Innovation Observatory

NHS National Institute for Health Research

HEALTH TECHNOLOGY BRIEFING
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Sotagliflozin for type 2 diabetes mellitus

NIHRIO ID	4993	**NICE ID**	9764
Developer/Company	Sanofi	**UKPS ID**	646913

Licensing and market availability plans	Currently in phase III clinical trials.

SUMMARY

Sotagliflozin is in clinical development for the treatment of type 2 diabetes mellitus (T2DM). T2DM is a common, lifelong condition that causes the level of glucose in the blood to become too high. It is caused by problems with a chemical in the body (hormone) called insulin, which is produced in the pancreas and is responsible for controlling the amount of glucose in the blood. There are two main types of diabetes: type 1 – where the pancreas does not produce any insulin, and type 2 - where the pancreas does not produce enough insulin or body cells do not react to insulin.

Sotagliflozin is one of a new class of drugs that increase elimination of glucose in the urine. They offer the advantages of a reduced risk of low blood sugar. Sotagliflozin reduces the reabsorption of glucose from the intestines and kidneys, thus improving blood glucose control in diabetes mellitus. If licensed, sotagliflozin will offer an additional treatment option for patients with T2DM.

PROPOSED INDICATION

Type 2 diabetes mellitus (T2DM)[a]

TECHNOLOGY

DESCRIPTION

Sotagliflozin (Zynquista, SAR439954, LX4211) is an antihyperglycemic drug which inhibits the sodium-glucose co-transporters (SGLTs) SGLT1 and SGLT2. SGLT1 is the primary transporter responsible for the absorption of glucose and galactose in the intestine, while SGLT2 and SGLT1 are both involved in the renal reabsorption of glucose.[1] Both of these proteins appear to be upregulated in individuals with diabetes, who present with elevated levels of intestinal glucose absorption and reduced glycosuria. This is a maladaptive response, contributing to the maintenance of pathological hyperglycaemia. SGLT1 and SGLT2 inhibitors including sotagliflozin supress glucose reabsorption from the intestines and kidneys, thus improving glycaemic control diabetes mellitus.[2]

Sotagliflozin is currently in development for the treatment of T2DM. In the phase III clinical trials (NCT02926937, NCT03066830, NCT03285594, NCT02926950, NCT03242018, NCT03242252, NCT03332771, NCT03386344, NCT03521934), sotagliflozin is administered orally in tablet form, once daily. The treatment regimen varies between trials.[3-11]

INNOVATION AND/OR ADVANTAGES

SGLT2 inhibitors are a new class of oral antidiabetic drugs, acting by increasing urinary glucose excretion (UGE). They offer the advantages of a reduced risk of hypoglycaemia, a decrease in body weight and blood pressure and an efficacy at all stages of T2DM. Sotagliflozin is a first-in-class dual SGLT1/SGLT2 inhibitor. By a potential additional mechanism of action on intestinal glucose absorption linked to SGLT1 inhibition, sotagliflozin differentiates from SGLT2 inhibitors by reducing postprandial glucose excursion and insulin secretion, as well as by increasing glucagon-like peptide-1 (GLP-1) secretion. Despite a weaker effect on UGE than selective SGLT2 inhibitors, sotagliflozin is as effective as SGLT2 inhibitors on HbA1C reduction, with a similar safety profile in short-term studies.[1]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Sotagliflozin does not currently have Marketing Authorisation in the EU/UK for any indication, however on February 28th 2019 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for sotgliflozin, for the treatment of type 1 diabetes mellitus as an adjunct to insulin.[12]

Sotagliflozin is in phase III clinical development for cardiovascular events in patients with T2DM post worsening heart failure[11] and on glucose control in patients with T2DM, severe impairment of kidney function and inadequate blood sugar control.[7]

[a] Information provided by Sanofi on UK PharmaScan

PATIENT GROUP

DISEASE BACKGROUND

T2DM is a common, lifelong condition that causes the level of glucose in the blood to become too high. It is caused by problems with a chemical in the body (hormone) called insulin, which is produced in the pancreas and is responsible for controlling the amount of glucose in the blood. There are two main types of diabetes: type 1 – where the pancreas does not produce any insulin, and type 2 - where the pancreas does not produce enough insulin or body cells do not react to insulin.[13]

Risk factors for T2DM are: increased age (>40 years), having a parent or sibling with diabetes, ethnicity (being of South Asian, African-Caribbean or Black African decent), having high blood pressure and being overweight.[14]

Symptoms of T2DM include: urinating more than usual, particularly at night, feeling thirsty all the time, feeling very tired, losing weight without trying to, itching around the penis or vagina, or repeatedly getting thrush; cuts or wounds taking longer to heal and blurred vision.[15]

If T2DM is not adequately controlled, this may result in hyperglycaemia (high blood glucose), which in itself has numerous associated complications. These can include kidney failure, nerve damage, damage to vision (sometimes even causing blindness), heart disease, stroke, peripheral arterial disease, foot ulcers (which can eventually lead to foot or lower leg amputation), persistent or regular infections (e.g. skin or urine infections) and dementia.[16]

Hypoglycaemia (low blood glucose) can also be a complication of T2DM where blood glucose levels become too low (which can be caused by not eating enough carbohydrate while taking insulin, missing meals or medications, drinking too much alcohol or doing more physical activity than usual). Symptoms of hypoglycaemia include feeling hungry, increased sweating, heart palpitations, anxiety and irritability, tingling lips, feeling tired and confused and blurred vision. If hypoglycaemia is not treated, this can result in fits, loss of consciousness and death.[16]

There is evidence that microvascular complications (complications affecting the small blood vessels) of T2DM can impact negatively on quality of life, in terms of having worse general health, more problems with usual activities, reduced vigour, more tension and mood disturbance, compared to those without a microvascular complication.[17]

CLINICAL NEED AND BURDEN OF DISEASE

In 2017-18, the total number of registrations of diabetes in England was 3,222,559,[18] representing 6.8% of the population.[19] If 90% of these cases are T2DM,[20] this equates to approximately 2,900,303 registrations and 6.1% of the population with T2DM.

The Hospital Episodes Statistics for England 2017/2018 recorded 42,832 finished consultant episodes (FCE), 24,917 hospital admissions, 176,378 bed days and 3,021 day cases due to non-insulin dependent (Type 2) diabetes mellitus (ICD 10 code E11).[21]

In England and Wales, people with T2DM have 34.5% greater risk of mortality compared to the general population. For T2DM, life expectancy for someone diagnosed in their 50s is reduced by an average of 6 years. It is currently estimated that 10% of NHS budget is spent on diabetes which equates to about £10 billion. The total cost (including direct and indirect costs) associated with diabetes in the UK is currently £23.7 billion and this is expected to rise to 39.8 billion in 2035/2036.[22]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

NICE guidelines recommend that clinicians should adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with T2DM, taking into account their personal preferences, comorbidities, risks from polypharmacy, and their ability to benefit from long-term interventions because of reduced life expectancy.[23]

Structured education is an integral part of diabetes care, and should be offered to patients at time of diagnosis, with annual reinforcement and review. Other key priorities include dietary advice, blood pressure management, blood glucose management, drug treatment, and the monitoring of complications.[23]

CURRENT TREATMENT OPTIONS

The following anti-diabetic medication options are recommended by NICE:[24]

Initial drug treatment with metformin: offer standard-release metformin as the initial drug treatment for adults with type 2 diabetes. If initial drug treatment with metformin has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider dual therapy with:

- metformin and a DPP-4 inhibitor or
- metformin and pioglitazone1 or
- metformin and a sulfonylurea

In adults with type 2 diabetes, do not offer or continue pioglitazone if they have any of the following:

- heart failure or history of heart failure
- hepatic impairment
- diabetic ketoacidosis
- current, or a history of, bladder cancer
- uninvestigated macroscopic haematuria

Treatment with SGLT-2 inhibitors may be appropriate for some adults with type 2 diabetes if metformin is contraindicated or not tolerated.

Treatment with combinations of medicines including SGLT-2 inhibitors (ertugliflozin, canagliflozin, dapagliflozin) may be appropriate for some people with type 2 diabetes. Ertugliflozin, canagliflozinor dapagliflozin in a dual-therapy regimen in combination with metformin are recommended as options for treating type 2 diabetes, only if:

- a sulfonylurea is contraindicated or not tolerated or
- the person is at significant risk of hypoglycaemia or its consequences

If patients and their clinicians consider ertugliflozin, canagliflozin, dapagliflozin or empagliflozin as suitable treatment options, the least expensive should be chosen.

PLACE OF TECHNOLOGY

If licensed, sotagliflozin will offer an additional treatment option for patients with T2DM.

CLINICAL TRIAL INFORMATION

Trial	**Sotagliflozin, NCT02926937; adults aged ≥18 years; sotagliflozin vs placebo; phase III**
Sponsor	Sanofi
Status	Ongoing
Source of Information	Trial registry,[3] manufacturer[b]
Location	USA, Canada, Mexico
Design	Randomised, double-blind, placebo-controlled, parallel-group
Participants	n=400 (planned); aged ≥18 years; T2DM; treated with diet and exercise only during the 12 weeks prior to screening
Schedule	Randomised to 2 X 200mg tablets once daily before the first meal of the day (sotagliflozin dose 1, 400 mg); or 1 X 200mg tablet of sotagliflozin plus 1 placebo tablet once daily, before the first meal of the day (sotagliflozin dose 2); or 2 placebo tablets, once daily before the first meal of the day
Follow-up	Active treatment for 26 weeks, follow-up 4 weeks
Primary Outcomes	Change from baseline in HbA1c in comparison of sotagliflozin dose 1 versus placebo [Time frame: Baseline to week 26]
Secondary Outcomes	**Baseline to week 26:** • Change from baseline in 2-hour PPG following a mixed meal in comparison of sotagliflozin doses 1 (400mg) and 2 (200mg) versus placebo • Change from baseline in FPG in comparison of sotagliflozin dose 1 (400mg) versus placebo • Change from baseline in body weight in comparison of sotagliflozin doses 1 (400mg) and 2 (200mg)versus placebo • Change from Baseline in HbA1c in comparison of sotagliflozin dose 2 (200mg) versus placebo **Baseline to week 12:** • Change from baseline in SBP for patients with baseline SBP ≥130 mmHg in comparison of sotagliflozin dose 1 (400mg) versus placebo • Change from baseline in SBP for all patients in comparison of sotagliflozin doses 1 (400mg) and 2 (200mg) versus placebo **At week 26:** • Percentage of patients with HbA1c <6.5% in comparison of sotagliflozin dose 1 (400mg)versus placebo • Percentage of patients with HbA1c <7.0% in comparison of sotagliflozin dose 1 (400mg) versus placebo
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as May 2019

Trial	**Sotagliflozin, NCT03066830; adults aged ≥18 years; sotagliflozin vs placebo; phase III**
Sponsor	Sanofi

[b] Information provided by Sanofi

Status	Ongoing
Source of Information	Trial registry[4]
Location	7 EU countries (incl UK), USA, Republic of Korea and Ukraine
Design	Randomised, double-blind, placebo-controlled, parallel-group
Participants	n=500 (planned); aged ≥18 years; T2DM; treated with a sulfonylurea (≥half the maximum recommended dose as per local label or maximum tolerated dose [documented]) as monotherapy or in combination with metformin (≥1500 mg per day or maximum tolerated dose [documented]) each at a stable dose for at least 12 weeks without a dose adjustment before screening
Schedule	Randomised to 2 x 200mg sotagliflozin tablets, once daily, before the first meal of the day (sotagliflozin dose 1, 400mg); or 2 placebo tablets, once daily, before the first meal of the day
Follow-up	Active treatment for 26 weeks, extension for 53 weeks, follow up 2 weeks
Primary Outcomes	Change from baseline in HbA1c [Time frame: Baseline to week 26]
Secondary Outcomes	**Baseline to week 26:** • Change from baseline in Fasting Plasma Glucose • Change from baseline in body weight **Baseline to week 12:** • Change from baseline in Systolic Blood Pressure (SBP) for patients with baseline SBP ≥130 mmHg • Change from baseline in SBP for all patients **At week 26:** • Percentage of patients with HbA1c <6.5% • Percentage of patients with HbA1c <7.0%
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as May 2019

Trial	**Sotagliflozin, NCT03285594,** EudraCT2016 - 001804 - 43; adults aged ⩾18 years; sotagliflozin vs placebo; phase III
Sponsor	Sanofi
Status	Ongoing
Source of Information	Trial registries,[5,25]manufacturer[b]
Location	5 EU countries (incl UK), USA, Canada, Czechia
Design	Randomised, placebo-controlled
Participants	n=560 (estimated); aged ≥18 years; T2DM; using any types of basal insulin alone or in combination with up to 2 OADs (oral antidiabetic drugs)
Schedule	Randomised to 2 x 200mg sotagliflozin tablets, once daily, before the first meal of the day background therapy with insulin glargine (Lantus) (with or without OADs) will continue throughout the study (sotagliflozin dose 1, 400mg); or 1 x 200mg sotagliflozin tablet plus one placebo tablet, taken orally once daily, before first meal of the day. Background therapy with insulin glargine (Lantus) (with or

	without OADs) will continue throughout the study (sotagliflozin dose 2, 200mg); or 2 placebo tablets, once daily, before the first meal of the day background therapy with insulin glargine (Lantus) (with or without OADs) will continue throughout the study (placebo)
Follow-up	Active treatment for 52 weeks, follow up 2 weeks
Primary Outcomes	**Change in HbA1c [Time frame: Baseline to week 18]** • Absolute change from baseline in hemoglobin A1c (HbA1c) (for sotagliflozin dose 1 (400mg))
Secondary Outcomes	**Baseline to week 12:** • Change in systolic blood pressure (SBP) for all patients • Change in SBP for patients with Baseline SBP ⩾130 mmHg **Baseline to week 18:** • Change in Fasting plasma glucose • Change in body weight • Change in HbA1c **Baseline to week 52:** • Change in Body Weight • Change in HbA1c • Adverse events
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as August 2019

Trial	**Sotagliflozin, NCT02926950, EudraCT2016-001800-49; adults aged ≥18 years; sotagliflozin vs placebo; phase III**
Sponsor	Sanofi
Status	Ongoing
Source of Information	Trial registries,[6,26]manufacturer[b]
Location	2 EU countries (excl UK), USA and Canada
Design	Randomised, double-blind, placebo-controlled, parallel-group
Participants	n=500 (planned); aged ≥18 years; patients with T2DM currently treated with diet and exercise and on metformin at a stable dose ⩾1500 mg/day for at least 12 weeks
Schedule	Randomised to 2 x 200mg tablets of sotagliflozin, once daily, before the first meal of the day (sotagliflozin dose 1, 400mg). Metformin will be administered per principal investigator; or 2 placebo tablets, once daily, before the first meal of the day. Metformin will be administered per principal investigator.
Follow-up	Active treatment for 26 weeks, 53 week extension, follow up 4 weeks
Primary Outcomes	Change from baseline in HbA1c [Time frame: Baseline to week 26]

Secondary Outcomes	**Baseline to week 12:** • Change from baseline in systolic blood pressure (SBP) for all patients • Change from baseline in SBP for patients with baseline SBP ⩾ 130 mmHg **Baseline to week 26:** • Change from Baseline in 2-hour PPG following a mixed meal • Change from Baseline in Fasting Plasma Glucose **At week 26:** • Percentage of patients with HbA1c <6.5% • Percentage of patients with HbA1c <7.0%
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as April 2019

Trial	**Sotagliflozin, NCT03242018,** EudraCT2016-004906-32; adults aged ⩾18 years; sotagliflozin vs placebo; phase III
Sponsor	Sanofi
Status	Ongoing
Source of Information	Trial registry,[7,27]manufacturer[b]
Location	Six EU countries (excl UK), USA and other countries
Design	Randomised,double-blind, placebo-controlled, parallel-group
Participants	n=276 (planned); aged ≥18 years; patients with T2DM and documented severe renal insufficiency
Schedule	Randomised to sotagliflozin 2 x 200mg tablets orally once daily (sotagliflozin dose 1, 400mg); 1 x 200mg sotagliflozin tablet and one placebo tablet orally once daily (sotagliflozin dose 2, 200mg); two placebo tablets orally once daily
Follow-up	Active treatment for 52 weeks, follow up 4 weeks
Primary Outcomes	Change in HbA1c [Time frame: Baseline to week 26]
Secondary Outcomes	**Baseline to week 12:** • Change in Systolic Blood Pressure (SBP) for patients with SBP ⩾130 mmHg • Change in SBP **Baseline to week 26:** • Change in HbA1c • Change in Fasting Plasma Glucose (FPG) • Change in urinary albumin-to-creatinine ratio (UACR) **At week 26:** • Patients with HbA1c less than 6.5% • Patients with HbA1c less than 7.0% **Week 52:** • Adverse events

Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as December 2019

Trial	**Sotagliflozin, NCT03242252,** EudraCT2016-004889-26**;** adults aged ⩾18 years; sotagliflozin vs placebo; phase III
Sponsor	Sanofi
Status	Ongoing
Source of Information	Trial registry,[8,28]manufacturer[b]
Location	Seven EU countries (excl UK), USA, Canada and other countries
Design	Randomised, double-blind, placebo-controlled, parallel-group
Participants	n=780 (planned); aged ≥18 years; patients with T2DM and documented moderate renal insufficiency
Schedule	Randomised to 1 x 200mg sotagliflozin tablet and 1 placebo tablet, once daily before the first meal of the day (sotagliflozin dose 1, 200mg); or 2 x 200mg sotagliflozin tablets, once daily before the first meal of the day (sotagliflozin dose 2, 400mg); or 2 placebo tablets once daily before the first meal of the day
Follow-up	Active treatment for 52 weeks, follow up 4 weeks
Primary Outcomes	Change in HbA1c [Time frame: Baseline to week 26]
Secondary Outcomes	**Baseline to week 12:** • Change in Systolic Blood Pressure (SBP) for patients with SBP ⩾130 mmHg • Change in Systolic Blood Pressure **Baseline to week 26:** • Change in Fasting Plasma Glucose (FPG) • Change in body weight • Change in urinary albumin-to-creatinine ratio (UACR) **At week 26:** • Patients with HbA1c less than 6.5% • Patients with HbA1c less than 7.0% **Week 52:** • Adverse events
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as October 2019

Trial	**Sotagliflozin, NCT03332771,** EudraCT2016-001801-17; adults aged ⩾18 years; sotagliflozin vs glimepiride vs placebo; phase III
Sponsor	Sanofi

Status	Ongoing
Source of Information	Trial registry,[9,29]manufacturer[b]
Location	Three EU countries (excl UK), USA
Design	Randomised, double-blind, double-dummy, active and placebo-controlled, parallel-group
Participants	n=930 (planned); aged ≥18 years; patients with T2DM treated with metformin at a stable dose ⩾1500 mg/day or maximum tolerated dose (documented) for at least 12 weeks prior to screening visit
Schedule	Randomised 2 x 200mg sotagliflozin tablets, and two glimepiride-matching placebo capsules, taken orally once daily before the first meal of the day (sotagliflozin dose 1, 400mg); or 1 x 200 mg sotagliflozin tablet and one sotagliflozin-matching placebo tablet, and two glimepiride-matching placebo capsules, taken orally once daily before the first meal of the day (sotagliflozin dose 2, 200mg); or two sotagliflozin-matching placebo tablets, and combination of 2 glimepiride capsules with adequate dose strengths per dose titration (titrated up to 6mg), taken orally once daily before the first meal of the day (active comparator: glimepiride); or two sotagliflozin-matching placebo tablets and two glimepiride-matching placebo capsules, taken orally once daily before the first meal of the day (placebo)
Follow-up	Active treatment for 52 weeks, follow up 2 weeks
Primary Outcomes	Change in hemoglobin A1c (for sotagliflozin dose1) [Time frame: Baseline to week 52]
Secondary Outcomes	**Baseline to week 12:** • Change in SBP for all patients (for sotagliflozin dose1) • Change in SBP (systolic blood pressure) for patients with baseline SBP ⩾130 mmHg (for sotagliflozin dose1) **Baseline to week 26:** • Change in hemoglobin A1c (for sotagliflozin dose1) • Change in body weight (for sotagliflozin dose1) • Change in hemoglobin A1c (for sotagliflozin dose 2) **Baseline to week 52:** • Change in body weight (for sotagliflozin dose1) • At least one documented symptomatic hypoglycemic event (⩽ 70 mg/dL) (for sotagliflozin dose1) • Change in hemoglobin A1c (for sotagliflozin dose 2) • Adverse events
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as August 2019

Trial	**Sotagliflozin, NCT03386344; adults aged ≥55 years; sotagliflozin vs placebo; phase III**

Sponsor	Sanofi
Status	Ongoing
Source of Information	Trial registry,[10]manufacturer[b]
Location	USA, Canada, and other countries
Design	Randomised, double-blind, placebo-controlled, parallel-group
Participants	n=360 (planned); aged ≥55 years; patients with T2DM managed with diet and exercise only or with a stable antidiabetes regimen (in monotherapy or combination therapy that can include oral antidiabetes medications, insulin, or glucagon-like peptide-1 agonists) for more than 12 weeks
Schedule	Randomised to 2 X200mg sotagliflozin tablets on top of baseline antidiabetic therapy (sotaglifin dose 1, 400mg); or 1 X 200mg sotagliflozin tablet and one sotagliflozin matching placebo tablet on top of baseline antidiabetic therapy (sotaglifin dose 2, 200mg); or two sotagliflozin matching placebo tablets on top of baseline antidiabetic therapy
Follow-up	Active treatment for 26-weeks, a 78-week extension period, 2-week follow up
Primary Outcomes	Change in hemoglobin A1C (HbA1c) [Time frame: Baseline to week 26]
Secondary Outcomes	**Baseline to week 12:** • Change in systolic blood pressure (SBP) **Baseline to week 26:** • Change in HbA1c • Change in body weight (BW) • Change in Fasting Plasma Glucose (FPG) • Percent change in BMD of total hip • Percent change in BMD of femoral neck **Week 26:** • Patients with HbA1c < 7.0% **Up to week 52:** • Adverse events
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as December 2020

Trial	**Sotagliflozin, NCT03521934,** EudraCT2017-003510-16; adults aged ⩾18 years to ⩽85 years; sotagliflozin vs placebo; phase III
Sponsor	Sanofi
Status	Ongoing
Source of Information	Trial registry,[11,30]manufacturer[b]
Location	EU countries (incl UK), Canada, USA and other countries

Design	Randomised, double-blind, placebo-controlled, parallel-group
Participants	n=4,000 (planned); aged ⩾18 years to ⩽85 years; patients with T2DM; admitted to the hospital, or urgent heart failure visit for worsening heart failure
Schedule	Randomised to sotagliflozin dose 1 X 200mg sotagliflozin, once daily with possible uptitration in the first 8 months to 2 X 200mg (400mg) of sotagliflozin; or 1 placebo tablet, once daily with possible uptitration in the first 8 months to 2 X placebo tablets
Follow-up	The estimated study duration for a given patient will be approximately 3 to 32 months
Primary Outcomes	Cardiovascular (CV) death or hospitalization for heart failure (HHF) [time frame: baseline to approximately 32 months] CV death or hospitalization for heart failure (HHF) [time frame: baseline to approximately 32 months]
Secondary Outcomes	**Baseline to approximately 32 months:** • Total number of heart failure events • Time to first composite renal event • CV death • All cause mortality
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study estimated completion date reported as January 2021

ESTIMATED COST

ADDITIONAL INFORMATION

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal in development. Empagliflozin for reducing the risk of cardiovascular events in type 2 diabetes (ID1037). Expected date of issue to be confirmed.
- NICE technology appraisal. Dapagliflozin in triple therapy for treating type 2 diabetes. (TA418). November 2016.
- NICE technology appraisal. Dapagliflozin in combination therapy for treating type 2 diabetes (TA288). June 2013. Last updated November 2016.

- NICE technology appraisal. Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes (TA390). May 2016.
- NICE technology appraisal. Empagliflozin in combination therapy for treating type 2 diabetes (TA336). March 2015.
- NICE technology appraisal. Canagliflozin in combination therapy for treating type 2 diabetes (TA315). June 2014.
- NICE clinical guideline. Type 2 diabetes in adults: management (NG28). December 2015. Last updated May 2017.
- NICE quality standard. Diabetes in adults. (QS6). March 2011. Last updated August 2016.
- NICE public health guidance. Type 2 diabetes: prevention in people at high risk (PH38). July 2012. Last updated September 2017.
- NICE public health guidance. Type 2 diabetes prevention: population and community-level interventions (PH35). May 2011.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013/14 NHS Standard Contract for Specialised Endocrinology Services (Adult). A03/S/a.

OTHER GUIDANCE

- Scottish Intercollegiate Guidelines Network. Management of diabetes. SIGN 116. September 2013.[31]

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