) is a SGLT-2 inhibitor, which blocks the reabsorption of glucose in the kidneys and promotes excretion of excess glucose in the urine. Through this mechanism, ertugliflozin may help control glycaemia independently of insulin pathways. It is administered orally.

Ertugliflozin has a marketing authorisation in the UK for treating adults aged 18 years and older with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control:

- as monotherapy in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications
- in addition to other medicinal products for the treatment of diabetes.

Intervention	Ertugliflozin alone or in a dual therapy regimen
Population	<p><u>Ertugliflozin monotherapy:</u> Adults with type 2 diabetes that is inadequately controlled with diet and exercise alone and in whom the use of metformin is considered inappropriate due to intolerance or contraindications</p> <p><u>Ertugliflozin in a dual therapy regimen:</u> Adults with type 2 diabetes that is inadequately controlled with monotherapy</p>

Comparators	<p>The following interventions as monotherapy:</p> <ul style="list-style-type: none"> • sulfonylureas • pioglitazone • DPP-4 inhibitors • other SGLT-2 inhibitors (if a DPP-4 inhibitor would otherwise be prescribed and a sulfonylurea or pioglitazone is not appropriate) <p>The following interventions in a dual therapy regimen:</p> <ul style="list-style-type: none"> • sulfonylureas • DPP-4 inhibitors • pioglitazone • SGLT-2 inhibitors
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • mortality • complications of diabetes, including cardiovascular, renal and eye • HbA1c/glycaemic control • body mass index • frequency and severity of hypoglycaemia • changes in cardiovascular risk factors • adverse effects of treatment, including urinary tract infections, genital infections and malignancies • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>

<p>Other considerations</p>	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>‘Dapagliflozin in triple therapy for treating type 2 diabetes’ (2016) NICE Technology Appraisal 418. Review date November 2019.</p> <p>‘Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes’ (2016) NICE Technology Appraisal 390. Review date May 2019.</p> <p>‘Empagliflozin in combination therapy for treating type 2 diabetes’ (2015) NICE Technology Appraisal 336. Review proposal in progress.</p> <p>‘Canagliflozin in combination therapy for treating type 2 diabetes’ (2014). NICE Technology Appraisal 315. Review proposal in progress.</p> <p>‘Dapagliflozin in combination therapy for treating type 2 diabetes’ (2013). NICE Technology Appraisal 288. Review proposal in progress.</p> <p>Related Technology Appraisals in development:</p> <p>‘Ertugliflozin in triple therapy for treating type 2 diabetes’ NICE technology appraisals guidance [ID1160]. Publication expected TBC.</p> <p>Related Guidelines:</p> <p>‘Type 2 diabetes in adults: management’ (2015 updated 2016) NICE guideline NG28. Currently under review.</p> <p>Guidelines in development</p> <p>‘Type 2 diabetes management’ [partial update of NG28]. NICE guideline. Publication expected December 2017.</p> <p>Related Quality Standards:</p> <p>Quality Standard No. 6, Mar 2011, updated 2016 ‘Diabetes in adults’.</p> <p>Related NICE Pathways:</p> <p>NICE Pathway: Diabetes, Pathway created: May 2011: https://pathways.nice.org.uk/pathways/diabetes.</p>

Related National Policy	NHS England Manual for Prescribed Specialised Services 'Adult specialist endocrinology services' (chapter 9) https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017
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References

1. [Quality and outcomes framework \(QOF\) for 2016-17](#) (2017). Accessed May 2018.