NICE National Institute for Health and Care Excellence

NICE Pathways

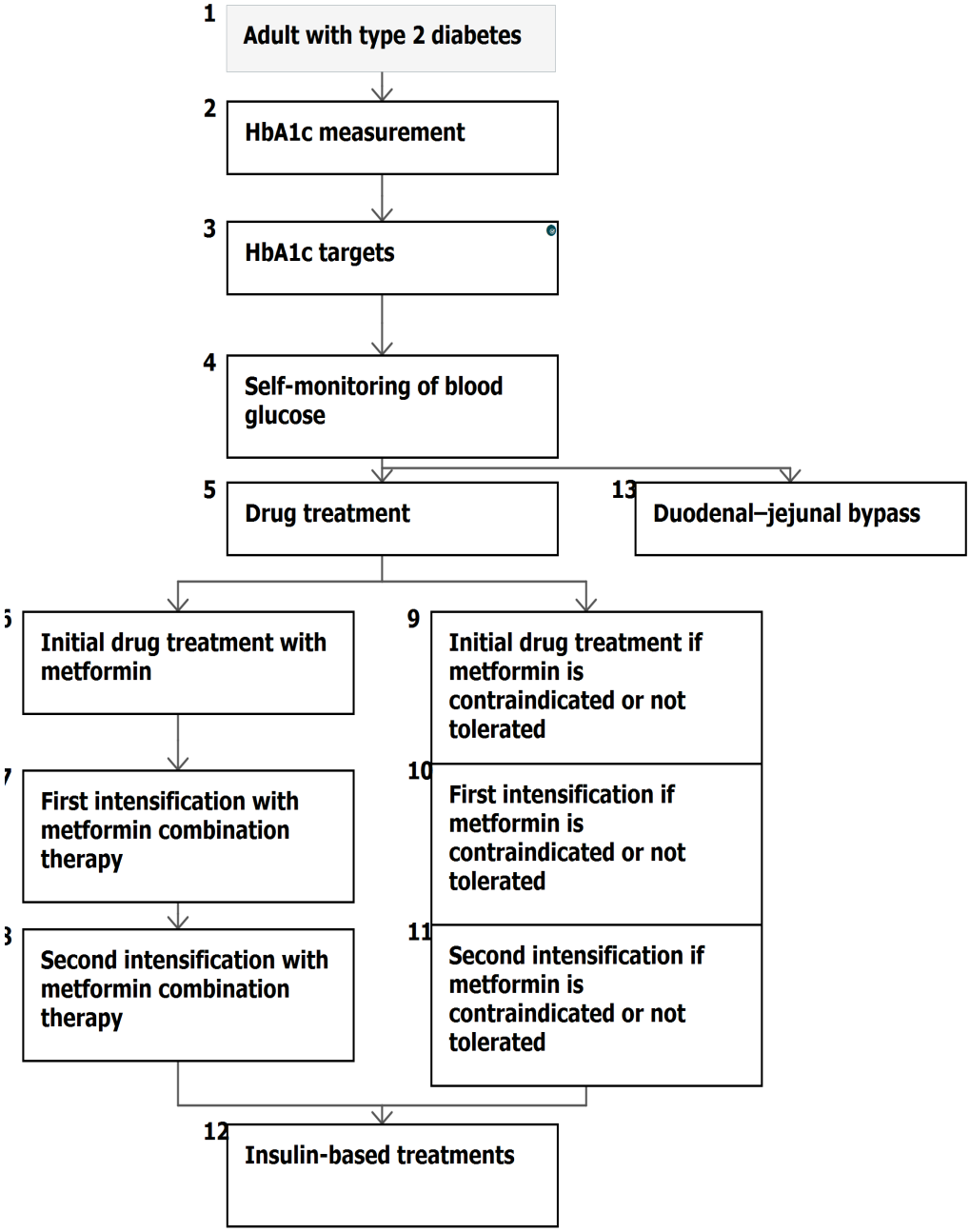
Managing blood glucose in adults with type 2 diabetes

NICE Pathways bring together everything NICE says on a topic in an interactive flowchart. NICE Pathways are interactive and designed to be used online.

They are updated regularly as new NICE guidance is published. To view the latest version of this NICE Pathway see:

http://pathways.nice.org.uk/pathways/type-2-diabetes-in-adults
NICE Pathway last updated: 26 March 2019

This document contains a single flowchart and uses numbering to link the boxes to the associated recommendations.



1 Adult with type 2 diabetes

No additional information

2 HbA1c measurement

In adults with type 2 diabetes, measure HbA1c levels at:

- 3–6-monthly intervals (tailored to individual needs), until the HbA1c is stable on unchanging therapy
- 6-monthly intervals once the HbA1c level and blood glucose lowering therapy are stable.

Use methods to measure HbA1c that have been calibrated according to International Federation of Clinical Chemistry (IFCC) standardisation.

If HbA1c monitoring is invalid because of disturbed erythrocyte turnover or abnormal haemoglobin type, estimate trends in blood glucose control using one of the following:

- quality-controlled plasma glucose profiles
- total glycated haemoglobin estimation (if abnormal haemoglobins)
- fructosamine estimation.

Investigate unexplained discrepancies between HbA1c and other glucose measurements. Seek advice from a team with specialist expertise in diabetes or clinical biochemistry.

3 HbA1c targets

Involve adults with type 2 diabetes in decisions about their individual HbA1c target. Encourage them to achieve the target and maintain it unless any resulting adverse effects (including hypoglycaemia), or their efforts to achieve their target, impair their quality of life.

Offer lifestyle advice and drug treatment to support adults with type 2 diabetes to achieve and maintain their HbA1c target (see patient education and lifestyle advice). For more information about supporting adherence, see what NICE says on medicines optimisation.

For adults with type 2 diabetes managed either by lifestyle and diet, or by lifestyle and diet combined with a single drug not associated with hypoglycaemia, support the person to aim for an HbA1c level of 48 mmol/mol (6.5%). For adults on a drug associated with hypoglycaemia,

support the person to aim for an HbA1c level of 53 mmol/mol (7.0%).

In adults with type 2 diabetes, if HbA1c levels are not adequately controlled by a single drug and rise to 58 mmol/mol (7.5%) or higher:

- reinforce advice about diet, lifestyle and adherence to drug treatment **and**
- support the person to aim for an HbA1c level of 53 mmol/mol (7.0%) **and**
- intensify drug treatment.

If adults with type 2 diabetes achieve an HbA1c level that is lower than their target and they are not experiencing hypoglycaemia, encourage them to maintain it. Be aware that there are other possible reasons for a low HbA1c level, for example, deteriorating renal function or sudden weight loss.

When to consider relaxing the target level

Consider relaxing the target HbA1c level on a case-by-case basis, with particular consideration for people who are older or frail, for adults with type 2 diabetes:

- who are unlikely to achieve longer-term risk-reduction benefits, for example, people with a reduced life expectancy
- for whom tight blood glucose control poses a high risk of the consequences of hypoglycaemia, for example, people who are at risk of falling, people who have impaired awareness of hypoglycaemia, and people who drive or operate machinery as part of their job
- for whom intensive management would not be appropriate, for example, people with significant comorbidities.

Targets in pregnancy

For guidance on HbA1c targets for women with type 2 diabetes who are pregnant or planning to become pregnant, see what NICE says on diabetes in pregnancy.

Quality standards

The following quality statement is relevant to this part of the interactive flowchart.

4. First intensification of blood glucose lowering therapy in type 2 diabetes

4 Self-monitoring of blood glucose

Take the DVLA At a glance guide to the current medical standards of fitness to drive into account when offering self-monitoring of blood glucose levels for adults with type 2 diabetes.

Do not routinely offer self-monitoring of blood glucose levels for adults with type 2 diabetes unless:

- the person is on insulin **or**
- there is evidence of hypoglycaemic episodes **or**
- the person is on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery **or**
- the person is pregnant, or is planning to become pregnant. For more information, see the what NICE says on diabetes in pregnancy.

Consider short-term self-monitoring of blood glucose levels in adults with type 2 diabetes (and review treatment as necessary):

- when starting treatment with oral or intravenous corticosteroids **or**
- to confirm suspected hypoglycaemia.

Be aware that adults with type 2 diabetes who have acute intercurrent illness are at risk of worsening hyperglycaemia. Review treatment as necessary.

If adults with type 2 diabetes are self-monitoring their blood glucose levels, carry out a structured assessment at least annually. The assessment should include:

- the person's self-monitoring skills
- the quality and frequency of testing
- checking that the person knows how to interpret the blood glucose results and what action to take
- the impact on the person's quality of life
- the continued benefit to the person
- the equipment used.

5 Drug treatment

Recommendations that cover DPP-4 inhibitors, GLP-1 mimetics and sulfonylureas refer to each of these groups of drugs at a class level.

The NICE guideline has an algorithm for blood glucose lowering therapy in adults with type 2 diabetes.

For adults with type 2 diabetes, discuss the benefits and risks of drug treatment, and the options available. Base the choice of drug treatment(s) on:

- the effectiveness of the drug treatment(s) in terms of metabolic response
- safety (see Medicines and Healthcare products Regulatory Agency [MHRA] guidance) and tolerability of the drug treatment(s)
- the person's individual clinical circumstances, for example, comorbidities, risks from polypharmacy
- the person's individual preferences and needs
- the licensed indications or combinations available
- cost (if 2 drugs in the same class are appropriate, choose the option with the lowest acquisition cost).

Rescue therapy at any phase of treatment

If an adult with type 2 diabetes is symptomatically hyperglycaemic, consider insulin (see insulin-based treatments [See page 19]) or a sulfonylurea, and review treatment when blood glucose control has been achieved.

6 Initial drug treatment with metformin

In these recommendations, initial drug treatment means treatment with a single non-insulin blood glucose lowering therapy (monotherapy).

Offer standard-release metformin as the initial drug treatment for adults with type 2 diabetes.

Gradually increase the dose of standard-release metformin over several weeks to minimise the risk of gastrointestinal side effects in adults with type 2 diabetes.

If an adult with type 2 diabetes experiences gastrointestinal side effects with standard-release metformin, consider a trial of modified-release metformin.

In adults with type 2 diabetes, review the dose of metformin if the eGFR is below 45 ml/minute/1.73m^2:

- Stop metformin if the eGFR is below 30 ml/minute/1.73m^2.

- Prescribe metformin with caution for those at risk of a sudden deterioration in kidney function and those at risk of eGFR falling below 45 ml/minute/1.73m^2.

7 First intensification with metformin combination therapy

In these recommendations, first intensification of drug treatment means treatment with 2 non-insulin blood glucose lowering therapies in combination (dual therapy).

In 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 pioglitazone[1] **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[2,3] may be appropriate for some adults with type 2 diabetes if metformin is contraindicated or not tolerated (see initial drug treatment if metformin is contraindicated or not tolerated [See page 14]).

Treatment with combinations of medicines including SGLT-2 inhibitors' may be appropriate for some people with type 2 diabetes; see below.

Ertugliflozin

The following recommendations are from NICE technology appraisal guidance on ertugliflozin as monotherapy or with metformin for treating type 2 diabetes.

Ertugliflozin in a dual-therapy regimen in combination with metformin is recommended as an option for treating type 2 diabetes, only if:

[1] When prescribing pioglitazone, exercise particular caution if the person is at high risk of the adverse effects of the drug. Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture. Known risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers' summaries of product characteristics for details. Medicines and Healthcare products Regulatory Agency (MHRA) guidance (2011) advises that 'prescribers should review the safety and efficacy of pioglitazone in individuals after 3–6 months of treatment to ensure that only patients who are deriving benefit continue to be treated'.

[2] MHRA guidance (2017) warned that canagliflozin may increase the risk of lower-limb amputation (mainly toes) in people with type 2 diabetes. At the time of publication (March 2017) evidence did not show an increased risk for dapagliflozin and empagliflozin, but the MHRA advised that the risk may be a class effect.

[3] MHRA guidance (2016) warned that serious, life-threatening, and fatal cases of diabetic ketoacidosis have been reported rarely in people taking an SGLT-2 inhibitor (a substantial proportion of the cases concerned off-label use in people with type 1 diabetes, which is not recommended). In several cases, blood glucose levels were only moderately elevated. The MHRA advised that healthcare professionals should test for raised ketones in people with ketoacidosis symptoms who are receiving an SGLT-2 inhibitor, even if their plasma glucose levels are near-normal.

- 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 to be 1 of a range of suitable treatments including canagliflozin, dapagliflozin and empagliflozin, the least expensive should be chosen.

These recommendations are not intended to affect treatment with ertugliflozin 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.

See why we made the recommendations on ertugliflozin.

NICE has written information for the public on ertugliflozin.

Empagliflozin

The following recommendations are an extract from NICE technology appraisal guidance on empagliflozin in combination therapy for treating type 2 diabetes.

Empagliflozin in a dual therapy regimen in combination with metformin is recommended as an option 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.

People currently receiving treatment initiated within the NHS with empagliflozin that is not recommended for them by NICE in this guidance should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on empagliflozin.

Canagliflozin

The following recommendations are an extract from NICE technology appraisal guidance on canagliflozin in combination therapy for treating type 2 diabetes.

Canagliflozin in a dual therapy regimen in combination with metformin is recommended as an option 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.

People currently receiving treatment initiated within the NHS with canagliflozin that is not recommended for them by NICE in this guidance should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on canagliflozin.

Dapagliflozin

The following recommendations are an extract from NICE technology appraisal guidance on dapagliflozin in combination therapy for treating type 2 diabetes.

Dapagliflozin in a dual therapy regimen in combination with metformin is recommended as an option 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.

People currently receiving dapagliflozin in a dual therapy regimen that is not recommended for them should be able to continue treatment until they and their clinician consider it appropriate to stop.

NICE has written information for the public on dapagliflozin.

Alogliptin

NICE has published an evidence summary on type 2 diabetes: alogliptin.

8 Second intensification with metformin combination therapy

In these recommendations, second intensification of drug treatment means treatment with either 3 non-insulin blood glucose lowering therapies in combination (triple therapy) or any treatment combination containing insulin.

In adults with type 2 diabetes, if dual therapy with metformin and another oral drug (see first intensification with metformin combination therapy [See page 7]) has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider either:

- triple therapy with:

- metformin, a DPP-4 inhibitor and a sulfonylurea **or**
- metformin, pioglitazone[1] and a sulfonylurea **or**

- starting insulin-based treatment (see insulin-based treatments [See page 19])

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[2,3] may be appropriate for some adults with type 2 diabetes if metformin is contraindicated or not tolerated (see initial drug treatment if metformin is contraindicated or not tolerated [See page 14]).

If triple therapy with metformin and 2 other oral drugs (see above) is not effective, not tolerated or contraindicated, consider combination therapy with metformin, a sulfonylurea and a GLP-1 mimetic for adults with type 2 diabetes who:

- have a BMI of 35 kg/m^2 or higher (adjust accordingly for people from black, Asian and other minority ethnic groups) **and** specific psychological or other medical problems associated with obesity **or**
- have a BMI lower than 35 kg/m^2 **and**
  - for whom insulin therapy would have significant occupational implications **or**
  - weight loss would benefit other significant obesity-related comorbidities.

Only continue GLP-1 mimetic therapy if the person with type 2 diabetes has had a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months).

In adults with type 2 diabetes, only offer a GLP-1 mimetic in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team[4].

Treatment with combinations of medicines including SGLT-2 inhibitors' may be appropriate for some people with type 2 diabetes; see below.

[1] When prescribing pioglitazone, exercise particular caution if the person is at high risk of the adverse effects of the drug. Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture. Known

risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers' summaries of product characteristics for details. Medicines and Healthcare products Regulatory Agency (MHRA) guidance (2011) advises that 'prescribers should review the safety and efficacy of pioglitazone in individuals after 3–6 months of treatment to ensure that only patients who are deriving benefit continue to be treated'.

[2] MHRA guidance (2017) warned that canagliflozin may increase the risk of lower-limb amputation (mainly toes) in people with type 2 diabetes. At the time of publication (March 2017) evidence did not show an increased risk for dapagliflozin and empagliflozin, but the MHRA advised that the risk may be a class effect.

[3] MHRA guidance (2016) warned that serious, life-threatening, and fatal cases of diabetic ketoacidosis have been reported rarely in people taking an SGLT-2 inhibitor (a substantial proportion of the cases concerned off-label use in people with type 1 diabetes, which is not recommended). In several cases, blood glucose levels were only moderately elevated. The MHRA advised that healthcare professionals should test for raised ketones in people with ketoacidosis symptoms who are receiving an SGLT-2 inhibitor, even if their plasma glucose levels are near-normal.

[4] A consultant-led multidisciplinary team may include a wide range of staff based in primary, secondary and community care.

Empagliflozin

The following recommendation is an extract from NICE technology appraisal guidance on empagliflozin in combination therapy for treating type 2 diabetes.

Empagliflozin in a triple therapy regimen is recommended as an option for treating type 2 diabetes in combination with:

- metformin and a sulfonylurea **or**
- metformin and a thiazolidinedione.

NICE has written information for the public on empagliflozin.

Canagliflozin

The following recommendation is an extract from NICE technology appraisal guidance on canagliflozin in combination therapy for treating type 2 diabetes.

Canagliflozin in a triple therapy regimen is recommended as an option for treating type 2 diabetes in combination with:

- metformin and a sulfonylurea **or**
- metformin and a thiazolidinedione.

NICE has written information for the public on canagliflozin.

Dapagliflozin

The following recommendations are from NICE technology appraisal guidance on dapagliflozin in triple therapy for treating type 2 diabetes.

Dapagliflozin in a triple therapy regimen is recommended as an option for treating type 2 diabetes in adults, only in combination with metformin and a sulfonylurea.

This guidance is not intended to affect the position of patients whose treatment with dapagliflozin in other triple therapy regimens was started within the NHS before this guidance was published. Treatment of those patients may continue without change to whatever funding arrangements were in place for them before this guidance was published until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on dapagliflozin.

Evidence summaries

NICE has published evidence summaries on:

- type 2 diabetes: dulaglutide
- type 2 diabetes: lixisenatide
- type 2 diabetes: alogliptin.

9 Initial drug treatment if metformin is contraindicated or not tolerated

In these recommendations, initial drug treatment means treatment with a single non-insulin blood glucose lowering therapy (monotherapy).

In adults with type 2 diabetes, if metformin is contraindicated or not tolerated, consider initial drug treatment[1] with:

- a DPP-4 inhibitor **or**
- pioglitazone[2] **or**
- 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[3,4] may be appropriate for some adults with type 2 diabetes if metformin is contraindicated or not tolerated; see below.

Ertugliflozin

The following recommendations are from NICE technology appraisal guidance on ertugliflozin as monotherapy or with metformin for treating type 2 diabetes.

Ertugliflozin as monotherapy is recommended as an option for treating type 2 diabetes in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not

[1] Be aware that, if metformin is contraindicated or not tolerated, repaglinide is both clinically effective and cost effective in adults with type 2 diabetes. However, discuss with any person for whom repaglinide is being considered, that there is no licensed non-metformin-based combination containing repaglinide that can be offered at first intensification.

[2] When prescribing pioglitazone, exercise particular caution if the person is at high risk of the adverse effects of the drug. Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture. Known risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers' summaries of product characteristics for details. Medicines and Healthcare products Regulatory Agency (MHRA) guidance (2011) advises that 'prescribers should review the safety and efficacy of pioglitazone in individuals after 3–6 months of treatment to ensure that only patients who are deriving benefit continue to be treated'.

[3] MHRA guidance (2017) warned that canagliflozin may increase the risk of lower-limb amputation (mainly toes) in people with type 2 diabetes. At the time of publication (March 2017) evidence did not show an increased risk for dapagliflozin and empagliflozin, but the MHRA advised that the risk may be a class effect.

[4] MHRA guidance (2016) warned that serious, life-threatening, and fatal cases of diabetic ketoacidosis have been reported rarely in people taking an SGLT-2 inhibitor (a substantial proportion of the cases concerned off-label use in people with type 1 diabetes, which is not recommended). In several cases, blood glucose levels were only moderately elevated. The MHRA advised that healthcare professionals should test for raised ketones in people with ketoacidosis symptoms who are receiving an SGLT-2 inhibitor, even if their plasma glucose levels are near-normal.

provide adequate glycaemic control, only if:

- a DPP-4 inhibitor would otherwise be prescribed and
- a sulfonylurea or pioglitazone is not appropriate.

If patients and their clinicians consider ertugliflozin to be 1 of a range of suitable treatments including canagliflozin, dapagliflozin and empagliflozin, the least expensive should be chosen.

These recommendations are not intended to affect treatment with ertugliflozin 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.

See why we made the recommendations on ertugliflozin.

NICE has written information for the public on ertugliflozin.

Canagliflozin, dapagliflozin and empagliflozin as monotherapies

The following recommendations are from NICE technology appraisal guidance on canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes.

Canagliflozin, dapagliflozin and empagliflozin as monotherapies are recommended as options for treating type 2 diabetes in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if:

- a DPP-4 inhibitor would otherwise be prescribed and
- a sulfonylurea or pioglitazone is not appropriate.

Adults whose treatment with canagliflozin, dapagliflozin or empagliflozin as monotherapy is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

NICE has written information for the public on canagliflozin, dapagliflozin and empagliflozin.

10 First intensification if metformin is contraindicated or not tolerated

In these recommendations, first intensification of drug treatment means treatment with 2 non-

insulin blood glucose lowering therapies in combination (dual therapy).

In adults with type 2 diabetes, if metformin is contraindicated or not tolerated and initial drug treatment has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider dual therapy[1] with:

- a DPP-4 inhibitor and pioglitazone[2] **or**
- a DPP-4 inhibitor and a sulfonylurea **or**
- pioglitazone 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[3,4] may be appropriate for some adults with type 2 diabetes if metformin is contraindicated or not tolerated (see initial drug treatment if metformin is contraindicated or not tolerated [See page 14]).

NICE has published an evidence summary on type 2 diabetes: alogliptin.

11 Second intensification if metformin is contraindicated or not tolerated

In these recommendations, second intensification of drug treatment means treatment with either 3 non-insulin blood glucose lowering therapies in combination (triple therapy) or any treatment combination containing insulin.

In adults with type 2 diabetes, if metformin is contraindicated or not tolerated, and if dual therapy with 2 oral drugs (see first intensification if metformin is contraindicated or not tolerated [See page 16]) has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider insulin-based treatment (see insulin-based treatments [See page 19]).

[1] Be aware that the drugs in dual therapy should be introduced in a stepwise manner, checking for tolerability and effectiveness of each drug.

[2] When prescribing pioglitazone, exercise particular caution if the person is at high risk of the adverse effects of the drug. Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture. Known risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers' summaries of product characteristics for details. Medicines and Healthcare products Regulatory Agency (MHRA) guidance (2011) advises that 'prescribers should review the safety and efficacy of pioglitazone in individuals after 3–6 months of treatment to ensure that only patients who are deriving benefit continue to be treated'.

[3] MHRA guidance (2017) warned that canagliflozin may increase the risk of lower-limb amputation (mainly toes) in people with type 2 diabetes. At the time of publication (March 2017) evidence did not show an increased risk for dapagliflozin and empagliflozin, but the MHRA advised that the risk may be a class effect.

[4] MHRA guidance (2016) warned that serious, life-threatening, and fatal cases of diabetic ketoacidosis have been reported rarely in people taking an SGLT-2 inhibitor (a substantial proportion of the cases concerned off-label use in people with type 1 diabetes, which is not recommended). In several cases, blood glucose levels were only moderately elevated. The MHRA advised that healthcare professionals should test for raised ketones in people with ketoacidosis symptoms who are receiving an SGLT-2 inhibitor, even if their plasma glucose levels are near-normal.

12 Insulin-based treatments

When starting insulin therapy in adults with type 2 diabetes, use a structured programme employing active insulin dose titration that encompasses:

- injection technique, including rotating injection sites and avoiding repeated injections at the same point within sites
- continuing telephone support
- self-monitoring
- dose titration to target levels
- dietary understanding
- DVLA guidance (At a glance guide to the current medical standards of fitness to drive)
- management of hypoglycaemia
- management of acute changes in plasma glucose control
- support from an appropriately trained and experienced healthcare professional.

When starting insulin therapy in adults with type 2 diabetes, continue to offer metformin for people without contraindications or intolerance. Review the continued need for other blood glucose lowering therapies[1].

Start insulin therapy for adults with type 2 diabetes from a choice of a number of insulin types and regimens:

- Offer NPH insulin injected at once or twice daily according to need.
- Consider starting both NPH and short-acting insulin (particularly if the person's HbA1c is 75 mmol/mol [9.0%] or higher), administered either:
  - separately **or**
  - as a pre-mixed (biphasic) human insulin preparation.
- Consider, as an alternative to NPH insulin, using insulin detemir or insulin glargine[2] if:
  - the person needs assistance from a carer or healthcare professional to inject insulin, and use of insulin detemir or insulin glargine would reduce the frequency of injections from twice to once daily **or**
  - the person's lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes **or**
  - the person would otherwise need twice-daily NPH insulin injections in combination with oral glucose-lowering drugs.
- Consider pre-mixed (biphasic) preparations that include short-acting insulin analogues, rather than pre-mixed (biphasic) preparations that include short-acting human insulin

[1] Medicines and Healthcare products Regulatory Agency (MHRA) guidance (2011) notes that cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for the development of cardiac failure. It advises that if the combination is used, people should be observed for signs and symptoms of heart failure, weight gain, and oedema. Pioglitazone should be discontinued if any deterioration in cardiac status occurs.

[2] These recommendations also apply to any current and future biosimilar product(s) of insulin glargine that have an appropriate marketing authorisation that allows the use of the biosimilar(s) in the same indication.

- preparations, if:
  - a person prefers injecting insulin immediately before a meal **or**
  - hypoglycaemia is a problem **or**
  - blood glucose levels rise markedly after meals.

Consider switching to insulin detemir or insulin glargine from NPH insulin in adults with type 2 diabetes:

- who do not reach their target HbA1c because of significant hypoglycaemia **or**
- who experience significant hypoglycaemia on NPH insulin irrespective of the level of HbA1c reached **or**
- who cannot use the device needed to inject NPH insulin but who could administer their own insulin safely and accurately if a switch to one of the long-acting insulin analogues was made **or**
- who need help from a carer or healthcare professional to administer insulin injections and for whom switching to one of the long-acting insulin analogues would reduce the number of daily injections.

Monitor adults with type 2 diabetes who are on a basal insulin regimen (NPH insulin, insulin detemir or insulin glargine) for the need for short-acting insulin before meals (or a pre-mixed [biphasic] insulin preparation).

Monitor adults with type 2 diabetes who are on pre-mixed (biphasic) insulin for the need for a further injection of short-acting insulin before meals or for a change to a basal bolus regimen with NPH insulin or insulin detemir or insulin glargine, if blood glucose control remains inadequate.

Treatment with combinations of medicines including SGLT-2 inhibitors[1,2] may be appropriate for some people with type 2 diabetes; see below.

Insulin delivery

For guidance on insulin delivery for adults with type 2 diabetes, see what NICE says on insulin delivery in type 1 diabetes in adults.

NICE technology appraisal guidance

Empagliflozin with insulin

The following recommendation is an extract from NICE technology appraisal guidance on empagliflozin in combination therapy for treating type 2 diabetes.

[1] MHRA guidance (2017) warned that canagliflozin may increase the risk of lower-limb amputation (mainly toes) in people with type 2 diabetes. At the time of publication (March 2017) evidence did not show an increased risk for dapagliflozin and empagliflozin, but the MHRA advised that the risk may be a class effect.

[2] MHRA guidance (2016) warned that serious, life-threatening, and fatal cases of diabetic ketoacidosis have been reported rarely in people taking an SGLT-2 inhibitor (a substantial proportion of the cases concerned off-label use in people with type 1 diabetes, which is not recommended). In several cases, blood glucose levels were only moderately elevated. The MHRA advised that healthcare professionals should test for raised ketones in people with ketoacidosis symptoms who are receiving an SGLT-2 inhibitor, even if their plasma glucose levels are near-normal

Empagliflozin in combination with insulin with or without other antidiabetic drugs is recommended as an option for treating type 2 diabetes.

NICE has written information for the public on empagliflozin.

Canagliflozin with insulin

The following recommendation is an extract from NICE technology appraisal guidance on canagliflozin in combination therapy for treating type 2 diabetes.

Canagliflozin in combination with insulin with or without other antidiabetic drugs is recommended as an option for treating type 2 diabetes.

NICE has written information for the public on canagliflozin.

Dapagliflozin with insulin

The following recommendation is an extract from NICE technology appraisal guidance on dapagliflozin in combination therapy for treating type 2 diabetes.

Dapagliflozin in combination with insulin with or without other antidiabetic drugs is recommended as an option for treating type 2 diabetes.

NICE has written information for the public on dapagliflozin.

Insulin pump therapy (CSII)

The following recommendation is an extract from NICE technology appraisal guidance on continuous subcutaneous insulin infusion for the treatment of diabetes mellitus.

CSII therapy **is not recommended** for the treatment of people with type 2 diabetes mellitus.

Evidence summaries

NICE has published evidence summaries on:

- type 2 diabetes mellitus in adults: high-strength insulin glargine 300 units/ml (Toujeo)
- diabetes mellitus type 1 and type 2: insulin glargine biosimilar (Abasaglar)
- type 2 diabetes: insulin degludec/liraglutide (Xultophy)
- type 2 diabetes: insulin degludec.

13 Duodenal–jejunal bypass

NICE has published interventional procedures guidance that implantation of a duodenal–jejunal bypass liner for managing type 2 diabetes should be used **only in the context of research**.

Glossary

ACE

angiotensin-converting enzyme

DPP-4

dipeptidyl peptidase-4

DVLA

Driver and Vehicle Licensing Agency

eGFR

estimated glomerular filtration rate

GLP-1

glucagon-like peptide-1

SGLT-2

sodium–glucose cotransporter 2

Sources

Type 2 diabetes in adults: management (2015 updated 2017) NICE guideline NG28

Ertugliflozin as monotherapy or with metformin for treating type 2 diabetes (2019) NICE technology appraisal guidance 572

Dapagliflozin in triple therapy for treating type 2 diabetes (2016) NICE technology appraisal guidance 418

Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes (2016) NICE technology appraisal guidance 390

Empagliflozin in combination therapy for treating type 2 diabetes (2015) NICE technology

appraisal guidance 336

Canagliflozin in combination therapy for treating type 2 diabetes (2014) NICE technology appraisal guidance 315

Dapagliflozin in combination therapy for treating type 2 diabetes (2013 updated 2016) NICE technology appraisal guidance 288

Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (2008) NICE technology appraisal guidance 151

Your responsibility

Guidelines

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and 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. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

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.

Technology appraisals

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take these recommendations fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this interactive flowchart 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.

Commissioners and/or providers have a responsibility to provide the funding required to enable the recommendations 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.

Medical technologies guidance, diagnostics guidance and interventional procedures guidance

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take these recommendations fully into account. However, the interactive flowchart does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the recommendations, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this interactive flowchart should be interpreted in a way that would be inconsistent with compliance with those duties.

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.