NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Teplizumab for delaying the onset of stage 3 type 1 diabetes in people 8 years and over with stage 2 type 1 diabetes [ID6259]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of teplizumab within its marketing authorisation for delaying the onset of stage 3 (symptomatic) type 1 diabetes in people aged 8 and over with stage 2 type 1 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 1 diabetes results from the body's own immune system destroying the cells that make insulin[1]. If not managed effectively, diabetes mellitus can lead to kidney failure, blindness, foot problems, and damage to the nervous system[2]. People with diabetes are also more at risk of cardiovascular disease[3].

Type 1 diabetes progresses across the following three stages[4]:

- **Stage 1 type 1 diabetes**: presence of 2 or more pancreatic islet autoantibodies, but a normal concentration of blood glucose. Clinical symptoms are not present at Stage 1.
- **Stage 2 type 1 diabetes**: 2 or more pancreatic islet autoantibodies and dysglycaemia (abnormalities in blood glucose levels) without reaching thresholds for hyperglycaemia. Clinical symptoms are not present at Stage 2.
- **Stage 3 (symptomatic) type 1 diabetes**, is defined by overt hyperglycaemia, accompanied by clinical symptoms. In Stage 3, people with type 1 diabetes will usually require lifelong insulin therapy as treatment.

Pancreatic islet autoantibodies can be measured using a blood sample. Dysglycaemia can be assessed in different ways including an oral glucose tolerance test or measurement of HbA1c.

In 2021-22, there were 9,760 people newly diagnosed with type 1 diabetes in England and Wales[5]. Most people with type 1 diabetes are diagnosed in stage 3. There is no national screening programme to identify people with stage 1 or 2 type 1 diabetes. Type 1 diabetes can present at any age, peaking in presentation around age 12 years[6]. Type 1 diabetes is slightly more common in males than females[6].

NICE's clinical guideline on the diagnosis and management of type 1 diabetes in adults (NG17) states that diabetes is typically diagnosed when people present with hyperglycaemia. The type of diabetes can be assessed using diabetes-specific autoantibodies and, if needed, non-fasting serum C-peptide. The management of

© National Institute for Health and Care Excellence 2024. All rights reserved.

type 1 diabetes in adults includes structured education, dietary management, physical activity, self-monitoring of blood glucose levels, insulin therapy, hypoglycaemia control, control of cardiovascular risk and treating complications.

NICE's clinical guideline on the diagnosis and management of type 1 and 2 diabetes in children and young people (NG18) highlights symptoms of stage 3 type 1 diabetes including: hyperglycaemia (random plasma glucose more than 11 mmol/litre), polyuria, polydipsia, weight loss, and excessive tiredness. The management of type 1 diabetes in children and young people includes education, dietary management, exercise, self-monitoring of blood glucose levels, insulin therapy, psychosocial support, and hypoglycaemia control.

There are no guidelines for the management of people with stage 2 type 1 diabetes but established clinical management will likely include monitoring blood glucose, psychosocial support and education about diabetes care.

The technology

Teplizumab (Tzield, Sanofi) does not currently have a marketing authorisation in the UK for delaying type 1 diabetes. It has been studied in clinical trials compared with placebo in people aged 8 and over with 2 or more pancreatic islet autoantibodies and abnormal glucose tolerance.

Intervention(s)	Teplizumab
Population(s)	People aged 8 and over with stage 2 type 1 diabetes (2 or more pancreatic islet autoantibodies and dysglycaemia)
Subgroups	If evidence allows, consideration may be given to subgroups based on age. If consideration is given to these subgroups, the committee will consider any equalities implications of its considerations.
Comparators	Established clinical management without tepilizumab including, but not limited to: • monitoring blood glucose • psychosocial support • education

© National Institute for Health and Care Excellence 2024. All rights reserved.

Outcomes	The outcome measures to be considered include: • progression from stage 2 to stage 3 type 1 diabetes • time to starting insulin treatment • levels of stimulated C-peptide • symptoms and complications of type 1 diabetes including incidence of diabetic ketoacidosis • mortality • adverse effects of treatment • 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. 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. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account The use of teplizumab is conditional on the presence of pancreatic islet autoantibodies. The economic modelling should include the costs associated with diagnostic testing for pancreatic islet autoantibodies in people who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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	**Related technology appraisals:** Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes. (2023) NICE Technology appraisal guidance TA943

© National Institute for Health and Care Excellence 2024. All rights reserved.

	Sotagliflozin with insulin for treating type 1 diabetes. (2020) NICE Technology appraisal guidance TA622 **Related NICE guidelines:** Diabetic foot problems: prevention and management. (2019) NICE guideline NG19 Diabetes (type 1 and type 2) in children and young people: diagnosis and management. (2022) NICE guideline NG18 Type 1 diabetes in adults: diagnosis and management. (2022) NICE guideline NG17 **Related interventional procedures:** Allogeneic pancreatic islet cell transplantation for type 1 diabetes mellitus. (2008) NICE Interventional procedures guidance IPG257 **Related quality standards:** Type 1 diabetes in adults. (2023) NICE quality standard QS208 Diabetes in children and young people. (2022) NICE Quality standard QS125 Diabetes in pregnancy. (2023) NICE Quality standard QS109
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan

References

1. NHS Diabetes. Accessed May 2024
2. Diabetes UK Complications of diabetes. Accessed May 2024
3. Diabetes UK Diabetes and heart disease. Accessed May 2024
4. Besser et al. (2022) ISPAD clinical practice consensus guidelines 2022: Stages of type 1 diabetes in children and adolescents. Accessed September 2024
5. NHS Digital National Diabetes Audit 2021-22, Report 1: Care Processes and Treatment Targets, Detailed Analysis Report. Accessed May 2024
6. NHS Digital. National Diabetes Audit, 2019-20 Type 1 Diabetes. Accessed September 2024

© National Institute for Health and Care Excellence 2024. All rights reserved.