NICE National Institute for Health and Care Excellence

NICE guidance

Sotagliflozin with insulin for treating type 1 diabetes

Technology appraisal guidance
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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Sotagliflozin with insulin is recommended as an option for treating type 1 diabetes in adults with a body mass index (BMI) of at least 27 kg/m^2, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy, only if:

- sotagliflozin is given as one 200 mg tablet daily
- they are on insulin doses of 0.5 units/kg of body weight/day or more and
- they have completed a structured education programme that is evidence based, quality assured, delivered by trained educators and includes information about diabetic ketoacidosis, such as:
  - how to recognise its risk factors, signs and symptoms
  - how and when to monitor blood ketone levels
  - what actions to take for elevated blood ketones and
- treatment is started and supervised by a consultant physician specialising in endocrinology and diabetes treatment, and haemoglobin A1c (HbA1c) levels are assessed after 6 months and regularly after this.

1.2 Stop sotagliflozin if there has not been a sustained improvement in glycaemic control (that is, a fall in HbA1c level of about 0.3% or 3 mmol/mol).

1.3 These recommendations are not intended to affect treatment with sotagliflozin that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Sotagliflozin (one 200 mg tablet daily) is an option for some people who cannot manage

their type 1 diabetes with insulin alone.

Evidence from clinical trials run for 1 year in this population shows improvements in blood glucose (HbA1c) and weight loss, and improvements in quality of life, with sotagliflozin plus insulin compared with people on placebo plus insulin. The company assumes that the improvement in HbA1c results in a lower risk of long-term complications over a person's lifetime. It's reasonable to assume some relationship between lowering HbA1c and reducing diabetic complications, and between lowering BMI and improving quality of life.

If sotagliflozin improves HbA1c for only 2 years, and no other physiological factors, the cost-effectiveness estimate for sotagliflozin plus insulin compared with insulin alone is within the range that NICE normally considers an acceptable use of NHS resources. Sotagliflozin with insulin is therefore recommended as an option for type 1 diabetes in adults. Because of the increased risk of diabetic ketoacidosis, sotagliflozin should be stopped if blood glucose control does not improve.

2 Information about sotagliflozin

Information about sotagliflozin

Marketing authorisation indication	Sotagliflozin is indicated 'as an adjunct to insulin therapy to improve glycaemic control in adults with type 1 diabetes mellitus with a body mass index (BMI) 27 kg/m^2 or more, who have failed to achieve adequate glycaemic control despite optimal insulin therapy'. Sotagliflozin should not be started in people with type 1 diabetes with a low insulin need. It should not be started in people with a glomerular filtration rate of less than 60 ml/min and should be stopped at a glomerular filtration rate persistently below 45 ml/min. Sotagliflozin should be initiated and supervised by a physician experienced in the management of type 1 diabetes mellitus. During treatment with sotagliflozin, insulin therapy should be continuously optimised to prevent ketosis and diabetic ketoacidosis, and the insulin dose should only be reduced to avoid hypoglycaemia.
Dosage in the marketing authorisation	Administered orally as a 200 mg tablet once daily before the first meal of the day. After at least 3 months, if additional glycaemic control is needed, in patients tolerating sotagliflozin 200 mg, the dose may be increased to 400 mg once daily.
Price	The list price of sotagliflozin is £39.20 for 30×200 mg tablets (company submission document B). The treatment cost at list price is £477.30 per year. Costs may vary in different settings because of negotiated procurement discounts.

3 Committee discussion

The appraisal committee considered evidence submitted by Sanofi and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

Clinical management

People normally have structured education and optimised insulin therapy

3.1 Type 1 diabetes is an autoimmune metabolic disease that destroys insulin-producing cells of the pancreas. This raises the levels of blood glucose, which increases the risk of long-term diabetes-related complications. These include, but are not limited to, retinopathy, neuropathy, cardiovascular disease and death. People with type 1 diabetes manage their condition by making choices about diet and physical activity and by injecting insulin. The NICE guideline on type 1 diabetes in adults recommends that people have individualised care, including structured education (for example, the Dose Adjustment For Normal Eating [DAFNE] programme), and advice on diet and physical activity (that is, lifestyle), and on managing blood glucose. The guideline advises on targets for haemoglobin A1c (HbA1c) levels, self-monitoring of blood glucose, and preventing and managing hypoglycaemia and diabetic ketoacidosis. It also encourages people to identify and control risk factors for cardiovascular disease, manage diabetes-related complications and optimise their insulin therapy. Optimised management of insulin may include injection technique and rotating sites, dosing of insulin, skills for self-monitoring, and using continuous subcutaneous insulin infusion ('insulin pump') instead of multiple injections of insulin. The clinical experts explained that people who optimally manage insulin would normally have done a structured education course, as described in NICE's quality standard on diabetes in adults. For people who, despite best efforts, cannot reach optimal glycaemic control, or who cannot improve control without it causing disabling hypoglycaemia, there were

no other pharmacological options in established clinical practice at the time of the first committee meeting for this appraisal. The NICE technology appraisal guidance on dapagliflozin with insulin for type 1 diabetes recommends dapagliflozin as an option for people with type 1 diabetes with a body mass index (BMI) of 27 kg/m^2 or more on insulin doses of 0.5 units/kg of body weight/day or more. This was published during the development of this appraisal, and so was not considered routine practice.

Experience of people with type 1 diabetes

There is a need for interventions that help people control their diabetes without adverse effects from treatment

3.2 Managing blood glucose involves, for most people, multiple blood glucose finger prick tests and multiple insulin injections every day. People adjust the dose of insulin according to their diet, activity level and other circumstances such as stress and illness. A clinical expert explained that although insulin pumps and structured education such as DAFNE are useful tools, managing the condition is demanding and requires a disciplined balance of insulin, diet and lifestyle. The risk of hypoglycaemia from injected insulin, and having to adjust doses, can considerably affect wellbeing and quality of life. Treatment with insulin can be associated with weight gain. The clinical experts further highlighted that only about 30% of people reach their glycaemic target, and there is an unmet clinical need for an additional treatment for people who cannot safely reach optimal glycaemic control. The clinical experts suggested that sodium-glucose cotransporter (SGLT) inhibitors such as sotagliflozin could increase the proportion of time someone spends in an appropriate blood glucose range. The committee concluded that there is an unmet need for treatments that help people control their diabetes without treatment-related adverse effects.

People who might take sotagliflozin

Sotagliflozin is clinically appropriate for a restricted population

3.3 Sotagliflozin is a dual inhibitor of sodium glucose cotransporter type 1 (SGLT1) and SGLT2. It has a marketing authorisation only for type 1 diabetes. The European Medicines Agency restricted the marketing authorisation for sotagliflozin with insulin to people with a BMI of 27 kg/m^2 or more who do not have adequate glycaemic control despite optimal insulin therapy because of the association between treatment with sotagliflozin and diabetic ketoacidosis. The summary of product characteristics for sotagliflozin states 'sotagliflozin should be initiated and supervised by a physician experienced in the management of type 1 diabetes mellitus', and that it 'should not be initiated when patients are at a higher risk of diabetic ketoacidosis', such as people with a 'low insulin need'. One of the clinical experts explained that it was important to identify people in whom the benefit of treatment outweighs the risk of diabetic ketoacidosis and this would require specialist knowledge. Low insulin need is defined as less than 0.5 units of insulin/kg of body weight/day in NICE's technology appraisal guidance on dapagliflozin with insulin for type 1 diabetes. In the same guidance, the clinical population consisted of people:

- with a BMI of 27 kg/m^2 or more
- who have completed a structured education programme
- with insulin needs of 0.5 units/kg of body weight/day or more
- with inadequate glycaemic control despite structured education as defined by NICE's quality standard on diabetes in adults
- with optimised insulin therapy

- who are aware of the increased risk of diabetic ketoacidosis and are able to do blood glucose and ketone testing to enable them to prevent, recognise and treat diabetic ketoacidosis and hypoglycaemia.

The committee was aware that dapagliflozin, an SGLT2 inhibitor, has properties in common with sotagliflozin. So it considered that the same criteria used to define the population for dapagliflozin would also apply to sotagliflozin. The committee concluded that sotagliflozin was clinically appropriate for a restricted population, and in line with the summary of product characteristics, sotagliflozin would need to be started and supervised by a consultant physician specialising in endocrinology and diabetes.

Clinical evidence

The key trials for sotagliflozin, inTandem1 and inTandem2, do not include dose escalation

3.4 The main evidence for sotagliflozin came from 2 trials, inTandem1 and inTandem2. These trials compared sotagliflozin plus insulin therapy at 2 doses (200 mg or 400 mg) with placebo plus insulin therapy over 52 weeks. They were randomised and included 1,575 people with inadequately controlled type 1 diabetes, of whom 916 had a BMI of 27 kg/m^2 or more. The primary endpoint in both trials was the difference between groups in the change in HbA1c from baseline at 24 weeks. The committee was aware that the summary of product characteristics for sotagliflozin stated that if someone needs additional glycaemic control after 3 months on sotagliflozin, the dose may be increased to 400 mg once daily. However, the company provided no clinical evidence for escalating the dose, as this was not included in the clinical trials. Therefore, the committee had not seen enough evidence to make recommendations on increasing the dose of sotagliflozin from one 200 mg to two 200 mg tablets daily.

The pooled inTandem trial data are appropriate for decision making

3.5 The committee heard from the clinical experts that inTandem1 was likely

to be less generalisable to the NHS than inTandem2, because inTandem1 had no UK sites, and it was based in the USA where there is higher use of continuous subcutaneous insulin infusion (insulin pumps) than the UK, and the average BMI is higher. inTandem2 had many sites in Europe and the UK. The committee considered that higher use of insulin pumps in inTandem1 and inTandem2 than in clinical practice may mean that the risk of diabetic ketoacidosis is higher in the trials than in the NHS. The company clarified that the average BMI in the pooled analyses of the inTandem1 and inTandem2 data for people with a BMI of 27 kg/m^2 or more was 32 kg/m^2, and that this was in line with the average BMI for the NHS for people with a BMI of 27 kg/m^2 or more based on the UK National Diabetes Audit data. The committee agreed that although inTandem1 was likely to be more generalisable to NHS practice than inTandem2, it was important to pool these trials to consider all of the relevant data. It concluded that the pooled inTandem results were generalisable to the NHS and appropriate for decision making.

The company limited the trial data to people who are likely to receive sotagliflozin in clinical practice

3.6 The committee considered whether the trial population reflected the restricted population that was clinically appropriate for sotagliflozin (see section 3.3). People were recruited to the inTandem1 and inTandem2 trials if their HbA1c levels were between 7% (about 53 mmol/mol) and 11% (about 97 mmol/mol). The trials included a 6-week lead-in period, during which insulin dose was optimised. After optimisation, HbA1c was less than 7% (about 53 mmol/mol) for 17% to 20% of people across the inTandem1 and inTandem2 trials. The clinical experts acknowledged that the target for glycaemic control in the NICE guideline on type 1 diabetes in adults was 6.5% (about 48 mmol/mol) but explained that an HbA1c target of 7% (about 53 mmol/mol) or less was reasonable, and they would be unlikely to intensify treatment in people with an HbA1c of less than 7% (about 53 mmol/mol). Furthermore, the committee recalled that sotagliflozin is clinically appropriate for a restricted population (see section 3.3). The company submitted evidence on the clinical effectiveness of sotagliflozin in the clinically appropriate restricted population (that is, people with a BMI of at least 27 kg/m^2, an HbA1c of greater than 7% (about 53 mmol/mol) after the optimisation period, and

with insulin requirements of 0.5 units/kg of body weight/day or more). The committee agreed that this population was similar to people who would have treatment with sotagliflozin in clinical practice (except that it would be used in people with insulin requirements of 0.5 units/kg of body weight/day or more) and that it would focus on these data.

In the short term, sotagliflozin improves HbA1c and BMI but the impact on other parameters is mixed

3.7 The company presented data for the subgroup eligible for treatment with sotagliflozin, as requested by the committee (see section 3.3). The pooled inTandem1 and inTandem2 trial results for this subgroup showed a larger reduction in HbA1c from baseline at 24 weeks in people randomised to sotagliflozin plus insulin therapy than people randomised to placebo plus insulin therapy. This difference was larger from 0 to 24 weeks (0.39%, about 14 mmol/mol) than from 24 and 52 weeks (0.28%, about 3 mmol/mol). The ERG explained that, based on the trial data, HbA1c was likely to return to baseline by the end of the second year. In addition, people randomised to sotagliflozin plus insulin therapy had a greater reduction in BMI than people randomised to placebo plus insulin therapy at 24 weeks (0.8 kg/m^2), which increased at 52 weeks (0.93 kg/m^2). The committee also saw that at 52 weeks randomisation to 200 mg of sotagliflozin lowered both systolic and diastolic blood pressure, had a mixed effect on cholesterol, and worsened the estimated glomerular filtration rate, reflecting reduced renal function. The committee was aware that, because the 52-week data had been calculated by the NICE team without confidence intervals, the statistical significance of the results was unknown and only limited conclusions could be drawn. It concluded that sotagliflozin with insulin modestly improved HbA1c and BMI compared with insulin alone, and the impact on other parameters was mixed.

Blood glucose and risk of diabetes-related complications

Lowering blood glucose (HbA1c) levels decreases the risk of

diabetes-related complications

3.8 HbA1c is a recognised surrogate endpoint for long-term complications of diabetes. Treatment to lower HbA1c levels in type 1 diabetes to near-normal levels decreases the risk of complications such as myocardial infarction, stroke and retinopathy. The Diabetes Control and Complications Trial (DCCT) showed an average relative decrease in HbA1c levels of 2% (about 22 mmol/mol) over 10 years in people who had intensive therapy, that is, multiple daily insulin injections (or an insulin pump) compared with those who had conventional glycaemic control, that is, no more than 2 injections. This reduced the risk of microvascular complications by over half. The DCCT's 30-year, observational, follow-on study (Epidemiology of Diabetes Interventions and Complications [EDIC]) showed that people who had previously been randomised to intensive therapy had a lower risk of macrovascular complications and death than people who had been randomised to conventional glycaemic control. The company used data from EDIC in its economic model to infer the risk of complications based on changes in physiological parameters such as HbA1c and BMI. The committee discussed whether the results of EDIC were generalisable to therapies such as sotagliflozin that lower blood glucose by a much smaller magnitude and with only short-term evidence. It agreed that this was an area of uncertainty, and that the company had not shown evidence of a beneficial impact of sotagliflozin on diabetes complications. The committee concluded that while there is no evidence of sotagliflozin reducing the risk of complications, sotagliflozin plus insulin lowered blood glucose more than insulin alone (see section 3.7), and data from EDIC could be used to show that lowering blood glucose levels decreases the risk of diabetes-related complications.

Adverse events

Diabetic ketoacidosis risk is higher with sotagliflozin plus insulin than with insulin alone

3.9 The committee noted that sotagliflozin was associated with an increased risk of adverse events including genital tract infection, urinary tract infection and, in particular, diabetic ketoacidosis. The committee was

aware that the European Medicines Agency limited the marketing authorisation to people with a BMI of 27 kg/m^2 or more, and excluded people with a 'low insulin need' (see section 3.3) to reduce the risk of this potentially life-threatening adverse effect. However, the company confirmed that sotagliflozin was still associated with an increased risk of diabetic ketoacidosis in this restricted population. The incidence in the inTandem1 and inTamden2 pooled population with a BMI of 27 kg/m^2 or more was 8 times higher (3.2 events for every 100 patient years) in the sotagliflozin plus insulin arm than in the insulin alone arm (0.4 events for every 100 patient years); these results included people with a low insulin need. The clinical experts explained that they would not offer sotagliflozin to someone who had not received structured education as defined in NICE's quality standard on diabetes in adults, and who could not recognise the signs and symptoms of diabetic ketoacidosis. The committee concluded that sotagliflozin should not be offered to someone who had not completed structured education to the specification defined in the NICE quality standard, and who was not able to detect diabetic ketoacidosis.

The company's economic model

The model uses risk equations to link changes in HbA1c and other parameters from the trials to diabetes complications over a lifetime

3.10 The company used a patient-level model (CORE Diabetes Model version 9) to simulate disease progression and complications over a lifetime time horizon. The company defined treatment effects after 1 year of treatment as changes in HbA1c, BMI, systolic blood pressure, serum lipids and, as confirmed in the committee's second meeting, diastolic blood pressure and renal function measured by estimated glomerular filtration rate. The company derived these from a pooled analysis of inTandem1 and inTandem2, limited to the committee's preferred population. To estimate complications linked to changes in HbA1c, systolic blood pressure, lipid parameters and renal function in the economic model, the company used risk equations based on the UKPDS 68 study. There was an additional adjustment to these equations

in the CORE model using data from the EDIC study for HbA1c and systolic blood pressure only and not the lipid parameters or renal function. The ERG explained that changes in the ratio of total cholesterol to high density lipoprotein cholesterol were linked to changes in ischaemic heart disease, myocardial infarction and stroke. Plasma triglycerides did not affect diabetes-related complications in the model. The ERG explained that other baseline characteristics in the model also affected the probability of having a complication and therefore could affect life length, quality of life or both. These baseline characteristics included BMI, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol and estimated glomerular filtration rate. The company's model assumed that sotagliflozin affected all physiological parameters in the economic model and predicted that sotagliflozin increased length of life and improved quality of life. The ERG noted that the key parameters driving the cost effectiveness of sotagliflozin were HbA1c followed by BMI. The committee was concerned that the company was not able to explain how changes in BMI affect complications in its model during the committee meeting. The committee recalled the evidence that sotagliflozin might affect all physiological parameters, but because it was not clear how the company's model worked, it agreed that it would be reasonable to consider analyses for sotagliflozin affecting all or some physiological variables, and analyses that affected only HbA1c.

Small changes seen in the inTandem trials may translate to a reduced risk of long-term complications in the economic model

3.11 The committee noted that the improvement in HbA1c level in DCCT and EDIC (for multiple daily injections of insulin compared with conventional glycaemic control) was substantially bigger (about a 2% [about 22 mmol/mol] reduction), and sustained for substantially longer (over 10 years) than the improvement in HbA1c level in the pooled inTandem trials (0.39% reduction [about 14 mmol/mol] over 1 year with sotagliflozin plus insulin compared with placebo plus insulin) in the preferred population. The committee was concerned that the company had assumed that the benefit associated with the smaller and shorter reduction in HbA1c seen from inTandem was proportional to the benefit of a sustained larger difference in HbA1c seen in DCCT and EDIC in terms of fewer complications (see section 3.8). The committee was concerned by the

company's approach that reducing HbA1c immediately lowered the incidence of microvascular and macrovascular complications. It heard from the clinical experts that, although there are data to show lowering HbA1c is associated with a decrease in diabetic complications, there are no data to show that weight loss alone would reduce diabetes-related complications. The committee was aware that in studies of type 2 diabetes, weight loss is associated with an improved quality of life. But the committee had not seen any evidence to support this in type 1 diabetes. The committee concluded that it was reasonable to assume some relationship between lowering HbA1c and reducing diabetic complications, and an association between lowering BMI and improving quality of life.

Cost-effectiveness estimate

The company's updated base case includes many of the committee's preferences

3.12 The company's revised base case included many of the committee's preferred assumptions:

- people with a BMI of 27 kg/m^2 or more, insulin needs of 0.5 units/kg of body weight/day or more and HbA1c of 7% (about 53 mmol/mol) or more after people optimised their insulin (see section 3.3)
- baseline characteristics from the pooled trial data (see section 3.5)
- treatment efficacy with sotagliflozin based on 52-week data improving HbA1c and BMI with treatment efficacy waning after the first year (see section 3.7)
- treatment with sotagliflozin for 2 years based on pooled trial data, which suggests that the effect of sotagliflozin on HbA1c returns to baseline at the end of the second year (see section 3.7) and treatment should stop if glycaemic control does not improve (see section 3.15)

- updated adverse events including case fatality for diabetic ketoacidosis to reflect the UK (0.7%), severe hypoglycaemia (4.45% in line with assumptions in NICE technology appraisal guidance on dapagliflozin with insulin for type 1 diabetes) and Fournier's gangrene.

  The probabilistic cost-effectiveness estimates for sotagliflozin compared with standard care for the company's revised base case were £16,093 per quality-adjusted life year (QALY) gained. Although the company had addressed most of the committee's preferences, the committee was concerned that the company had only used data at 24 weeks from the pooled inTandem trials and had not used the 52-week data. Furthermore, because of uncertainties associated with how the model worked, the committee concluded that it wanted to see scenarios limiting the benefit of treatment with sotagliflozin to improvement in HbA1c.

The ERG's scenario analyses explore the extrapolation of trial results over a patient's lifetime

3.13 The ERG updated the company's base case so that it was better aligned with all of the committee preferences. It:

- identified an error in the company model and changed the mortality probability for severe hypoglycaemia from 4% to 4.45% (see section 3.12)
- used 24- and 52-week data from inTandem1 and inTandem2 to estimate the treatment effect of sotagliflozin (see section 3.12).

  The impact of these adjustments increased the company's probabilistic base-case incremental cost-effectiveness ratio (ICER) for sotagliflozin compared with insulin from £16,093 to £19,046 per QALY gained.

  The committee had concerns that sotagliflozin was assumed to affect all physiological parameters in the economic model (see section 3.10). The ERG provided 2 scenario analyses to address these concerns:

- treatment effect for all physiological parameters

- treatment effect for HbA1c only.

These scenarios resulted in probabilistic ICERs of £15,163 and £25,115 per QALY gained respectively. The committee noted that both of these scenarios included a relationship between physiological parameters (see section 3.10) and the long-term risk of macrovascular and microvascular complications. The committee recalled its conclusions that sotagliflozin with insulin modestly improved HbA1c and BMI, compared with insulin alone (see section 3.7). It concluded that the most plausible ICER is between £15,163 per QALY gained and £25,115 per QALY gained.

Sotagliflozin with insulin appears to be cost effective when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy

3.14 The committee concluded that sotagliflozin with insulin appears to be a cost-effective use of NHS resources for treating type 1 diabetes in adults with a BMI of 27 kg/m^2 or more when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy. It also considered the recommendations for starting treatment used in NICE's technology appraisal guidance on dapagliflozin with insulin for type 1 diabetes would be relevant to this appraisal. The committee further concluded that all the following criteria should also be included in the recommendation:

- people are on insulin doses of 0.5 units/kg of body weight/day or more (see section 3.3)
- people have completed a structured education programme such as DAFNE, which includes training on diabetes ketoacidosis, before starting treatment (see section 3.3)
- treatment is started and supervised by a consultant physician specialising in endocrinology and diabetes (see section 3.3)
- HbA1c level is assessed after 6 months (and regularly after this), and sotagliflozin is stopped if there has not been a sustained improvement in glycaemic control, that is, a fall in HbA1c level of at least 0.3% (see section 3.15).

People should stop sotagliflozin if glycaemic control does not improve

3.15 The committee noted that the cost-effectiveness estimates (see section 3.13) did not include treatment discontinuation or a stopping rule if glycaemic control was not improved. The committee was aware that in NICE's technology appraisal guidance on dapagliflozin with insulin for type 1 diabetes, a clinically meaningful reduction in HbA1c levels was defined as at least 0.3 percentage points. The clinical experts explained that it would be reasonable to stop treatment if there was not a clinically meaningful decrease in glycaemic control, defined as a change in HbA1c level of at least 0.3 percentage points. The committee recognised that, in general, ongoing treatment in the absence of a clinically meaningful improvement in HbA1c level would subject the person to risks of diabetic ketoacidosis and the NHS to costs. It concluded that HbA1c should be assessed after 6 months of starting treatment and then regularly after this, and that sotagliflozin should be stopped if glycaemic control does not improve (that is, a fall in HbA1c level of at least 0.3%).

Equality issues

3.16 No equality issues were raised by stakeholders.

There are no additional benefits not adequately captured in the QALY

3.17 The committee recognised that there is an unmet need for people with inadequately controlled type 1 diabetes despite optimised insulin therapy. It agreed that sotagliflozin is innovative, but all health benefits are likely to be captured in the model. Furthermore, the committee did not consider sotagliflozin a step change in managing type 1 diabetes because of the modest benefits seen in the clinical trials (see section 3.7).

4 Implementation

4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication. However, the company has informed NICE that sotagliflozin is not yet available in the NHS. Therefore, the period during which the NHS in England has to comply with the recommendations has been extended to within 3 months of the commercial launch of sotagliflozin in England. This extension is made under Section 7(5b) of the Regulations.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document. However, the company has informed NICE that sotagliflozin is not yet available in the NHS. Therefore, the period during which the NHS in Wales has to comply with the recommendations has been extended to within 2 months of the commercial launch of sotagliflozin in Wales.

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 type 1 diabetes and the doctor responsible for their care thinks that sotagliflozin is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Appraisal committee members and NICE project team

Appraisal committee members

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

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

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

NICE project team

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

Jessica Cronshaw
Technical lead

Eleanor Donegan and Carl Prescott
Technical advisers

Jeremy Powell
Project manager

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Accreditation