NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

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

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using teplizumab in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Issue date: August 2025

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using teplizumab in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 08 September 2025
- Second evaluation committee meeting: 07 October 2025
- Details of membership of the evaluation committee are given in section 4

1 Recommendations

1.1 Teplizumab should not be used for delaying the onset of stage 3 type 1 diabetes in people 8 years and over with stage 2 type 1 diabetes.

1.2 This recommendation is not intended to affect treatment with teplizumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop. For children or young people, this decision should be made jointly by the healthcare professional, the child or young person, and their parents or carers.

What this means in practice

Teplizumab is not required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because there is not enough evidence to determine whether teplizumab is value for money in this population.

Why the committee made these recommendations

There is no treatment available for delaying the onset of stage 3 type 1 diabetes in people 8 years and older with stage 2 type 1 diabetes.

For most people, type 1 diabetes is diagnosed at stage 3. But it may be diagnosed at stage 2. Usual treatment for stage 2 type 1 diabetes includes blood glucose monitoring, education and psychosocial support.

Clinical trial evidence shows that, compared with placebo, teplizumab delays progression to stage 3 type 1 diabetes.

But there are uncertainties in the economic model about the:

- population eligible for teplizumab
- costs of managing stage 3 type 1 diabetes
- effects of stage 3 type 1 diabetes on quality of life.

Because of the uncertainties in the economic model, it is not possible to determine the most likely cost-effectiveness estimates for teplizumab.

So, teplizumab should not be used.

2 Information about teplizumab

Anticipated marketing authorisation indication

2.1 Teplizumab (Tzield, Sanofi) is expected to be indicated to 'delay the onset of stage 3 type 1 diabetes in adult and paediatric patients 8 years of age and older with Stage 2 type 1 diabetes'.

Dosage in the marketing authorisation

2.2 The dosage schedule will be available in the summary of product characteristics for teplizumab.

Price

2.3 The proposed list price of teplizumab is confidential so cannot be reported here.

2.4 The company has a commercial arrangement, which would have applied if teplizumab had been recommended.

Carbon Reduction Plan

2.5 Information on the Carbon Reduction Plan for UK carbon emissions for Sanofi will be included here when guidance is published.

3 Committee discussion

The evaluation committee considered evidence submitted by Sanofi, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Details of condition and treatment options

3.1 Type 1 diabetes (T1D) is a chronic metabolic condition caused by the immune system destroying the cells that make insulin, which leads to elevated blood glucose levels (hyperglycaemia). T1D can be categorised as 3 progressive stages depending on blood glucose levels, the presence of autoantibodies and the presence of symptoms. Stage 1 and stage 2 T1D are asymptomatic, but 2 or more pancreatic islet autoantibodies will be present. Stage 3 T1D is symptomatic and is defined by significantly raised blood sugar levels (hyperglycaemia) that requires insulin to manage. T1D is not routinely diagnosed by stage in clinical practice and mostly it is diagnosed at stage 3, when clinical symptoms start to appear. After progression to stage 3, lifelong insulin therapy is usually needed. T1D has been associated with reduced life expectancy and can lead to health complications including diabetic ketoacidosis, kidney failure, cardiovascular disease, blindness, foot problems and damage to the nervous system. The patient experts explained that the demands of lifelong self-management of T1D are all-encompassing and place significant psychological burden on people with the condition and their carers. The challenges of managing T1D are particularly pronounced when also caring for children with the condition and are sustained as the child gets older. There are currently no treatment options available to delay the onset of stage 3 T1D. The patient experts explained that delaying the onset of stage 3 may lead to fewer long-term complications. They emphasised that delaying onset of stage 3 would give people more time to prepare for the challenges of managing T1D once symptoms arise.

This additional time would be particularly beneficial for people who are less able to independently manage their condition, such as children and young people, and allow them more time to mature and focus on passing through key developmental milestones. The committee acknowledged that T1D has a large impact on people with the condition and their carers. It concluded there is an unmet need for treatment options to delay the onset of stage 3 T1D.

Treatment pathway

3.2 Most people enter the T1D treatment pathway at stage 3 after symptom onset. Management of stage 3 T1D includes insulin, blood glucose monitoring, carbohydrate counting and exercise. Because stage 2 is asymptomatic it is not usually identified in routine practice but may be diagnosed in research studies (see section 3.3). Once stage 2 T1D has been identified, established clinical management may include monitoring of blood glucose levels, psychosocial support and education. The clinical experts explained that until recently, there have been no treatments like teplizumab for people in stage 2 T1D. Submissions from professional organisations and NHS England stated there is no widespread testing or national pathway of care for pre-symptomatic T1D (that is, stage 1 and stage 2). They explained that, if teplizumab were recommended, a new pathway of care would need to be established. This would need to include standardised methods of autoantibody testing to identify people with stage 2 T1D, appropriate follow up for those identified, resources for administering teplizumab in secondary care and additional training for clinical staff. They stated that this would place a significant additional demand on the NHS. The committee acknowledged the need for additional infrastructure in the NHS to support any potential recommendation of teplizumab.

Identifying the eligible population for teplizumab

3.3 In its submission, the company defined the eligible population as people aged 8 years and over with stage 2 T1D (defined as those with 2 or more islet autoantibodies and dysglycaemia) who are at risk of progression to stage 3 T1D. This is in line with the anticipated licensed indication and the population from the clinical trial, TN-10 (see section 3.5). But because people with stage 2 T1D are asymptomatic, and there are no national screening programmes to identify people with stage 2 T1D, the EAG was concerned about how people eligible for teplizumab would be identified in practice. It emphasised the importance of identifying selection criteria for diagnostic testing and explained that the method of identifying people eligible for treatment could significantly impact the treatment benefits. It suggested that screening should be included as part of the intervention (that is, in addition to teplizumab) or that the population eligible for teplizumab should be limited to people aged 8 and over in whom stage 2 T1D has been incidentally detected. The company had decided the inclusion of screening was outside the remit of the evaluation, so did not include screening costs in the model. The company explained that children and young people with stage 2 T1D are being identified in both the NHS and in research trials. The clinical experts explained there are 4 distinct populations that may be tested and subsequently identified as having stage 2 T1D. These are people who:

- are identified in research studies
- are tested because of clinical concerns about hyperglycaemia (for example, as a consequence of steroid use for other autoimmune conditions)
- have a first-degree relative with T1D
- request autoantibody testing.

The clinical experts explained that for about 50% of people with stage 2 T1D, it is diagnosed in routine clinical practice (that is, they are offered testing because of clinical concerns or having a first-degree relative

with T1D, or they request autoantibody testing). So, there is a population of people already diagnosed with stage 1 T1D who could benefit from teplizumab after progression to stage 2. The clinical experts also explained that the current demand for antibody testing is low because there is no available treatment to delay the onset of stage 3 T1D. If a treatment to delay stage 3 T1D becomes available there would likely be an increase in the number of people coming forward for autoantibody testing. But the size of this increase is not known. The committee questioned the potential population size and the proportion of people that would have stage 2 T1D if tested. The clinical experts explained that in the general population the expected risk of having T1D at any stage (that is, people having autoantibodies) is 1 in 300 to 1 in 400, and this risk substantially increases to 1 in 10 to 1 in 20 for people with a first-degree relative with T1D. They also explained that some people initially have a negative autoantibody result and then have a positive result at a later date. But these are mostly younger children who would not be eligible for teplizumab. The committee noted there was significant uncertainty about how much autoantibody testing would occur if teplizumab were recommended and the subsequent impacts to the NHS, which may be significant (see section 3.2). The committee understood that more primary research is needed on the effects of screening in T1D and it is unlikely that a coordinated national screening programme would be introduced in the near future. The committee acknowledged that if teplizumab were recommended, there would be an expected increase in people requesting autoantibody testing with subsequent diagnosis of stage 2 T1D. It also recognised that some incidental diagnosis of stage 2 T1D is already happening in NHS practice. The consideration of a national screening programme is outside the committee's remit, so it agreed the costs of a national screening programme should not be included in the model. But it decided that the potential increase in demand for ad-hoc autoantibody testing and the associated costs, if teplizumab were recommended,

should have been captured in the model. The committee also decided that the lack of data on the size and composition of the population eligible for teplizumab was a significant uncertainty. It concluded that it needed more information on the number of people in each of the identified populations that might present for autoantibody testing. It would also like more information on how autoantibody testing would be commissioned in practice.

Appropriateness of established clinical management as a comparator

3.4 The comparator in the company's submission was established clinical management without teplizumab, which includes blood glucose monitoring, education and psychosocial support. The EAG questioned whether this was the appropriate comparator because people with stage 2 T1D are not routinely identified in NHS practice (see section 3.2). The EAG explained that if the population is not being identified in routine practice because there is no screening, then the appropriate comparator would be no management. It suggested that if screening was included with teplizumab, with no routine screening or management as the comparator, the costs in the comparator arm would be zero. The committee decided not to include screening costs in the intervention (see section 3.3). It noted some people may be identified after presenting for testing within the NHS (see section 3.2). It decided there are costs associated with monitoring people with diagnosed stage 2 T1D. The committee concluded that established clinical management is an appropriate comparator.

Clinical effectiveness

TN-10 trial

3.5 The clinical-effectiveness evidence for teplizumab came from TN-10, a multicentre, randomised, double-blind, placebo-controlled phase 2 trial of teplizumab. TN-10 included 76 people aged 8 and over with stage 2 T1D who were first-degree relatives of people with stage 3 T1D. The primary

outcome in the trial was time from randomisation to onset of stage 3 T1D as defined by the American Diabetes Association. Secondary outcomes included C-peptide levels, insulin secretion and adverse events. In the primary analysis (median follow up of 24.5 months), the time to stage 3 T1D onset was 49.5 months in the teplizumab arm and 24.9 months in the placebo arm (difference 24.6 months; hazard ratio 0.41, p=0.0066). In the extended follow up (median 30.3 months), the time to stage 3 T1D onset was 59.6 months in the teplizumab arm and 27.1 months in the placebo arm (difference 32.5 months; hazard ratio 0.457, p=0.01). The committee concluded that treatment with teplizumab leads to a statistically significant delay in progression to stage 3 T1D in the trial population (that is, people with stage 2 T1D who are first-degree relatives of people with stage 3 T1D).

Generalisability

3.6 The population of TN-10 was selected from a larger study, TN-01. This is an ongoing screening and monitoring study in people with diagnosed stage 2 T1D who are relatives of people with stage 3 T1D. The EAG advised that the number of people in TN-10 (n=76) was small relative to the number of people assessed for trial eligibility from TN-01 (n=146). It also noted that the process of selecting eligible participants from TN-01 was unclear. Combined with the uncertainty in identifying the stage 2 T1D population in NHS practice (see section 3.3), the EAG was concerned about how representative the TN-10 population (relatives of people with stage 3 T1D) was of the full stage 2 T1D population in NHS practice. The company clarified that the eligibility criteria were wider for TN-01 than TN-10. It explained some of the reasons why people from TN-01 were not eligible. These included having stage 1 T1D, less than 2 diabetes-related autoantibodies, not meeting the minimum age for the TN-10 trial population (8 years) and participation in other trials. The committee considered whether the rate of progression from stage 2 to stage 3 T1D differs based on family history of T1D. The company stated that family

history of T1D was not significantly associated with risk of progression. The clinical experts explained that there was no evidence to suggest differences in progression based on family history. The committee concluded that data from TN-10 is suitable for decision making, but acknowledged that the generalisability of the clinical trial data may be affected by uncertainties in identifying the stage 2 T1D population in NHS practice.

Adverse events

3.7 TN-10 investigated adverse events associated with teplizumab, including treatment-emergent adverse events of special interest (AESIs). Adverse events occurred more often in the teplizumab arm compared with placebo (the incidence of AESIs is confidential and cannot be reported here). The EAG noted that teplizumab appears to be associated with increased risk of infection and of blood and lymphatic system disorders, particularly severe neutropenia (grade 3 and above). It was also concerned that because TN-10 had a small patient population, the potential impact of AESIs from teplizumab on the immune system was unclear. The clinical experts explained that the effect of teplizumab is immunomodulatory rather than immunosuppressive, and the observed impact on white blood cells from teplizumab in TN-10 is in line with what would be expected in clinical practice. They also clarified that levels of lymphocytes and neutrophils would be expected to recover within the initial 14-day period of teplizumab administration. The company included the costs of the most common adverse events reported during treatment with teplizumab in its model. The committee noted that the model included the cost of medicines to prevent cytokine release syndrome (CRS), such as nonsteroidal anti-inflammatory drugs, but CRS was not included as an adverse event in the model. The committee considered whether the costs of all the relevant adverse events had been captured in the model. The company explained that 1 person in the teplizumab arm of TN-10 had a grade 2 (moderate) adverse event of CRS that was considered likely

related to teplizumab. It also stated that an integrated safety analysis from 5 clinical trials of people with stage 2 or stage 3 T1D (n=1,018) showed a CRS rate of 5.8% in people having teplizumab. The clinical experts explained that most cases of CRS with teplizumab are mild and are managed with ibuprofen and paracetamol, with most occurring in the first 5 days of teplizumab infusion in hospital where people are regularly monitored. The committee decided that the costs of adverse events are not fully captured in the model. It concluded that the costs of CRS should be included in the teplizumab arm of the model, in line with the incidence rate of 5.8% from the integrated safety analysis. But it acknowledged that because CRS tends to occur early on and is managed in hospital with over-the-counter medicines, this is unlikely to be a significant driver of the cost-effectiveness estimates.

Economic model

Company's modelling approach

3.8 The company developed a Markov model with 3 mutually exclusive health states; stage 2 T1D, stage 3 T1D and death. The model used a lifetime horizon (up to a maximum age of 100 years) and a cycle length of 6 months. People were assumed to enter the model in the stage 2 health state and could transition to either stage 3 or death. After moving into the stage 3 health state people in the model could not move back to stage 2. The mortality rate was greater in the stage 3 T1D health state than in stage 2, in which general population mortality was assumed to apply. The committee concluded that the model structure was suitable for decision making.

Assumptions

Modelling progression to stage 3 T1D

3.9 The company modelled long-term estimates of time to onset of stage 3 T1D for teplizumab and established clinical management by using

independent parametric distributions fitted to data from TN-10. The company's base case used a log-normal distribution for teplizumab and an exponential distribution for established clinical management. It explained that the chosen distributions had the best visual and statistical fit to the data, and that the estimated proportions of people progressing from stage 2 to stage 3 in established clinical management were in line with estimates from literature. But the EAG was concerned that the exponential distribution for the comparator arm was not appropriate because non-constant hazards are observed. It preferred to use the same type of parametric model for both teplizumab and established clinical management. The EAG chose the gamma distribution for both arms because it was a good statistical fit to the data. It also explained that the gamma distribution provided more conservative estimates of long-term progression to stage 3, which it preferred because of the uncertainty in the long-term data. The committee decided that the exponential curve for the established clinical management arm was not plausible based on the underlying hazard. It noted that in the teplizumab arm, the observed hazard functions for progression over time increased up to 2 years and decreased after this point. The committee considered whether the log-normal distribution, which assumes the risk of progression is higher earlier and decreases in the longer term, may more plausibly match the observed data and hazards for teplizumab. The committee noted that the TN-10 trial data is not mature and it would expect the difference in progression between treatment arms to increase with longer-term data. It considered whether a more optimistic distribution such as the log-normal, relative to the gamma distribution, may be appropriate for the teplizumab arm. The committee concluded that although the log-normal distribution for teplizumab and the gamma distribution for established clinical management appear plausible, it would like to see further exploration of hazard functions and curve fitting to verify this.

Utility values

Approach to estimating decline in disutility

3.10 The company modelled the impact of stage 3 T1D on quality of life by applying 3 different disutilities to age-dependent utility estimates of the general population:

- a one-off initial disutility during the cycle of onset of stage 3 to reflect the initial negative impact and subsequent adjustment to having symptomatic T1D
- a fixed disutility during all cycles to reflect the impact of having symptomatic T1D compared with the general population or asymptomatic stage 2 T1D
- an increasing disutility over time since onset of stage 3 T1D to reflect the accumulating impact of T1D health complications.

The EAG preferred to remove the one-off initial disutility but acknowledged this was not a major driver of cost effectiveness. The committee noted there can be difficulty in adjusting to symptomatic T1D (see section 3.1) and considered that the one-off disutility at stage-3 onset was appropriate to include in the model. The EAG preferred to remove the time-dependent, complication-related disutility because it was concerned about double counting a decline in utility that may be related to ageing. The committee noted that the cohorts in the analysis were age and sex matched and the company confirmed this. So, the regression model was not double counting age-related effects on utility. The committee decided that a time-dependent disutility was appropriate but, after reviewing the informing evidence, it considered whether applying the same rate of decline across stage 3 disease was appropriate. The clinical experts explained that complications associated with stage 3 T1D take 10 years to manifest and the disutility in the informing evidence was similar for the first 8 years. The committee considered that including a constant disutility across all

cycles of stage 3 T1D may be double counting its impact on quality of life. The committee concluded that although the one-off disutility and time-dependent disutility were appropriate to include, it had concerns about the inclusion of a constant disutility. So, the committee would like to see exploration of the rate of disutility over time in stage 3 T1D, and how this interacts with the one-off disutility and constant disutility values applied.

Carer disutility

3.11 Carer disutility was included in the model for children only, with a disutility value of -0.04 relative to the general population. This was based on self-reported data from literature on quality of life for carers of children with stage 3 T1D having outpatient care. An average of 1.76 carers was assumed. The committee raised a concern that this disutility was not fully representative of carer disutility and may be an overestimate. This is because people in the model have a first-degree relative with T1D. For example, someone could be a parent with T1D caring for a child with T1D, so the disutility captured is the relative effect of a parent having T1D themselves. Or there could be multiple children in a family with T1D, so the disutility may not be directly additive. The company explained that they had explored scenarios in which caregiver disutility was removed and explained that the disutility may be an underestimate because of 'ceiling' effects. The patient expert explained that having a child with T1D may cause significant additional stress when the parent also has T1D. They also pointed out that this concern would not end at age 18. The committee concluded that the approach to modelling carer disutility was likely to be reasonable and unlikely to be a significant driver of cost effectiveness, but this was uncertain. So it would like to see scenarios in which disutility is halved, or absent, and also in which carer disutility ends at age 25.

Costs

Estimating costs in stage 3 T1D

3.12 The initial average monthly cost per person of managing stage 3 T1D (£415.22) was taken from literature on direct healthcare costs of diabetes in the UK (Hex et al. 2024). The company assumed this monthly cost increased over time in line with a piece-wise regression model, fitted to observed data from literature reporting trends in total and healthcare cost data (Ou et al. 2016). But the EAG noted that the data came from a prevalent population and was concerned that the company's approach significantly overestimated the costs of stage 3 T1D. This is because the annual cost per person over 60 years was significantly higher than the annual cost in the prevalent population (£4,982) from Hex et al. In the EAG's base case, the monthly cost of £415.22 was applied as a fixed cost regardless of time spent in the stage 3 health state. But the EAG acknowledged that this fixed approach was likely to overestimate costs in people with newly diagnosed stage 3 T1D and underestimate costs at a later stage. It also suggested a recalibration of the regression model so that the average monthly cost of stage 3 T1D over 60 years was equal to £415.22. But the initial cost estimates were not possible to validate with this approach. The committee decided that use of consistent costs over time in stage 3 T1D was not plausible if it is also assumed that quality of life in stage 3 worsens over time (see section 3.10). The committee also thought that the data used to model increasing costs for an incident population over time may not be appropriate. Although the data is based on a UK prevalent population, it is combined with modelled cost-trajectory data from an incident population in Taiwan that may not be applicable to the population seen in the NHS. Also, there may be other costs of managing stage 3 T1D that have not been included. The clinical experts explained that the costs of managing T1D have significantly increased since the data collection period of 2021 to 2022 used in Hex et al. This is because hybrid closed loop systems for managing blood glucose levels in type 1 diabetes are now being used in the NHS, with an uptake of around 80 to 90%. The clinical experts estimated that the costs of hybrid closed loop systems would add about £5,000 to costs annually. The committee

also considered that if the use of hybrid closed loops has an impact on the rate of complications, this may impact the rate of utility decline (see section 3.10) and the rate at which stage 3 costs are accumulated. The committee concluded that it is plausible to assume the costs of managing stage 3 T1D increase over time in line with an increase in complications. But the modelling approaches presented are highly uncertain. The committee also concluded the cost of hybrid closed loops should be included, and the impact of this on the trajectory of accumulation of stage 3 T1D costs would need to be captured in the modelling. The committee would like to see plausible estimates for the cost of managing stage 3 T1D based on a more recent data source that includes the costs and benefits of hybrid closed loop systems.

General population mortality life tables

3.13 In its submission, the company highlighted that the 2020 to 2022 life tables used to estimate general population mortality were concurrent with the COVID-19 pandemic, which would have had an impact on overall survival. In a scenario analysis, the company used 2017 to 2018 life tables to estimate general population mortality. This approach was used by the EAG in its base case. The committee acknowledged that the impact of this change on the cost-effectiveness estimates was minimal. It concluded that using the 2017 to 2018 life tables for general population mortality was appropriate for decision making.

Cost-effectiveness estimates

Company and EAG cost-effectiveness estimates

3.14 The cost-effectiveness estimates used by the committee for decision making took into account the available confidential discounts. In the company's base case, the deterministic incremental cost-effectiveness ratio (ICER) was £27,534 and the probabilistic ICER was £29,488. In the EAG's base case, the deterministic ICER was £165,387 and the probabilistic ICER was £171,788.

Committee's preferred analyses

3.15 The committee could not identify a preferred ICER because of uncertainties in the economic model and the need for additional analyses. The committee would like to see analyses on:

- the numbers and proportions of people making up the populations that could potentially be identified in NHS practice (that is, people who would be eligible for teplizumab), as well as information on who would be offered testing (see section 3.3)
- further exploration of hazard functions and curve fitting for modelling progression to stage 3 T1D (see section 3.9)
- exploration of utility decline, because the use of combined age-dependent disutility and constant utility may not be appropriate (see section 3.10)
- scenarios examining the impact of carer disutility on the cost-effectiveness estimates, specifically when carer disutility is halved or absent, and when carer disutility is included up to age 25 (see section 3.11)
- modelling of stage 3 T1D costs using a more recent data source that includes the cost and benefit of hybrid closed loop systems (see section 3.12).

Other factors

Equality

3.16 The committee discussed whether there were any further considerations based on its duties under the equality legislation. It noted the following points raised by stakeholders:

- The clinical-effectiveness data is mainly based on White populations. But there are differences in continuous glucose monitoring and diabetes progression across ethnic groups that may influence the effectiveness of teplizumab.

- Young people and younger adults are at higher risk of more severe T1D and premature death from T1D compared with the general population, so there may be additional benefit in this population.
- Some people may find engaging with insulin therapy difficult (including people who are neurodivergent or have learning difficulties), so delaying progression may be particularly beneficial in these groups.
- People living in more deprived areas may benefit more from teplizumab because of having fewer opportunities for participation in structured diabetes education and specialist diabetes services.
- There may be potential barriers to accessing teplizumab because of a lack of a national screening programme, particularly in areas with limited healthcare resources. Variation in access may introduce inequalities based on geography, education or knowledge of early-stage diabetes.
- First-degree relatives of people with T1D are more likely to have been screened for pancreatic islet autoantibodies.
- The 14-day infusion course of teplizumab could cause difficulties because of the cost of travel and accommodation.

The committee also noted that caregiver responsibilities for T1D may disproportionately fall on women and that delaying the onset of T1D may mitigate this additional caregiver burden. Age, sex, disability and ethnicity are all protected characteristics under the Equality Act 2010. But the committee noted that teplizumab was being considered within its full marketing authorisation and issues related to differences in prevalence or incidence of a condition, or access to care, are not issues that can be addressed by a NICE technology appraisal recommendation. It took into account the potential particular benefits of teplizumab in some population groups in its decision making.

Uncaptured benefits

3.17 The committee considered whether there were any uncaptured benefits of teplizumab. The clinical experts explained that short-term control of T1D can reduce the risk of complications in the long term despite diabetes progression. They noted that delaying progression to stage 3 may also reduce the risk of complications in the long term, but the size of this potential benefit is uncertain. The committee concluded that teplizumab may potentially reduce long-term complications in stage 3 T1D but the impact of this on the cost-effectiveness estimates was uncertain.

Conclusion

Recommendation

3.18 The committee noted the uncertainties in the company's modelling and cost-effectiveness estimates. It concluded that further information was needed before it could decide on all its preferred modelling assumptions and understand the full impact of the uncertainties. The committee was unable to establish that teplizumab was a cost-effective use of NHS resources. So, it did not recommend teplizumab for delaying the onset of stage 3 type 1 diabetes in people aged 8 years and over with stage 2 type 1 diabetes.

Managed access

3.19 Having concluded that teplizumab could not be recommended for routine use, the committee considered if it could be recommended for use during a managed access period. The committee considered whether a recommendation with managed access could be made and discussed if uncertainty surrounding testing could be addressed. The company did not make a proposal for managed access. So, the committee was unable to consider a recommendation with managed access.

4 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

James Fotheringham
Vice chair, technology appraisal committee A

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

Emma McCarthy
Technical lead

Caron Jones
Technical adviser

Greg O'Toole
Project manager

Ian Watson

Associate director

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