NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final draft guidance

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

1 Recommendation

1.1 Teplizumab can be used, within its marketing authorisation, as an option for delaying the onset of stage 3 type 1 diabetes in people 8 years and over with stage 2 type 1 diabetes. Teplizumab is only recommended if the company provides it according to the commercial arrangement (see section 2).

What this means in practice

Teplizumab must be funded in the NHS in England for the condition and population in the recommendations, if it is considered the most suitable treatment option. Teplizumab must be funded in England within 90 days of final publication of this guidance.

There is enough evidence to show that teplizumab provides benefits and value for money, so it can be used routinely across the NHS in this population.

Why the committee made this recommendation

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

Issue date: June 2026

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.

There are some uncertainties in the economic model. But the most likely cost-effectiveness estimates for teplizumab are within the range NICE considers an acceptable use of NHS resources. So, teplizumab can be used.

2 Information about teplizumab

Marketing authorisation indication

2.1 Teplizumab (Tzield, Sanofi) is 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 (T1D)'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of teplizumab is £10,939.12 per 2-mg vial (excluding VAT, BNF online, accessed May 2026).

2.4 The company has a commercial arrangement, (simple discount patient access scheme). This makes teplizumab available to the NHS with a discount. The size of the discount is commercial in confidence.

Sustainability

2.5 For information, the Carbon Reduction Plan for UK carbon emissions is published on Sanofi's webpage on environmental impact.

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 need managing with insulin. 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. It can also 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 for carers of 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 emphasised that delaying the 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. It would also allow them more time to mature and focus on passing through key developmental milestones. The patient experts explained that delaying the onset of stage 3 may lead to fewer long-term complications. 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 T1D is asymptomatic, it is not usually identified in routine practice but may be diagnosed in research studies (see section 3.3). When 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 with stage 2 T1D. Submissions from professional organisations and NHS England stated that there is no widespread testing or national pathway of care for presymptomatic T1D (that is, stages 1 and 2). This this was confirmed at all committee meetings. 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
- additional training for clinical staff.

They stated that this would place a significant additional demand on the NHS. At the second committee meeting, the clinical experts explained that implementation would be challenging. But they said that the impact would not be as significant because the population eligible would be small and would be split across tertiary centres. They estimated that about 4 to 5 patients would be offered teplizumab at each tertiary centre annually. They also advised that the population being diagnosed with stage 2 T1D and having teplizumab would still present to the NHS eventually when clinical symptoms appear at stage 3. But they said that they would be identified at an earlier stage. The clinical experts also acknowledged the difficulty in setting up the weekend services that would be needed for 14-day consecutive administration of teplizumab. The committee acknowledged the need for additional infrastructure in the NHS to support any potential recommendation for teplizumab use.

Identifying the eligible population for teplizumab

3.3 In its submission, the company defined the eligible population as people 8 years and over with stage 2 T1D (defined as people with 2 or more islet autoantibodies and dysglycaemia) who are at risk of progression to stage 3 T1D. This is in line with the licensed indication and the population from the clinical trial, TN-10 (see section 3.7). But people with stage 2 T1D are asymptomatic and there are no national screening programmes to identify them. So, 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. It also explained that the method of identifying people eligible for treatment could significantly affect the cost effectiveness. The EAG suggested that:

- screening should be included as part of the intervention (that is, in addition to teplizumab), or
- the population eligible for teplizumab should be limited to people 8 years and over in whom stage 2 T1D has been incidentally detected.

The company had decided that the inclusion of screening was outside the remit of the evaluation, so did not include screening costs in the model. It 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 subpopulations 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 corticosteroid use for other autoimmune conditions)
- have a first-degree relative with T1D
- are members of the public who request autoantibody testing.

The clinical experts explained that, in about 50% of people currently identified with stage 2 T1D, it is diagnosed in routine clinical practice. That is, these people 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. They highlighted that, 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. In responses to the draft guidance consultation and at the second committee meeting, the company and experts from NHS England also agreed that there would be an increase in 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. This risk substantially increases to 1 in 10 to 1 in 20 for people with a first-degree relative with T1D. At the second committee meeting, the company explained that the results of the recently published ELSA study showed that the expected risk of having T1D in the first-degree-relative cohort was closer to 1 in 30. It also showed that the rate in the general population is about 1 in 200. The clinical experts 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. It also noted the uncertainty about the subsequent effects on 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. It also recognised that a coordinated national screening programme is unlikely to 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 that 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 requested more information on the number of people in each identified populations that might present for autoantibody testing and on how autoantibody testing would be commissioned in practice.

In response to draft guidance consultation, NHS England provided estimates of the number of people in the 4 distinct subpopulations outlined in the draft guidance who may present for antibody testing. These figures included estimates for:

- first-degree relatives (with estimates based on 2 and 5 people tested per person with T1D, as well as a central estimate)
- first-degree relatives plus an additional 1% uplift outside this population to account for increased testing requests, clinical concerns and people identified from research.

NHS England explained that it provided a range of estimates depending on the number of first-degree relatives tested per person with T1D. It noted that the size of the increase in number of people coming forward for testing is still unknown. It also explained that the whole eligible population would not be tested immediately. The clinical experts explained that people identified from research studies (such as ELSA, a screening study aimed at identifying T1D in people aged 2 to 17 years) would already be eligible to have teplizumab. They advised that ELSA has been extended until 2030, which could help to provide the NHS with time to set up the necessary infrastructure for testing. The committee also noted that some people in the 4 subpopulations may already be identified in practice because of clinical concerns or identified in a research study. But it decided that additional testing costs, specifically for first-degree relatives and people requesting autoantibody testing, should be captured in the model. The committee recalled from the first meeting that the expected risk of

having T1D in the first-degree-relative population was around 1 in 30. So, after the second committee meeting, it concluded that it would like to see further analysis including testing costs using a detection rate of 1 in 30 (that is, 30 tests per person having teplizumab).

Funding for testing in first-degree relatives

3.4 At the third committee meeting, the company revised its base case to include the costs of additional testing for first-degree relatives only in line with a 1 in 30 population risk (see section 3.3). It applied the testing costs to both arms of the model, with the justification that the decision problem was based on people already diagnosed with stage 2 disease. So, it stated that the additional benefits of testing had already been included in the modelling. It also assumed that only 13% of these additional testing costs would be applied to the NHS. This figure came from a UK study of paediatric diabetes units (Swaby 2025), in which 13% of respondents reported having autoantibody testing because of family screening in secondary care. The company explained that it expected the remaining proportion of testing to be covered in research studies like ELSA, or by testing for other clinical concerns. It also said that it is expected that stage 2 T1D will mainly be identified through research studies while the testing pathway is established. The EAG preferred to apply the testing costs to the teplizumab arm only. This was because the introduction of teplizumab is the reason for additional testing, so the additional cost to the intervention should be captured in the model. It also highlighted that assuming 13% of testing costs would be paid for by the NHS was based on current testing practice. The EAG stated it was unclear how this figure informed the percentage of additional testing that would be for first-degree relatives. The EAG explained that the claim contradicted the company's previous statements that only the first-degree-relative population would need further testing. The committee understood that the additional testing offered, if teplizumab was recommended, would be in first-degree relatives. It thought that, if the number of people being tested who were

first-degree relatives increased with the recommendation of teplizumab but the number tested in the remaining eligible populations (see section 3.3) did not, then everyone having teplizumab who would not have otherwise been tested would be first-degree relatives.

The clinical experts explained that, in practice, first-degree relatives of people with T1D would be directed towards research studies, when available. They also explained that there will likely be an increase in the number of first-degree relatives coming forward for testing over time, and that this increase would be larger if teplizumab is recommended. But they predicted that most of this extra demand would likely be covered by research studies. The committee thought that it was plausible that most people who would have testing in practice would be first-degree relatives, and it was unlikely that the general population would be able to request autoantibody testing in clinical practice. It acknowledged clinical expert opinion that people would be directed towards research studies but noted that the potential pool of first-degree relatives of people with T1D is much larger than the current ELSA study cohort. It acknowledged that that there is already some testing happening in the NHS and that this would continue if teplizumab were recommended. But thought that this could be significantly outweighed by the potential increase for testing in first-degree relatives, if many people were to come forward for testing. The committee decided that the extent to which research studies like ELSA would be able to cover the increase in testing if teplizumab were recommended is uncertain. This is because the potential demand for testing is unknown. The committee also acknowledged that the NHS would incur the additional testing costs, if research studies have capacity or resource constraints, or finish. The committee decided that an increase in testing in the first-degree-relative population after the recommendation of teplizumab, who would otherwise not have been tested, could be proportionally large enough to make testing in any other populations (including the population identified through existing testing, and those in

the comparator arm) essentially negligible. The committee concluded that, for the purposes of decision-making, it preferred to assume that additional testing costs would be applied to 100% of people having teplizumab, who would all be having NHS-funded tests. It also concluded that these additional testing costs should be applied to the teplizumab arm only. It acknowledged that assuming everyone having teplizumab would accrue extra testing costs as NHS-funded first-degree relatives, while the research studies are open and there is some existing testing in the NHS, was conservative. But it decided it was appropriate to capture the upper limit of potential risk to the NHS from an increase in testing for first-degree relatives.

Testing costs

3.5 In its response to the draft guidance consultation, NHS England submitted the estimated testing costs associated with the testing of the populations outlined in the draft guidance (see section 3.3). It assumed 1 autoantibody test per person. It also assumed that testing costs would include phlebotomy appointments, blood tests, an oral glucose tolerance test and diabetes service costs. The overall testing costs per person were:

- first-degree relatives: £668.53 for children, £212.73 for adults
- first-degree relatives plus ad-hoc uplift: £637.35 for children, £193.26 for adults.

The company said that NHS England's approach to estimating testing costs was an overestimate, and included costs that went beyond the scope of testing and into the diagnostic pathway. The company's base case included only the cost of a single confirmatory autoantibody test per person at £29.04 for people already diagnosed with stage 2 T1D. It stated that the costs of antibody testing related to identifying patients should be excluded from the modelling. But it presented budget-impact scenarios based on the estimated costs of an increase in uptake of

first-degree-relative testing. These were also based on the cost of a single autoantibody test per person. The company noted that the existing tariff costs are based on managing stage 3, not stage 2, T1D, and that stage 2 costs are likely to be lower. The NHS England expert agreed that NHS England's estimated costs cover a wider context than testing alone. They explained that the tariffs used for diabetes service costs, which are based on a person seeing a consultant for testing, are the only tariffs currently available. They advised that the costs may change over time if a treatment pathway for stage 2 T1D is set up. An Integrated Care Board expert explained that the costs presented by NHS England were likely to be an overestimate of the anticipated costs of the testing pathway for stage 2 T1D. The committee concluded that any testing costs included in the model should incorporate the wider costs of testing for stage 2 T1D in addition to autoantibody testing in any populations identified through testing (for example, first-degree relatives). But it decided that the costs provided by NHS England may be an overestimate. It requested more plausible estimates of testing costs in line with anticipated practice. This may include the costs of glucose testing and blood tests carried out in a community clinic. It requested additional analysis that included testing costs, in line with the requested analysis using a risk proportion of 1 in 30 (see section 3.3).

At the third committee meeting, the company presented an assumed testing pathway with a total estimated testing cost of £1,724.26, assuming that:

- 30 people are invited to and have exploratory antibody testing, at a total cost of £46.92 per person tested
- 1.1 people have confirmatory testing, which includes a specialist diabetes nurse follow up, a venous test and a blood glucose (HbA1c) test, at a cost of £140.96 per person

- 1 person is diagnosed with stage 2 T1D, and staged using an oral glucose tolerance test (and also has a diagnosis consultation with a specialist diabetes nurse), at a cost of £184.

The company highlighted that the updated testing pathway was based on an NHS community clinic setting and validated by the company's clinical expert opinion. The EAG stated that the testing pathway is plausible. But it highlighted that more than 30 people may need to be tested for every person treated with teplizumab. This would depend on anticipated teplizumab uptake, and the proportion of people categorised as having stage 1 T1D who are followed up to stage 2. The EAG presented some additional scenarios with testing numbers informed by presymptomatic T1D staging, stage 1 monitoring and teplizumab uptake figures. These figures were from an additional expert communication submitted in response to the draft guidance consultation (with accompanying model input from the company). The clinical experts explained that the uptake of teplizumab was likely to be higher than the value provided. They estimated that uptake would be around 70%. They also explained that they would not expect significant loss to follow up of people diagnosed at stage 1 and monitored until stage 2 if teplizumab is recommended.

The committee decided that the presented testing pathway is reasonable but an assumed teplizumab uptake of 100% is not plausible. It acknowledged the difficulties that may be associated with having teplizumab, such as the need to travel daily for the 14-day infusion course (see section 3.20). The committee was inclined to accept a detection rate of 1 in 30 (based on a first-degree-relative population; see section 3.3). But it preferred to assume a greater expected uptake of teplizumab than the value proposed in the additional expert communication. It thought that 70% uptake, in line with the clinical expert opinion, was plausible. It also preferred to

assume that everyone diagnosed at stage 1 is monitored up to stage 2 with no loss to follow up, instead of the proportion proposed in the additional expert communication. It noted that its preferred monitoring and uptake proportions meant that a greater percentage of tested first-degree relatives would be treated with teplizumab. So, fewer tests would be needed for every person identified and treated. If everyone diagnosed with stage 1 T1D progresses to stage 2, this would result in a total of 43 tests needed for every person treated with teplizumab. So, the committee concluded that the costs of autoantibody testing for 43 people per person treated with teplizumab should be captured in the model. But it acknowledged that this estimate was based on optimistic monitoring rates and teplizumab uptake figures.

Appropriateness of established clinical management as a comparator

3.6 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, 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 acknowledged that some people may be identified after presenting for testing in the NHS and that there are costs associated with monitoring for people with diagnosed stage 2 T1D. The committee concluded that established clinical management is an appropriate comparator.

Clinical effectiveness

TN-10 trial

3.7 The clinical-effectiveness evidence for teplizumab came from TN-10. This is a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial of teplizumab. It included 76 people 8 years 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 [HR] 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; HR 0.457, p=0.01). The committee concluded that treatment with teplizumab led 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 of TN-10

3.8 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 compared with 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. When taking account of 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, including:

- having stage 1 T1D
- having less than 2 diabetes-related autoantibodies
- not meeting the minimum age for the TN-10 trial population (8 years)
- 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 said 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 acknowledged that the generalisability of the clinical trial data may be affected by uncertainties in identifying the stage 2 T1D population in NHS practice. But it concluded that data from TN-10 is suitable for decision making.

Generalisability of ELSA

3.9 At the second committee meeting, the committee was concerned about how well the population eligible for teplizumab, including potentially populations who are underserved, are represented in ELSA (see section 3.3). The clinical experts explained that ELSA has good representation. The committee requested additional evidence that ELSA is generalisable to the wider UK population. At the third committee meeting, the company presented additional data on the generalisability of ELSA (n=24,875). This included demographic data on the ELSA study population compared with the general population (see section 3.3). It acknowledged that people from Black and Asian ethnic groups and people from less advantaged socioeconomic backgrounds are slightly underrepresented. But it also highlighted that recruitment for ELSA is occurring in various settings and supports recruitment from ethnic minority groups, people living in areas of high deprivation and people without a family history of T1D. The committee recalled that stage 2 T1D is expected to be identified mainly through research studies, such as ELSA

(see section 3.3). The clinical experts explained that only about 31 people had been identified as stage 2 T1D in ELSA. But the committee recalled previous NHS England estimates of the first-degree-relative population potentially eligible for testing and noted that these were significantly higher. It acknowledged the significance of the need for teplizumab in a first-degree-relative population in which additional testing costs outside of ELSA have been captured. The committee concluded that the additional ELSA data presented showed that the study is sufficiently generalisable to the UK population.

Adverse events

3.10 TN-10 investigated adverse events associated with teplizumab, including treatment-emergent adverse events of special interest (AESIs). Adverse events occurred more often with teplizumab than with placebo (the incidence of AESIs is confidential and cannot be reported here). The EAG noted that teplizumab appears to be associated with an increased risk of infection, and of blood and lymphatic system conditions, particularly severe neutropenia (grade 3 and above). It was also concerned that, because TN-10 was small, 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. They added that the observed impact on white blood cells from teplizumab in TN-10 was 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 non-steroidal 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 thought likely related to teplizumab. It also said 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. Also, most occur in the first 5 days of teplizumab infusion in hospital, where people are regularly monitored. The committee decided that the costs of adverse events were 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 was unlikely to be a significant driver of the cost-effectiveness estimates. After the draft guidance consultation, the company revised its base case to include the costs of CRS at a rate of 4.6%. The company explained that this was the appropriate proportion to use. This was because the model captured the excess risk of adverse events and CRS was reported in 1.2% of people from the integrated safety analysis. The EAG agreed with this approach and noted that the cost-effectiveness results were not sensitive to changes in the proportion of people having CRS in the model. The committee concluded that assuming a CRS incidence of 4.6% in the teplizumab arm of the model was appropriate for decision making.

Economic model

Company's modelling approach

3.11 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

3.12 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 T1D 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 of the non-constant hazards seen. 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 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 assumed the risk of progression was higher earlier and decreased in the longer term, were possibly a more plausible

match to the observed data and hazards for teplizumab. The committee noted that the TN-10 trial data is not mature. It said 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.

At the first committee meeting, the committee concluded that the log-normal distribution for teplizumab and the gamma distribution for established clinical management appeared plausible. But it said that it would like to see further exploration of hazard functions and curve fitting to verify this. After the draft guidance consultation, the company presented additional scenarios exploring flexible spline extrapolation models. It revised its base case to assume a gamma distribution for the established clinical-management arm in line with the committee's preference at the first committee meeting. It also maintained a log-normal distribution for the teplizumab arm based on goodness of fit. The committee was satisfied with the exploration of alternative extrapolations. It concluded that the company's revised approach of using the log-normal distribution for teplizumab and the gamma distribution for established clinical management was appropriate for decision making.

Utility values

Approach to estimating decline in disutility

3.13 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 decided it was appropriate to include the one-off disutility at stage-3 onset 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 T1D 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 decided 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 the one-off disutility and time-dependent disutility were appropriate to include. But it had concerns about the inclusion of a constant disutility. It requested 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.

After the draft guidance consultation, the company revised its base case to use smaller time-dependent disutility values and a piece-wise

approach for time-dependent disutility. In this approach, the size of the time-dependent disutility applied in each cycle increased after 10 years (that is, the time taken for symptoms to manifest). The EAG agreed the company's approach was reasonable. It noted that changes to the inflexion point at time points other than 10 years had a minimal impact on the cost-effectiveness estimates. The committee concluded that the company's updated approach to handling stage 3 disutility was appropriate for decision making.

Carer disutility

3.14 In the company's original base case, 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 was concerned that this disutility was not fully representative of carer disutility and may be an overestimate. This was because people in the model had 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 was 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 it had explored scenarios in which caregiver disutility was removed. It also 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 years. The clinical experts agreed with this. They highlighted that a parent may continue to have some involvement in care past age 18 years (for example, in ordering prescriptions or attending appointments) even as the person with T1D becomes gradually more independent in managing their condition.

After the draft guidance consultation, the company revised its base case to increase the age at which carer disutility ends in the model from age 18 to 25 years. It modelled scenarios in which caregiver disutility was halved or absent. It maintained a base-case disutility of -0.04 and an average of 1.76 carers. The EAG thought that the disutility value applied could have been too large because the starting age of the model was 13.6 years and the source of the disutility value came from a study in children. The company explained that the average age of the population in the study from which the disutility was sourced was 11 years. The committee decided there would not be a significant difference in utility between this age and the average starting age of the model. It also agreed that applying the caregiver disutility up to age 25 years was likely to be reasonable. But it noted that the evidence provided for carer disutility was based only on a single primary caregiver per patient. So, it decided that applying a disutility to someone other than a primary caregiver may not be appropriate.

At the third committee meeting, the company provided additional evidence for the inclusion of a secondary caregiver and maintained its preferred number of 1.76 caregivers. The additional evidence was a company-sponsored survey on secondary caregiver involvement, with data collected from caregivers of a child or young person with T1D up to age 25 years. The company explained that the results of the survey indicated that a proportion of primary caregivers have caregiver support (the proportion in the survey is confidential so cannot be reported here). The EAG agreed it was plausible that multiple caregivers would be involved in the care of a child or young person with T1D. But it preferred a different value for the number of caregivers, based on the company's survey data (this value is confidential so cannot be reported here). The EAG's preferred number of caregivers was estimated by adding the reported proportion of time secondary caregivers spend on caregiving relative to primary caregivers in the survey, to the proportion of time spent providing

care across all primary caregivers, when including sole caregivers. It thought that it was unclear why the company's preferred number of carers had not been adjusted in line with the ratio of secondary caregiver contributions from the survey. The company explained that its preferred number of caregivers was an accurate representation of the multifaceted caregiver burden of T1D. But, on balance, it accepted the EAG's preferred value. The patient experts explained that the impact of living with T1D in a family is significant and the additional caregiving needed for a child with T1D is constant. The committee was satisfied with the additional evidence provided for the relative contributions of a secondary caregiver. So, it thought that including multiple caregivers in the model was reasonable. It concluded that the caregiver disutility of -0.04 should be applied up to age 25 years, with the number of caregivers and relative contribution of second caregivers in line with the EAG's base case.

Stage 2 disutility

3.15 After the draft guidance consultation, the company's revised base case included an ongoing disutility for stage 2 T1D in addition to the disutility at stage 3 (see section 3.13). The size of the disutility differed by model arm (-0.049 for teplizumab and -0.124 for established clinical management). It was based on utility data obtained from a UK-specific vignette study of 300 adults (Guenther et al. 2025, conference abstract). The committee considered whether a stage 2 disutility would be plausible given that T1D is asymptomatic at this stage. It also questioned whether the presence of teplizumab as a treatment option would affect the size of the stage 2 disutility applied. The company explained that the stage 2 disutility reflected the initial shock and adjustment of diagnosis of stage 2 T1D. The EAG advised that the relative effect for stage 2 T1D in the model was not plausible, particularly relative to the stage 3 T1D disutility values applied (see section 3.13). It preferred not to apply a disutility at stage 2 T1D. The EAG also explained that it was unable to fully assess the validity of the methods used because it had only seen the conference abstract and not

the full study. The committee decided that it was uncertain about the plausibility of a stage 2 disutility. It was also uncertain that the effect on utility from diagnosis and adjustment may already have been captured in the one-off disutility applied at stage 3 T1D in the model. It also noted that the results of vignette studies can be sensitive to how the questions asked are framed. So, it was essential to evaluate the full methods used in the study.

Before the third committee meeting, the company provided additional details of the vignette study. This assessed the perceptions of the impact of T1D on health-related quality of life. The company explained that the stage 2 disutility was distinct from the one-off initial disutility at stage 3 onset. That one-off disutility relates to the adjustment in managing symptoms after reaching the symptomatic stage of T1D. It also explained that it was clinically plausible that stage 2 disutility would be larger than stage 3 onset disutility because the shock of diagnosis occurs earlier. The EAG highlighted that the company's argument related to initial shock but was applied continuously throughout stage 2 in the model. In the EAG's revised base case, it preferred to apply the stage 2 disutility for 6 months (or 1 model cycle). The committee thought that the larger disutility at stage 2 was likely because of using a vignette method to get utility values. It noted that the study did not include evidence for a long-term effect on health-related quality of life in stage 2 T1D.

The patient experts explained that there would be ongoing anxiety in stage 2 T1D caused by awareness of having been diagnosed with a chronic condition without certainty of when symptoms would start to occur. The committee acknowledged that it was plausible that being diagnosed at stage 2 may affect health-related quality of life. It also thought that the impact on quality of life may be reduced with the availability of a disease-modifying treatment such as teplizumab. But it still thought that using a vignette study as the source of disutility was uncertain. This was

emphasised by the difference in the stage 3 utility from the vignette study and what the company chose to use in the economic model. The committee also recalled its earlier assumption that 100% of people eligible for teplizumab are first-degree relatives getting a diagnosis through NHS testing (see section 3.4). It added that, without teplizumab, people would be undiagnosed and so would not have a disutility at stage 2. So, applying a disutility for established clinical management was not plausible. But it also thought that applying a disutility for the teplizumab arm only would introduce uncertainty because of the impact of testing instead of capturing disutility related to the introduction of teplizumab. Because of the uncertainty and to maintain consistency with previous conclusions around testing, the committee concluded that it preferred not to apply a stage 2 disutility in either arm.

Non-reference discounting rate

3.16 In the company's call for evidence response submitted before the third committee meeting, it made a case that teplizumab met the criteria for the non-reference case discount rate of 1.5%. The committee acknowledged that all the following criteria in section 4.5.3 of the NICE health technology evaluations: the manual must be met for a 1.5% discount rate to be used:

- The technology is for people who would otherwise die or have a very severely impaired life.
- The technology is likely to restore them to full or near-full health.
- The benefits are likely to be sustained over a very long period.

The company explained that teplizumab prolongs the period in which people are in full health, and may lead to reduced complications over the long term, even after progression to stage 3 T1D. The committee noted that the assumption of restoration to full or near-full health was contradicted by the company's modelled projections of stage 3 costs (see section 3.17), which remained high in the teplizumab arm. The

committee also decided it was not plausible that a treatment which only delays the onset of symptomatic T1D could be thought to:

- restore people to full, or near-full health, and
- also be indicated for people who would otherwise die or have a severely impaired life.

So, the committee concluded that teplizumab did not meet the criteria for a 1.5% discount rate. It preferred to use a discount rate of 3.5% for both health effects and costs, in line with the NICE reference case.

Costs

Estimating costs in stage 3 T1D

3.17 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. It was concerned that the company's approach significantly overestimated the costs of stage 3 T1D. This was 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 have:

- overestimated costs in people with newly diagnosed stage 3 T1D
- underestimated costs at a later stage.

It also suggested a recalibration of the regression model, so that the average monthly cost of stage 3 T1D in people 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 using 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 3.13). It noted that data estimated from a prevalent population being used to model increasing costs for an incident population over time may not be appropriate. Also, the data was based on a UK prevalent population. But it was 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. Also, if using hybrid closed loops affects complication rates, the committee thought that it may affect the rates of utility decline (see section 3.13) and stage 3 cost accumulation. It concluded that it is plausible to assume that the costs of managing stage 3 T1D increase over time in line with an increase in complications. But it thought that the modelling approaches presented were highly uncertain. The committee also concluded that the costs of hybrid closed loops should be included. It added that the impact of this on the trajectory of stage 3 T1D cost accumulation would need to be captured in the modelling.

After the draft guidance consultation, the company submitted new data on stage 3 costs based on a Danish registry study with 19 years of data available. It applied a linear regression model with a quadratic term to

data collected for between 5 and 19 years of follow up, to extrapolate stage 3 costs beyond this point. It also accounted for the impact of hybrid closed loops on costs using the Core Diabetes Model and assumed a 100% uptake of hybrid closed loop systems. The EAG agreed that the Danish registry data was an appropriate source of stage 3 cost data. But it thought that the company's revised approach overestimated extrapolated costs beyond 19 years. It also noted that the average estimated monthly costs were greater than the £415.22 costs presented at the first committee meeting (the company's estimated monthly costs are confidential so cannot be reported here). It preferred to apply a linear extrapolation of costs without a quadratic term. It also assumed a 54% uptake of hybrid closed loop systems, based on uptake data submitted by NHS England. The company explained that its approach showed an upward cost trajectory, which would align with an increase in complications over time. It noted that the EAG's approach showed a trajectory which was unlikely to align with the expected increase in costs associated with accumulating comorbidities over the long term. The committee acknowledged that stage 3 T1D costs were likely to increase over time and that the costs in the EAG's approach were likely to be too low. But it noted that the extent to which extrapolated stage 3 T1D costs increased in the company's approach may not be appropriate and had not been validated against any real-world data sources. The committee requested more suitable data to justify the expected increase in costs beyond 20 years.

At the third committee meeting, the company updated its base case to assume an 84% uptake of hybrid closed loop systems. This was in line with a clinical expert opinion on the expected plateau in uptake from March 2026 onwards. But it kept its quadratic modelling approach submitted at draft guidance consultation. The company explained that this approach was validated by the company's clinical experts. Also, a

quadratic extrapolation had the best fit for people with stage 3 T1D, as well as healthy controls. It highlighted that it did not expect the average per person cost of stage 3 T1D to increase over the long term. This was because the model was cohort-based and a smaller proportion of people were alive to accrue stage 3 costs. It presented a scenario in which stage 3 costs were capped after 65 years in stage 3 T1D, but did not cap stage 3 costs in its base case.

The EAG acknowledged that a non-linear increase in costs is plausible. It revised its base case to assume a 72% uptake of hybrid closed loop systems. This was based on a clinical expert opinion of current uptake in the company's submission before the third committee meeting. But it thought that the modelled T1D specific costs may have been an overestimate. This was because of the uncertainty in the extrapolations of costs for people with T1D and people who were healthy. The difference between the 2 extrapolations was used to calculate costs used for stage 3 T1D in the model. The EAG highlighted that the general population would develop age-related comorbidities over time that will increase healthcare costs. So, the difference in the costs between this population and the T1D population are likely to be smaller than projected. In the EAG's base case, it preferred to introduce a cap on stage 3 T1D costs after 40 years spent at stage 3. This was to account for the uncertainty in projected costs. The committee noted that the changes to the annual projected cost of stage 3 T1D over time, as shown by the company, showed that an increase in stage 3 costs in the model would affect the cost-effectiveness estimates (the company's values are confidential so cannot be reported here). The committee also considered how the duration of stage 3 T1D and age of people in stage 3 might drive estimated costs. The clinical experts explained that both these factors are independent and may influence stage 3 costs.

The committee thought that the company's quadratic approach and

assumed uptake of hybrid closed loops were reasonable. It also thought that a small percentage of people surviving stage 3 T1D for a very long period could be accumulating high costs. But it thought that the size of these costs is uncertain because of the uncertainty in the projections. It thought that survival in stage 3 T1D is likely to be shorter if more complications occur. Also, people surviving for a very long period are expected to incur fewer stage 3 T1D costs associated with complications This may not have been captured in extrapolations based on data with under 20 years of follow up. The committee thought that a cap on stage 3 costs could mitigate some of this uncertainty. For decision making, it concluded that it preferred the company's scenario that used a quadratic modelling approach with an uptake of 84% for hybrid closed loops. But it thought there should be a cap on stage 3 T1D costs after 65 years in that stage.

General population mortality life tables

3.18 In its submission, the company noted that the 2020 to 2022 life tables used to estimate general population mortality were concurrent with the COVID-19 pandemic. This 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

Acceptable ICER

3.19 NICE's manual on health technology evaluations notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £25,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will

take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted the high level of remaining uncertainty, specifically around the:

- size of the potential increase in demand for testing (see section 3.3)
- projected costs of stage 3 T1D over time (see section 3.17).

But it also noted unmet need, and that delaying the onset of symptomatic T1D would save the NHS costs in the long term because of a reduction in complications. It also thought that delaying the onset of symptomatic T1D during key stages of development in the paediatric population within the marketing authorisation may be particularly beneficial (see section 3.1). It thought that the preferred approach to accounting for testing costs was conservative and captured the risk to the NHS, which mitigated some of the uncertainty around the expected demand in testing. So, the committee concluded that an acceptable ICER would be towards the upper end of the range NICE considers a cost-effective use of NHS resources (£25,000 to £35,000 per QALY gained).

The committee's preferences and cost-effectiveness estimates

3.20 The exact cost-effectiveness estimates used by the committee for decision making cannot be reported here because there are confidential discounts for teplizumab and hybrid closed loops. For decision making, the committee preferred the model to include:

- testing costs in the teplizumab arm only, with 43 tests per person having teplizumab, based on a detection rate of 1 in 30 and teplizumab uptake of 70% (see sections 3.3 and 3.4)

- the assumption that additional testing costs are applied to 100% of people having teplizumab, with all additional testing funded by the NHS (see section 3.4)
- an incidence rate of 4.6% for CRS in the teplizumab arm of the model (see section 3.10)
- a log-normal distribution for time to onset of stage 3 T1D in the teplizumab arm (see section 3.12)
- a gamma distribution for time to onset of stage 3 T1D in the teplizumab arm (see section 3.12)
- the company's revised approach to stage 3 disutility in the model (that is, the piece-wise approach for time-dependent disutility presented at the second committee meeting) (see section 3.13)
- carer disutility of -0.04 applied up to age 25 years, with an assumed number of caregivers and the relative contribution of second carers in line with the EAG's preference (see section 3.14)
- no stage 2 disutility (see section 3.15)
- a discount rate of 3.5% for health effects and costs (see section 3.16)
- a quadratic approach to modelling stage 3 T1D costs, with costs capped after 65 years (see section 3.17)
- an assumed hybrid closed loop uptake of 84% (see section 3.17).

With the committee's preferred assumptions, the cost-effectiveness estimate for teplizumab was within the range that NICE considers an acceptable use of NHS resources.

Other factors

Equality

3.21 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 other 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 a learning difficulty). 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.
- People living in more deprived areas may have increased rates of diabetic ketoacidosis, so reducing this risk may have additional benefit in this population.
- Diabetes in caregivers of young people with T1D is associated with deprivation and protected characteristics.

The committee also considered the impact on health inequalities for people who are underserved do not have sufficient access to or are not represented in research studies. It requested extra evidence on the generalisability of ELSA to underserved populations, which was

provided before the third committee meeting (see section 3.9). 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. The committee noted that teplizumab was being considered within its full marketing authorisation. 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. But the committee took into account the potential benefits of teplizumab in particular population groups in its decision making.

Uncaptured benefits

3.22 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. The committee noted that delaying progression to stage 3 T1D may also reduce the risk of complications in the long term. But the size of this potential benefit is uncertain. At the first committee meeting, it also noted that there may be a potential utility benefit for secondary carers, which was not initially captured in the model. But, at the third committee meeting, the committee preferred to include it in the model after being presented with additional evidence for secondary caregivers (see section 3.14). 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

3.23 The committee concluded that teplizumab is clinically beneficial in delaying the onset of stage 3 T1D in people with stage 2 T1D. It acknowledged the unmet need in people with presymptomatic T1D. It decided there is some uncertainty around the testing and long-term costs

of T1D. But the most likely cost-effectiveness estimates for teplizumab are within the range NICE considers an acceptable use of NHS resources. So, teplizumab can be used, within its marketing authorisation, as an option for delaying the onset of stage 3 T1D in people 8 years and over with stage 2 T1D.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 90 days of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 60 days of the first publication of the final draft guidance.

4.3 When NICE recommends a treatment ‘as an option’, the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has stage 2 type 1 diabetes and the healthcare professional responsible for their care thinks that tirzepatide is the right treatment, it should be available for use, in line with NICE’s recommendations.

5 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, Jennifer Upton
Project managers

Ian Watson

Associate director

ISBN: [to be added at publication]