# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

## Dapagliflozin in triple therapy regimens for treating type 2 diabetes

## Final scope

### Remit

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

### Appraisal objective

This appraisal is a part-review of NICE technology appraisal (TA) 288, dapagliflozin combination treatment. It will only consider recommendation 1.3 in TA288, dapagliflozin triple therapy. The other recommendations in TA288 remain extant.

### Background

Type 2 diabetes is a chronic metabolic condition characterised by insulin resistance (that is, the body's inability to effectively use insulin) and insufficient pancreatic insulin production, resulting in high blood glucose levels (hyperglycaemia). Type 2 diabetes is commonly associated with obesity, physical inactivity, raised blood pressure, disturbed blood lipid levels and a tendency to develop thrombosis, and therefore is recognised to have an increased cardiovascular risk. It is associated with long-term microvascular and macrovascular complications, together with reduced quality of life and life expectancy

In 2014 there were approximately 2.8 million adults in England with diabetes, of whom 90% had type 2 diabetes[i]. However, many people with type 2 diabetes are undiagnosed, and so the number of people with the condition may be higher than reported (it is estimated that there are around 590,000 people in the UK who have diabetes but have not been diagnosed[i]). 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[i].

NICE guideline (NG) 28 ‘Type 2 diabetes in adults: management’ recommends an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes. It recommends beginning with dietary advice and increasing physical activity for all people with type 2 diabetes. If blood glucose is not adequately controlled by lifestyle interventions alone, the guideline recommends one or more oral anti-diabetic drugs, beginning with metformin. If blood glucose is not adequately controlled

following monotherapy, dual therapy should be considered followed by either the addition of insulin or triple therapy. For triple therapy, NG28 recommends considering a combination of metformin with: a dipeptidyl peptidase-4 (DPP-4) inhibitor and a sulfonylurea, and; pioglitazone and a sulfonylurea. If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, NG28 recommends considering combination therapy with metformin, a sulfonylurea and a glucagon-like peptide-1 (GLP-1) agonist for some people with type 2 diabetes. NICE technology appraisals (TA) 315 and 336 recommended canagliflozin and empagliflozin respectively for triple therapy in combination with metformin and a sulfonylurea, or metformin and a thiazolidinedione. TA288 recommended that dapagliflozin should not be used for triple therapy except as part of a clinical trial; this recommendation will be the subject of this appraisal (because there is new evidence now available about this recommendation).

**The technology**

Dapagliflozin (Forxiga, AstraZeneca) is a selective sodium glucose-cotransporter 2 (SGLT-2) inhibitor, which blocks the reabsorption of glucose in the kidneys and promotes excretion of excess glucose in the urine. Through this mechanism, dapagliflozin may help control glycaemia independently of insulin pathways. It is administered orally.

Dapagliflozin has a UK marketing authorisation in "adults aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control as:

- Monotherapy: When diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance.

- Add-on combination therapy: In combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control"

| | |
|---|---|
| **Intervention(s)** | Dapagliflozin in combination with 2 other oral anti-diabetic agents |
| **Population(s)** | Adults with type 2 diabetes that is inadequately controlled on dual therapy with either:<br>• metformin with a sulfonylurea<br>• metformin with a DPP-4 inhibitor |
| **Comparators** | The following in combination with 2 other oral antidiabetic agents:<br>• other SGLT2 inhibitors<br>• DPP-4 inhibitors<br>• pioglitazone |

| | |
|---|---|
| | • GLP-1 agonists<br>• a sulfonylurea<br>• insulin |
| **Outcomes** | The outcome measures to be considered include:<br>• mortality<br>• complications of diabetes, including cardiovascular, renal and eye<br>• HbA1c/glycaemic control<br>• body mass index<br>• frequency and severity of hypoglycaemia<br>• changes in cardiovascular risk factors<br>• adverse effects of treatment, including urinary tract infections, genital infections and malignancies<br>• health-related quality of life. |
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective. |
| **Other considerations** | 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. |
| **Related NICE recommendations and NICE Pathways** | Related Technology Appraisals:<br>'Empagliflozin in combination therapy for treating type 2 diabetes' (2015). NICE Technology Appraisal 336. Review proposal date March 2018.<br>'Canagliflozin in combination therapy for treating type 2 diabetes' (2014). NICE Technology Appraisal 315. Review proposal date May 2017.<br>'Dapagliflozin in combination therapy for treating type 2 |

| | |
|---|---|
| | diabetes' (2013). NICE Technology Appraisal 288. Review Proposal Date TBC.<br><br>Appraisals in development (including suspended appraisals)<br><br>'Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes'. NICE technology appraisals guidance [ID756]. Publication expected May 2016.<br><br>Related Guidelines:<br><br>'Type 2 diabetes in adults: management' (2015). NICE guideline 28. Review date December 2017.<br><br>'Diabetic foot problems: prevention and management' (2015). NICE Guideline 19. Review date February 2017.<br><br>'Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period' (2015). NICE guideline 3. Review date TBC.<br><br>'Diabetes in adults' (2011). NICE quality standard 6.<br><br>Related NICE Pathways: Diabetes (2011). NICE pathway |
| **Related National Policy** | NHS England (2014) 'Manual for Prescribed Specialised Services'. Chapter 67.<br><br>Department of Health (2001) 'National Service Framework: Diabetes'.<br><br>Department of Health (2014) 'NHS Outcomes Framework 2015-16'. Domains 1 to 5. |

## References

[i] Diabetes UK (2015) 'Diabetes: Facts and Stats'. Accessed December 2015.