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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Type 2 diabetes in adults: management

Draft for consultation, September 2021

This guideline covers care and management for adults (aged 18 and over) with type 2 diabetes. It focuses on providing education and dietary advice, managing cardiovascular risk, managing blood glucose levels, and identifying and managing long-term complications.

This guideline will update NICE guideline NG28 (published December 2015) and will replace it.

Who is it for?

- Healthcare professionals who care for adults with diabetes
- Commissioners and providers of diabetes services
- Adults with type 2 diabetes, and their families and carers

What does it include?

- the draft recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the 2021 recommendations and how they might affect practice
- the guideline context.

Information about how the guideline was developed is on the [guideline's webpage](#). This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

New and updated recommendations

We have reviewed the evidence on drug treatment for adults with type 2 diabetes. You are invited to comment on the new and updated recommendations. These are marked as **[2021]**.

You are also invited to comment on recommendations that we propose to delete from the 2015 guideline.

We have not reviewed the evidence for the recommendations marked **[2015]**, **[2009]**, **[2009, amended 2015]** or **[2009, amended 2020]** (shaded in grey) and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See [update information](#) for a full explanation of what is being updated.

Full details of the evidence and the committee's discussion on the 2021 recommendations are in the [evidence reviews](#). Evidence for the 2015 recommendations is in the [full version](#) of the 2015 guideline.

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1 Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [NICE's information on making decisions about your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

2

3 **1.1 Individualised care**

4 1.1.1 Adopt an individualised approach to diabetes care that is tailored to
5 the needs and circumstances of adults with type 2 diabetes, taking
6 into account their personal preferences, comorbidities, risks from
7 polypharmacy, and **their likelihood of benefiting from long-term**
8 **interventions**. Such an approach is especially important in the
9 context of multimorbidity. **[2015, amended 2021]**

10 1.1.2 Reassess the person's needs and circumstances at each review
11 and think about whether to stop any medicines that are not
12 effective. **[2015]**

13 1.1.3 Take into account any disabilities, including visual impairment,
14 when planning and delivering care for adults with type 2 diabetes.
15 **[2015]**

16 **1.2 Patient education**

17 1.2.1 Offer structured education to adults with type 2 diabetes and their
18 family members or carers (as appropriate) at the time of diagnosis,
19 with annual reinforcement and review. Explain to people that
20 structured education is an integral part of diabetes care. **[2009]**

1 1.2.2 Ensure that any structured education programme for adults with
2 type 2 diabetes:

- 3 • is evidence-based, and suits the needs of the person
- 4 • has specific aims and learning objectives, and supports the
5 person and their family members and carers to develop
6 attitudes, beliefs, knowledge and skills to self-manage diabetes
- 7 • has a structured curriculum that is theory driven, evidence-based
8 and resource-effective, has supporting materials and is written
9 down
- 10 • is delivered by trained educators who:
 - 11 – have an understanding of educational theory appropriate to
12 the age and needs of the person
 - 13 – are trained and competent to deliver the principles and
14 content of the programme
- 15 • is quality assured, and reviewed by trained, competent,
16 independent assessors who measure it against criteria that
17 ensure consistency
- 18 • has outcomes that are audited regularly. **[2015]**

19 1.2.3 Ensure the patient education programme provides the necessary
20 resources to support the educators, and that educators are properly
21 trained and given time to develop and maintain their skills. **[2009]**

22 1.2.4 Offer adults with type 2 diabetes group education programmes as
23 the preferred option. Provide an alternative of equal standard for
24 people who are unable or prefer not to take part in group education.
25 **[2009]**

26 1.2.5 Ensure that patient education programmes meet the cultural,
27 linguistic, cognitive and literacy needs of people in the local area.
28 **[2009]**

29 1.2.6 Ensure that all members of the diabetes healthcare team are
30 familiar with the patient education programmes available locally,

1 and that these programmes are integrated with the rest of the care
2 pathway. **[2009]**

3 1.2.7 Ensure that adults with type 2 diabetes and their family members
4 and carers (as appropriate) have the opportunity to contribute to
5 the design and provision of local patient education programmes.
6 **[2009]**

7 **1.3 *Dietary advice and bariatric surgery***

8 1.3.1 Provide individualised and ongoing nutritional advice from a
9 healthcare professional with specific expertise and competencies in
10 nutrition. **[2009]**

11 1.3.2 Provide dietary advice in a form sensitive to the person's needs,
12 culture and beliefs, being sensitive to their willingness to change
13 and the effects on their quality of life. **[2009]**

14 1.3.3 Encourage adults with type 2 diabetes to follow the same healthy
15 eating advice as the general population, which includes:

- 16 • eating high-fibre, low-glycaemic-index sources of carbohydrate,
17 such as fruit, vegetables, wholegrains and pulses
- 18 • choosing low-fat dairy products
- 19 • eating oily fish
- 20 • controlling their intake of saturated and trans fatty acids. **[2009]**

21 1.3.4 Integrate dietary advice with a personalised diabetes management
22 plan, including other aspects of lifestyle modification such as
23 increasing physical activity and losing weight. **[2009]**

24 1.3.5 For adults with type 2 diabetes who are overweight, discuss and
25 agree an initial body weight loss target of 5% to 10%. Remember
26 that a small amount of weight loss may still be beneficial, and a
27 larger amount will have advantageous metabolic impact in the long
28 term. **[2009]**

1 1.3.6 Individualise recommendations for carbohydrate and alcohol intake,
2 and meal patterns. Make reducing the risk of hypoglycaemia a
3 particular aim for people using insulin or an insulin secretagogue.

4 **[2009]**

5 1.3.7 Advise adults with type 2 diabetes that they can substitute a limited
6 amount of sucrose-containing foods for other carbohydrate in the
7 meal plan but should take care to avoid excess energy intake.

8 **[2009]**

9 1.3.8 Discourage adults with type 2 diabetes from using foods marketed
10 specifically for people with diabetes. **[2009]**

11 1.3.9 When adults with type 2 diabetes are admitted as inpatients to
12 hospital or any other care setting, implement a meal planning
13 system that provides consistency in the carbohydrate content of
14 meals and snacks. **[2009]**

15 1.3.10 For recommendations on lifestyle advice, see the [NICE guidelines](#)
16 [on preventing excess weight gain](#), [weight management](#), [obesity](#),
17 [physical activity](#), [stop smoking interventions and services](#), [smoking:](#)
18 [harm reduction](#), and [smoking: acute, maternity and mental health](#)
19 [services](#). **[2015]**

20 1.3.11 For recommendations on bariatric surgery for people with recent-
21 onset type 2 diabetes, see the [section on bariatric surgery for](#)
22 [people with recent-onset type 2 diabetes in the NICE guideline on](#)
23 [obesity](#). **[2015]**

24 **1.4 *Diagnosing and managing hypertension***

25 The recommendations on diagnosing and managing hypertension have been
26 removed. For recommendations on hypertension in people with type 2
27 diabetes, see the [NICE guideline on hypertension in adults](#). Diagnosis,
28 treatment and monitoring of hypertension is broadly the same for people with

1 type 2 diabetes as for other people. When a different approach is needed for
2 people with type 2 diabetes, this is specified in the hypertension guideline.

3 **1.5 *Antiplatelet therapy***

4 1.5.1 Do not offer antiplatelet therapy (aspirin or clopidogrel) to adults
5 with type 2 diabetes without cardiovascular disease. **[2015]**

6 1.5.2 For guidance on the primary and secondary prevention of
7 cardiovascular disease in adults with type 2 diabetes, see the [NICE](#)
8 [guidelines on cardiovascular disease](#) and [acute coronary](#)
9 [syndromes](#). **[2015]**

10 **1.6 *Blood glucose management***

11 **HbA1c measurement and targets**

12 **Measurement**

13 1.6.1 Measure HbA1c levels in adults with type 2 diabetes every:

- 14 • 3 to 6 months (tailored to individual needs) until HbA1c is stable
15 on unchanging therapy
- 16 • 6 months once the HbA1c level and blood glucose lowering
17 therapy are stable. **[2015]**

18 1.6.2 Measure HbA1c using methods calibrated according to
19 International Federation of Clinical Chemistry (IFCC)
20 standardisation. **[2015]**

21 1.6.3 If HbA1c monitoring is invalid because of disturbed erythrocyte
22 turnover or abnormal haemoglobin type, estimate trends in blood
23 glucose control using one of the following:

- 24 • quality-controlled plasma glucose profiles
- 25 • total glycated haemoglobin estimation (if abnormal
26 haemoglobins)
- 27 • fructosamine estimation. **[2015]**

1 1.6.4 Investigate unexplained discrepancies between HbA1c and other
2 glucose measurements. Seek advice from a team with specialist
3 expertise in diabetes or clinical biochemistry. **[2015]**

4 **Targets**

5 NICE has produced a patient decision aid to support discussions about
6 agreeing an individual HbA1c target. See [appendix A](#).

7 1.6.5 Discuss and agree with adults with type 2 diabetes an individual
8 HbA1c target (see figure 1). Encourage them to reach their target
9 and maintain it unless any resulting adverse effects (including
10 hypoglycaemia), or their efforts to achieve their target, impair their
11 quality of life. **[2015, amended 2021]**

12

1 **Figure 1 Your target HbA1c: weighing it up**

Make a mark on each of the lines to show how you feel about these statements. The more you agree with the statement on the left, the further to the left you should put your mark. The more you agree with the statement on the right, the further to the right you should put your mark. You and your diabetes team can use this to help decide the best target HbA1c for you.

Thinking about things like driving, having severe hypos would not be a problem for me*	-----	Thinking about things like driving, having severe hypos would be a big problem for me*
I'm not concerned about the chance of getting side effects from medicines	-----	Getting side effects from medicines would be a big problem for me
I'm willing to take more medicines if I need to	-----	I do not want to take any more medicines
I do not have any health issues apart from my diabetes	-----	I have lots of health issues as well as my diabetes
Thinking about my age and my health overall, my quality of life in the long term is important to me	-----	Thinking about my age and my health overall, my quality of life in the shorter-term is more important to me



*Hypos might also be a problem for you for other reasons, such as if you operate machinery, if you are at risk of falling, or if you find it difficult to recognise the warning symptoms of a hypo.

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1 1.6.6 Offer lifestyle advice and drug treatment to support adults with
2 type 2 diabetes to reach and maintain their HbA1c target (see the
3 sections on [dietary advice and bariatric surgery](#) and [drug](#)
4 [treatment](#)). For more information about supporting adherence, see
5 the [NICE guideline on medicines adherence](#). [2015]

6 1.6.7 For adults whose type 2 diabetes is managed either by lifestyle and
7 diet, or lifestyle and diet combined with a single drug not associated
8 with hypoglycaemia, support them to aim for an HbA1c level of
9 48 mmol/mol (6.5%). For adults on a drug associated with
10 hypoglycaemia, support them to aim for an HbA1c level of
11 53 mmol/mol (7.0%). [2015]

12 1.6.8 In adults with type 2 diabetes, if HbA1c levels are not adequately
13 controlled by a single drug and rise to 58 mmol/mol (7.5%) or
14 higher:

- 15 • reinforce advice about diet, lifestyle and adherence to drug
16 treatment **and**
- 17 • support the person to aim for an HbA1c level of 53 mmol/mol
18 (7.0%) **and**
- 19 • intensify drug treatment. [2015]

20 1.6.9 Consider relaxing the target HbA1c level (see
21 recommendations 1.6.7 and 1.6.8 [and NICE's patient decision aid](#)
22 [in appendix A](#)) on a case-by-case basis and in discussion with
23 adults with type 2 diabetes, with particular consideration for people
24 who are older or frail, if:

- 25 • they are unlikely to achieve longer-term risk-reduction benefits,
26 for example, people with a reduced life expectancy
- 27 • tight blood glucose control would put them at high risk if they
28 developed hypoglycaemia, for example, they are at risk of
29 falling, they have impaired awareness of hypoglycaemia, or they
30 drive or operate machinery as part of their job

- 1 • intensive management would not be appropriate, for example if
2 they have significant comorbidities. **[2015, amended 2021]**

3 1.6.10 If adults with type 2 diabetes reach an HbA1c level that is lower
4 than their target and they are not experiencing hypoglycaemia,
5 encourage them to maintain it. Be aware that there are other
6 possible reasons for a low HbA1c level, for example deteriorating
7 renal function or sudden weight loss. **[2015]**

8 1.6.11 For guidance on HbA1c targets for women with type 2 diabetes
9 who are pregnant or planning to become pregnant, see the [NICE](#)
10 [guideline on diabetes in pregnancy](#). **[2015]**

11 **Self-monitoring of blood glucose**

12 1.6.12 Take the [Driver and Vehicle Licensing Agency \(DVLA\)'s Assessing](#)
13 [fitness to drive: a guide for medical professionals](#) into account
14 when offering self-monitoring of blood glucose levels for adults with
15 type 2 diabetes. **[2015]**

16 1.6.13 Do not routinely offer self-monitoring of blood glucose levels for
17 adults with type 2 diabetes unless:

- 18 • the person is on insulin **or**
19 • there is evidence of hypoglycaemic episodes **or**
20 • the person is on oral medication that may increase their risk of
21 hypoglycaemia while driving or operating machinery **or**
22 • the person is pregnant or is planning to become pregnant (see
23 the [NICE guideline on diabetes in pregnancy](#)). **[2015]**

24 1.6.14 Consider short-term self-monitoring of blood glucose levels in
25 adults with type 2 diabetes, reviewing treatment as necessary:

- 26 • when starting treatment with oral or intravenous corticosteroids
27 **or**
28 • to confirm suspected hypoglycaemia. **[2015]**

1 1.6.15 Be aware that adults with type 2 diabetes who have acute
2 intercurrent illness are at risk of worsening hyperglycaemia. Review
3 treatment as necessary. **[2015]**

4 1.6.16 If adults with type 2 diabetes are self-monitoring their blood glucose
5 levels, carry out a structured assessment at least annually. The
6 assessment should include:

- 7 • the person's self-monitoring skills
- 8 • the quality and frequency of testing
- 9 • checking that the person knows how to interpret the blood
10 glucose results and what action to take
- 11 • the impact on the person's quality of life
- 12 • the continued benefit to the person
- 13 • the equipment used. **[2015]**

14 **1.7 Drug treatment**

15 Recommendations in this section that cover dipeptidyl peptidase-4 (DPP-4)
16 inhibitors, glucagon-like peptide-1 (GLP-1) mimetics, sulfonylureas and
17 sodium–glucose cotransporter-2 (SGLT2) inhibitors refer to each of these
18 groups of drugs at a class level.

There is [MHRA safety advice](#) on pioglitazone and SGLT2 inhibitors. Always check the BNF and SPC for any drug being prescribed.

19 **Choosing drug treatments**

20 We have included 4 visual summaries in this section to provide an overview
21 and additional information to support medicines choice:

- 22 • Visual summary 1. Prescribing guidance
- 23 • Visual summary 2. First-line treatment
- 24 • Visual summary 3. Disease progression
- 25 • Visual summary 4. Medicines table

1 1.7.1 Discuss with adults with type 2 diabetes the benefits and risks of
2 drug treatment and the options available. Base the choice of drug
3 treatments on:

- 4 • the person's individual clinical circumstances, for example,
5 comorbidities, **contraindications** and risks from polypharmacy
- 6 • the person's individual preferences and needs
- 7 • the effectiveness of the drug treatments in terms of metabolic
8 response and **cardiovascular protection**
- 9 • safety (see [MHRA guidance](#)) and tolerability of the drug
10 treatment
- 11 • **monitoring requirements**
- 12 • the licensed indications or combinations available
- 13 • cost (if 2 drugs in the same class are appropriate, choose the
14 option with the lowest acquisition cost). **[2015, amended 2021]**

15 See also the [NICE guideline on shared decision making](#) and the
16 [section on safety of medicines for diabetes before and during](#)
17 [pregnancy in the NICE guideline on diabetes in pregnancy](#).

18 **Rescue therapy at any phase of treatment**

19 1.7.2 If an adult with type 2 diabetes is symptomatically hyperglycaemic,
20 consider insulin (see the [section on insulin-based treatments](#)) or a
21 sulfonylurea, and review treatment when blood glucose control has
22 been achieved. **[2015]**

23 **First-line drug treatment**

24 Also see [Visual summaries 1, 2 and 4](#) for an overview and additional
25 information to support medicines choice.

26 1.7.3 Offer standard-release metformin as first-line drug treatment to
27 adults with type 2 diabetes. **[2015]**

28 1.7.4 Assess the person's cardiovascular status and risk to determine
29 whether they have congestive heart failure or established

1 atherosclerotic cardiovascular disease or are at [high risk of](#)
2 [developing cardiovascular disease](#).

3 See recommendations on using risk scores and QRISK2 to assess
4 cardiovascular disease risk in adults with type 2 diabetes in [NICE's](#)
5 [guideline on cardiovascular disease: risk assessment and](#)
6 [reduction, including lipid modification](#). **[2021]**

7 1.7.5 Based on the person's cardiovascular risk assessment:

- 8 • If they have congestive heart failure or established
9 atherosclerotic cardiovascular disease, offer an SGLT2 inhibitor
10 in addition to metformin.
- 11 • If they are at [high risk of developing cardiovascular disease](#),
12 consider an SGLT2 inhibitor in addition to metformin. **[2021]**

13 1.7.6 When starting dual therapy with metformin and an SGLT2 inhibitor
14 as first-line therapy, introduce the drugs sequentially, starting with
15 metformin, checking their tolerability. **[2021]**

16 1.7.7 Gradually increase the dose of standard-release metformin over
17 several weeks to minimise the risk of gastrointestinal side effects in
18 adults with type 2 diabetes. **[2015]**

19 1.7.8 If an adult with type 2 diabetes experiences gastrointestinal side
20 effects with standard-release metformin, consider a trial of
21 modified-release metformin. **[2015]**

22 1.7.9 For first-line drug treatment in adults with type 2 diabetes, if
23 metformin is contraindicated or not tolerated:

- 24 • If they have congestive heart failure or established
25 atherosclerotic cardiovascular disease, offer an SGLT2 inhibitor
26 alone.
- 27 • If they are at [high risk of developing cardiovascular disease](#),
28 consider an SGLT2 inhibitor alone. **[2021]**

1 1.7.10 For **first-line** drug treatment in adults with type 2 diabetes, if
2 metformin is contraindicated or not tolerated and **if they are not in**
3 **either of the groups in recommendation 1.7.9, consider:**

- 4 • a DPP-4 inhibitor **or**
- 5 • pioglitazone **or**
- 6 • a sulfonylurea **or**
- 7 • **an SGLT2 inhibitor for people who meet the criteria in [NICE](#)**
8 **[technology appraisal guidance 390](#), or [TA572](#) [2015, amended**
9 **2021]**

10 1.7.11 Be aware that, if metformin is contraindicated or not tolerated,
11 repaglinide is both clinically effective and cost effective in adults
12 with type 2 diabetes. However, discuss with any person for whom
13 repaglinide is being considered, that there is no licensed
14 non-metformin-based combination containing repaglinide that can
15 be offered **as dual therapy**. **[2015, amended 2021]**

16 1.7.12 Before starting an SGLT2 inhibitor, check:

- 17 • that the person is not following a very low carbohydrate or
18 ketogenic diet, because if combined with taking an SGLT2
19 inhibitor this can cause diabetic ketoacidosis (DKA)
- 20 • that the person is not pregnant, planning a pregnancy or
21 breastfeeding; ask if they would like advice on contraception and
22 planning for pregnancy (see [NICE's guideline on diabetes in](#)
23 [pregnancy](#)). **[2021]**

24
25 1.7.13 Be aware that SGLT2 inhibitors can cause fluid volume depletion
26 and have an adverse effect on renal function and this needs to be
27 monitored, taking into account individual clinical factors and
28 baseline renal function. **[2021]**

1 See also the [NICE guideline on chronic kidney disease in adults](#)
2 and [NICE's draft recommendations on treatment options for adults](#)
3 [with chronic kidney disease and type 2 diabetes](#).

4 1.7.14 Advise adults with type 2 diabetes who are taking an SGLT2
5 inhibitor:

- 6 • not to start a very low carbohydrate or ketogenic diet without
7 discussing it with their healthcare professional, because they
8 would first need to suspend SGLT2 inhibitor treatment to avoid
9 DKA
- 10 • to stop taking the SGLT2 inhibitor temporarily if they become ill
11 (for example, with fever, diarrhoea or vomiting). **[2021]**

12 Visual summary 1. Prescribing guidance

Choosing medicines for type 2 diabetes

Prescribing guidance

Choosing treatments

Base the choice of medicine on:

- the person's individual clinical circumstances and their preferences and needs
- the medicine's effectiveness in terms of metabolic response and cardiovascular protection
- the medicine's safety and tolerability
- the person's cardiovascular disease (CVD) risk and status
- which medicine has the lowest cost within its class.

Reviewing and changing treatments

At each point:

- stop medicines that have not worked or are not tolerated
- check adherence and optimise the person's current treatment regimen before thinking about adding or switching medicines (see the [NICE guidelines on medicines adherence, medicines optimisation and shared decision making](#))
- think about whether switching rather than adding medicines could be effective
- check adherence to diet and lifestyle advice.

Rescue therapy

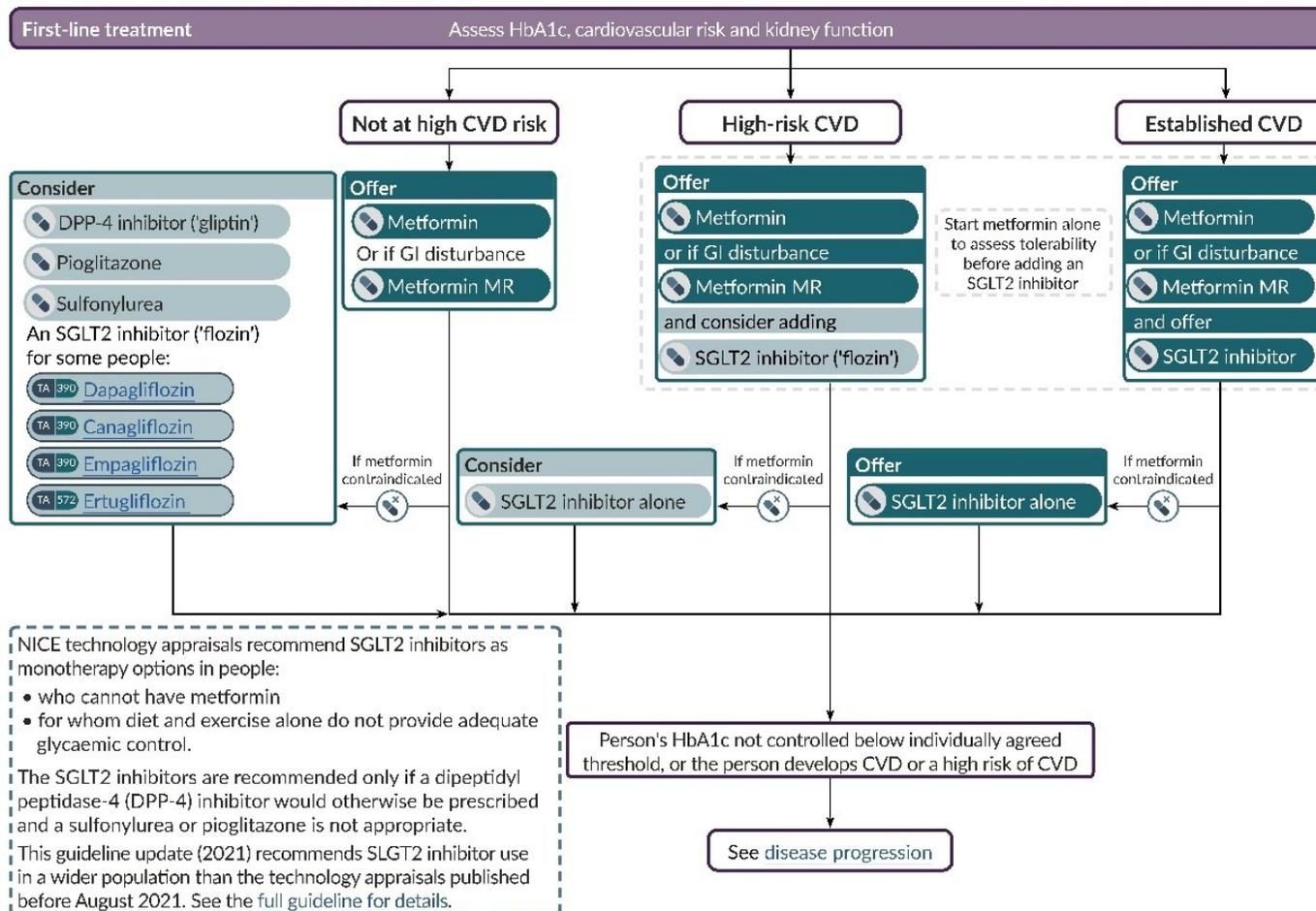
For symptomatic hyperglycaemia, consider insulin or a sulfonylurea, review when blood glucose control has been achieved.

13

14

1 **Visual summary 2. First-line treatment**

Choosing medicines for type 2 diabetes



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1 **Visual summary 4. Medicines table**

Choosing medicines for type 2 diabetes

Option	Form	Contraindications (check individual SPCs)	Renal impairment (check individual SPCs)	Hepatic impairment (check individual SPCs)	Effect on weight	Hypoglycaemia risk	Options and BNF link
DPP-4 inhibitor ('gliptin')	Tablet	Ketoacidosis (check individual SPCs)	Caution if severe Dose adjustment required if moderate to severe	Avoid if severe Caution if moderate	None	Low	Alogliptin Linagliptin Sitagliptin Saxagliptin Vildagliptin
GLP-1	Tablet or injection	Severe gastrointestinal disease, ketoacidosis, diabetic gastroparesis, inflammatory bowel disease (check individual SPCs)	Avoid or use with caution	No warnings	Loss	Low	Dulaglutide Exenatide Liraglutide Lixisenatide Semaglutide
Insulin	Injection	-	Response to hypoglycaemia is impaired. Insulin requirements may decrease, dose reduction may be needed	Insulin requirements may decrease	Gain	High	Insulin treatment summary See individual BNF monographs
Metformin	Tablet	Acute metabolic acidosis	Avoid if eGFR is less than 30 ml/minutes/1.73 m ²	Withdraw if tissue hypoxia likely	None	Low	Metformin
Pioglitazone	Tablet	History of heart failure, previous or active bladder cancer, uninvestigated macroscopic haematuria	No warnings	Avoid	Gain	Low	Pioglitazone See also MHRA warnings on cardiovascular risk and bladder cancer
SGLT2 inhibitor ('flozin')	Tablet	Ketoacidosis	Options and doses may change if eGFR is less than 60 ml/minute/1.73 m ² (see individual SPCs for more information)	Caution if severe	Loss	Low	Canagliflozin Dapagliflozin Empagliflozin Ertugliflozin See also MHRA warnings on diabetic ketoacidosis and genital infection
Sulfonylurea	Tablet	Ketoacidosis (and see individual SPCs)	Use with care if mild to moderate because of the risk of hypoglycaemia Use the lowest dose that adequately controls blood glucose Avoid where possible if severe	Avoid if severe	Gain	Moderate	Gliclazide Glimepiride Glipizide Tolbutamide

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.

This information is a summary of the recommendations, please consult the guideline for the full recommendations. All supplementary information is taken from the BNF or the SPCs.

This guideline update (2021) recommends SGLT2 inhibitor use in a wider population than the technology appraisals published before August 2021. See the [full guideline](#) for details.

2

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on first-line drug treatment](#).

Full details of the evidence and the committee's discussion are in [evidence review A: pharmacological therapies with cardiovascular and other benefits in people with type 2 diabetes](#).

1 **Reviewing drug treatments**

2 1.7.15 When reviewing or considering changing treatments for adults with
3 type 2 diabetes, think about and discuss the following with the
4 person:

- 5 • stopping medicines that have not worked or are not tolerated
- 6 • how to optimise their current treatment regimen before thinking
7 about changing treatments, taking into account factors such as:
 - 8 – adverse effects
 - 9 – adherence to existing medicines
 - 10 – prescribed doses and formulations
 - 11 – the recommendations on medication review in the [NICE](#)
12 [guideline on medicines optimisation](#) and on reviewing
13 medicines and supporting adherence in the [NICE guideline on](#)
14 [medicines adherence](#)
- 15 • whether switching rather than adding drugs could be effective
- 16 • the considerations about treatment choice in [recommendation](#)
17 [1.7.1. \[2021\]](#)

18 **Adding an SGLT2 inhibitor at any stage after first-line treatment has** 19 **been started**

20 1.7.16 For adults with type 2 diabetes already on drug therapy:

- 21 • If they have or develop congestive heart failure or established
22 atherosclerotic cardiovascular disease, offer an SGLT2 inhibitor

1 in addition to current treatment or replace an existing drug with
2 the SGLT2 inhibitor.

- 3 • If they are or become at [high risk of developing cardiovascular](#)
4 [disease](#), consider adding an SGLT2 inhibitor to current treatment
5 or replacing an existing drug with the SGLT2 inhibitor.

6 Take into account the person's current treatment regimen and
7 preferences and make a shared decision about switching
8 treatments or adding an SGLT2 inhibitor, as appropriate (also see
9 [recommendations 1.7.12](#) to [1.7.14](#) on starting an SGLT2 inhibitor).

10 **[2021]**

11

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on reviewing drug treatments](#).

Full details of the evidence and the committee's discussion are in [evidence review A: pharmacological therapies with cardiovascular and other benefits in people with type 2 diabetes](#).

12 **Treatment options if further interventions are needed**

13 Also see [Visual summaries 1, 3 and 4](#) for an overview and additional
14 information to support medicines choice.

15 1.7.17 Introduce drugs used in combination therapy in a stepwise manner,
16 checking for tolerability and effectiveness of each drug. **[2015]**

17 1.7.18 For adults with type 2 diabetes, if **monotherapy** has not continued
18 to control HbA1c to below the person's individually agreed
19 threshold for **further intervention, consider adding:**

- 20 • a DPP-4 inhibitor **or**
21 • pioglitazone **or**
22 • a sulfonylurea **or**

- 1 • an SGLT2 inhibitor for people who meet the criteria in [NICE](#)
2 [technology appraisal guidance 315](#), [TA572](#), [TA288](#), or [TA336](#)
3 **[2015, amended 2021]**

4 1.7.19 For adults with type 2 diabetes, if dual therapy with metformin and
5 another oral drug has not continued to control HbA1c to below the
6 person's individually agreed threshold for **further intervention**
7 consider either:

- 8 • triple therapy **by adding** a DPP-4 inhibitor, pioglitazone or a
9 sulfonylurea or an SGLT2 inhibitor for people who meet the
10 criteria in [NICE technology appraisal guidance 315](#), [TA418](#),
11 [TA336](#), or [TA583](#) **or**
12 • starting insulin-based treatment (see the [section on insulin-](#)
13 [based treatments](#)) **[2015, amended 2021]**

14 1.7.20 In adults with type 2 diabetes, if metformin is contraindicated or not
15 tolerated and dual therapy with 2 oral drugs has not continued to
16 control HbA1c to below the person's individually agreed threshold
17 for **intervention**, consider insulin-based treatment (see the [section](#)
18 [on insulin-based treatments](#)). **[2015, amended 2021]**

19 1.7.21 Do not offer GLP-1 mimetic therapy to adults with type 2 diabetes
20 solely for cardiovascular risk reduction. **[2021]**

21 1.7.22 If triple therapy with metformin and 2 other oral drugs is not
22 effective, not tolerated or contraindicated, consider **triple therapy**
23 **including** a GLP-1 mimetic for adults with type 2 diabetes who:

- 24 • have a BMI of 35 kg/m² or higher (adjust accordingly for people
25 from black, Asian and other minority ethnic groups) **and** specific
26 psychological or other medical problems associated with obesity
27 **or**
28 • have a BMI lower than 35 kg/m² **and**:

- 1 – for whom insulin therapy would have significant occupational
2 implications **or**
3 – weight loss would benefit other significant obesity-related
4 comorbidities. **[2015, amended 2021]**

5 1.7.23 Only continue GLP-1 mimetic therapy if the adult with type 2
6 diabetes has had a beneficial metabolic response (a reduction of at
7 least 11 mmol/mol [1.0%] in HbA1c and weight loss of at least 3%
8 of initial body weight in 6 months). **[2015]**

9 1.7.24 For adults with type 2 diabetes, only offer combination therapy with
10 a GLP-1 mimetic and insulin along with specialist care advice and
11 ongoing support from a [consultant-led multidisciplinary team](#).
12 **[2015]**

13 **Visual summary 1. Prescribing guidance**

Choosing medicines for type 2 diabetes

Prescribing guidance

Choosing treatments

Base the choice of medicine on:

- the person's individual clinical circumstances and their preferences and needs
- the medicine's effectiveness in terms of metabolic response and cardiovascular protection
- the medicine's safety and tolerability
- the person's cardiovascular disease (CVD) risk and status
- which medicine has the lowest cost within its class.

Reviewing and changing treatments

At each point:

- stop medicines that have not worked or are not tolerated
- check adherence and optimise the person's current treatment regimen before thinking about adding or switching medicines (see the [NICE guidelines on medicines adherence, medicines optimisation and shared decision making](#))
- think about whether switching rather than adding medicines could be effective
- check adherence to diet and lifestyle advice.

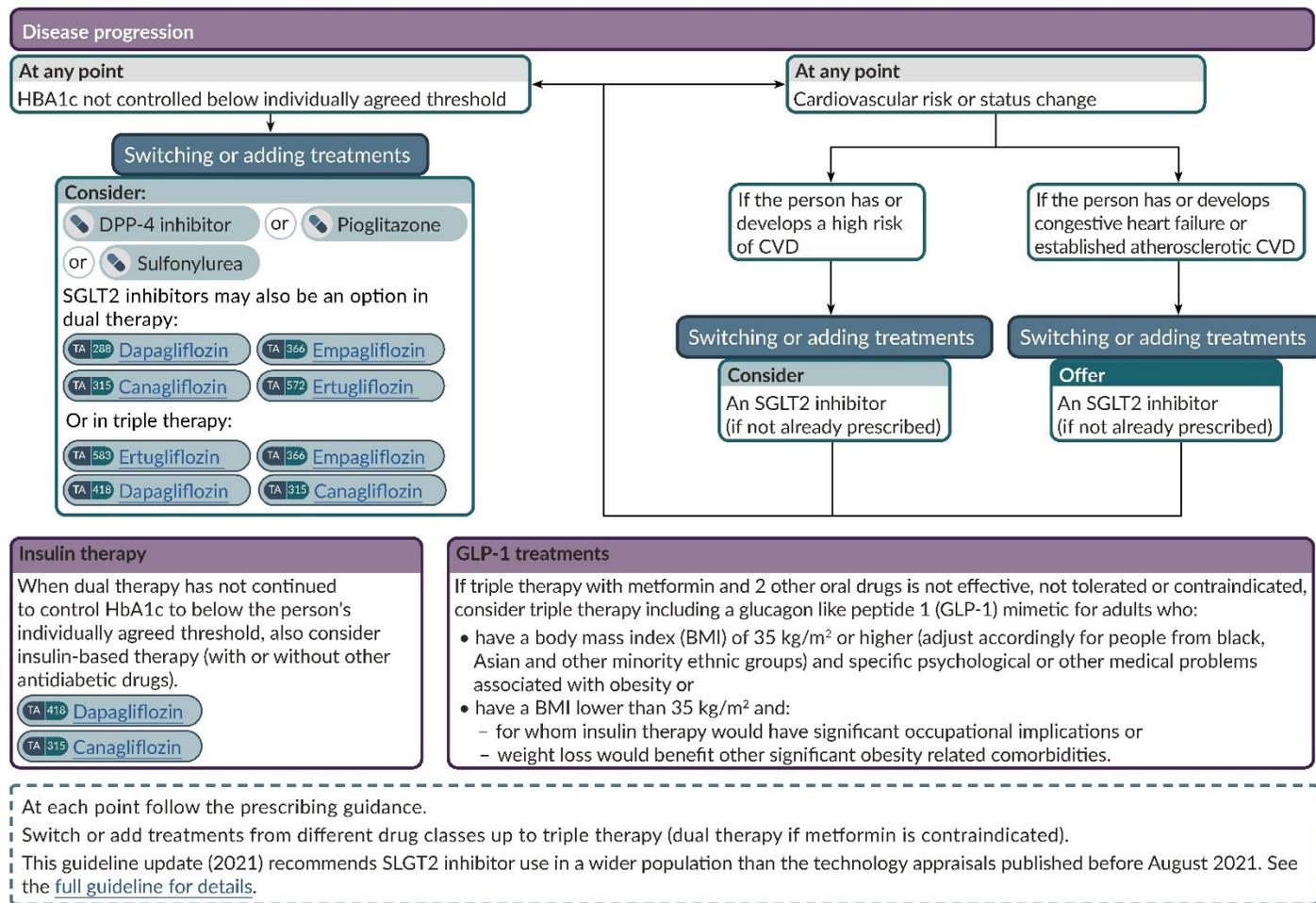
Rescue therapy

For symptomatic hyperglycaemia, consider insulin or a sulfonylurea, review when blood glucose control has been achieved.

14

1 **Visual summary 3. Disease progression**

Choosing medicines for type 2 diabetes



2

1 **Visual summary 4. Medicines table**

Choosing medicines for type 2 diabetes

Option	Form	Contraindications (check individual SPCs)	Renal impairment (check individual SPCs)	Hepatic impairment (check individual SPCs)	Effect on weight	Hypoglycaemia risk	Options and BNF link
DPP-4 inhibitor ('gliptin')	Tablet	Ketoacidosis (check individual SPCs)	Caution if severe Dose adjustment required if moderate to severe	Avoid if severe Caution if moderate	None	Low	Alogliptin Linagliptin Sitagliptin Saxagliptin Vildagliptin
GLP-1	Tablet or injection	Severe gastrointestinal disease, ketoacidosis, diabetic gastroparesis, inflammatory bowel disease (check individual SPCs)	Avoid or use with caution	No warnings	Loss	Low	Dulaglutide Exenatide Liraglutide Lixisenatide Semaglutide
Insulin	Injection	-	Response to hypoglycaemia is impaired. Insulin requirements may decrease, dose reduction may be needed	Insulin requirements may decrease	Gain	High	Insulin treatment summary See individual BNF monographs
Metformin	Tablet	Acute metabolic acidosis	Avoid if eGFR is less than 30 ml/minutes/1.73 m ²	Withdraw if tissue hypoxia likely	None	Low	Metformin
Pioglitazone	Tablet	History of heart failure, previous or active bladder cancer, uninvestigated macroscopic haematuria	No warnings	Avoid	Gain	Low	Pioglitazone See also MHRA warnings on cardiovascular risk and bladder cancer
SGLT2 inhibitor ('flozin')	Tablet	Ketoacidosis	Options and doses may change if eGFR is less than 60 ml/minute/1.73 m ² (see individual SPCs for more information)	Caution if severe	Loss	Low	Canagliflozin Dapagliflozin Empagliflozin Ertugliflozin See also MHRA warnings on diabetic ketoacidosis and genital infection
Sulfonylurea	Tablet	Ketoacidosis (and see individual SPCs)	Use with care if mild to moderate because of the risk of hypoglycaemia Use the lowest dose that adequately controls blood glucose Avoid where possible if severe	Avoid if severe	Gain	Moderate	Gliclazide Glimepiride Glipizide Tolbutamide

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.

This information is a summary of the recommendations, please consult the guideline for the full recommendations. All supplementary information is taken from the BNF or the SPCs.

This guideline update (2021) recommends SGLT2 inhibitor use in a wider population than the technology appraisals published before August 2021. See the [full guideline](#) for details.

2

For a short explanation of why the committee made these recommendations and how they might affect practice, see the [rationale and impact section on treatment options if further interventions are needed](#).

Full details of the evidence and the committee's discussion are in [evidence review A: pharmacological therapies with cardiovascular and other benefits in people with type 2 diabetes](#).

1 **Insulin-based treatments**

2 1.7.25 For adults with type 2 diabetes starting insulin therapy, provide a
3 structured programme using active insulin dose titration that
4 encompasses:

- 5 • injection technique, including rotating injection sites and avoiding
- 6 repeated injections at the same point within sites
- 7 • continuing telephone support
- 8 • self-monitoring
- 9 • dose titration to target levels
- 10 • dietary advice
- 11 • [the DVLA's Assessing fitness to drive: a guide for medical](#)
- 12 [professionals](#)
- 13 • managing hypoglycaemia
- 14 • managing acute changes in plasma glucose control
- 15 • support from an appropriately trained and experienced
- 16 healthcare professional. **[2015]**

17 1.7.26 For adults with type 2 diabetes starting insulin therapy, continue to
18 offer metformin for people without contraindications or intolerance.
19 Review the continued need for other blood glucose lowering
20 therapies. **[2015]**

21 1.7.27 Start insulin therapy for adults with type 2 diabetes from a choice of
22 the following insulin types and regimens:

- 1 • Offer NPH insulin injected once or twice daily according to need.
- 2 • Consider starting both NPH and short-acting insulin (particularly
- 3 if the person's HbA1c is 75 mmol/mol [9.0%] or higher),
- 4 administered either:
- 5 – separately **or**
- 6 – as a pre-mixed (biphasic) human insulin preparation.
- 7 • Consider, as an alternative to NPH insulin, using insulin detemir
- 8 or [insulin glargine](#) if:
- 9 – the person needs help from a carer or healthcare professional
- 10 to inject insulin, and use of insulin detemir or insulin
- 11 glargine^{Error! Bookmark not defined.} would reduce the frequency of
- 12 injections from twice to once daily **or**
- 13 – the person's lifestyle is restricted by recurrent symptomatic
- 14 hypoglycaemic episodes **or**
- 15 – the person would otherwise need twice-daily NPH insulin
- 16 injections in combination with oral glucose-lowering drugs.
- 17 • Consider pre-mixed (biphasic) preparations that include
- 18 short-acting insulin analogues, rather than pre-mixed (biphasic)
- 19 preparations that include short-acting human insulin
- 20 preparations, if:
- 21 – the person prefers injecting insulin immediately before a meal
- 22 **or**
- 23 – hypoglycaemia is a problem **or**
- 24 – blood glucose levels rise markedly after meals. **[2015]**

25 1.7.28 Consider switching to insulin detemir or insulin glargine from NPH

26 insulin in adults with type 2 diabetes:

- 27 • who do not reach their target HbA1c because of significant
- 28 hypoglycaemia **or**
- 29 • who experience significant hypoglycaemia on NPH insulin
- 30 irrespective of the level of HbA1c reached **or**

- 1 • who cannot use the device needed to inject NPH insulin but
2 could administer their own insulin safely and accurately if a
3 switch to one of the long-acting insulin analogues was made **or**
4 • who need help from a carer or healthcare professional to
5 administer insulin injections and for whom switching to one of
6 the long-acting insulin analogues would reduce the number of
7 daily injections. **[2015]**

8 1.7.29 Monitor adults with type 2 diabetes who are on a basal insulin
9 regimen (NPH insulin, insulin detemir or insulin glargine) for the
10 need for short-acting insulin before meals (or a pre-mixed [biphasic]
11 insulin preparation). **[2015]**

12 1.7.30 Monitor adults with type 2 diabetes who are on pre-mixed
13 (biphasic) insulin for the need for a further injection of short-acting
14 insulin before meals or for a change to a basal bolus regimen with
15 NPH insulin or insulin detemir or insulin glargine, if blood glucose
16 control remains inadequate. **[2015]**

17 For guidance on using insulin in combination with SGLT2 inhibitors, see:

- 18 • the [section on drug treatment](#)
19 • [NICE technology appraisal 315](#), [TA288](#), and [TA336](#).

There is [MHRA safety advice](#) on SGLT2 inhibitors. Always check the BNF and SPC for any drug being prescribed.

20 **Insulin delivery**

21 1.7.31 For guidance on insulin delivery for adults with type 2 diabetes, see
22 the [section on insulin delivery in the NICE guideline on type 1](#)
23 [diabetes](#). **[2015]**

1 **1.8 Managing complications**

2 **Gastroparesis**

There is [MHRA safety advice](#) on domperidone and metoclopramide.
Always check the BNF and SPC for any drug being prescribed.

3

4 1.8.1 Think about a diagnosis of gastroparesis in adults with type 2
5 diabetes who have erratic blood glucose control or unexplained
6 gastric bloating or vomiting, taking into account possible alternative
7 diagnoses. **[2009, amended 2015]**

8 1.8.2 For adults with type 2 diabetes who have vomiting caused by
9 gastroparesis, explain that:

- there is no strong evidence that any available antiemetic therapy is effective
 - some people have had benefit with domperidone, erythromycin or metoclopramide
 - the strongest evidence for effectiveness is for domperidone, but prescribers must take into account its safety profile, in particular its cardiac risk and potential interactions with other medicines.
- [2015]**

In December 2015, the use of erythromycin was off label.

See [NICE's information on prescribing medicines](#).

20 1.8.3 To treat vomiting caused by gastroparesis in adults with type 2
21 diabetes:

- consider alternating the use of erythromycin and metoclopramide

22

23

- 1 • consider domperidone only in exceptional circumstances (if
2 domperidone is the only effective treatment) and in accordance
3 with [MHRA guidance](#). **[2015]**

4 In December 2015, the use of erythromycin was off label.
5 See [NICE's information on prescribing medicines](#).

6 1.8.4 If gastroparesis is suspected, consider referring adults with type 2
7 diabetes to specialist services if:

- 8 • the differential diagnosis is in doubt **or**
9 • the person has persistent or severe vomiting. **[2009]**

10 **Painful diabetic neuropathy**

11 1.8.5 For guidance on managing painful diabetic peripheral neuropathy in
12 adults with type 2 diabetes, see the [NICE guideline on neuropathic
13 pain in adults](#). **[2015]**

14 **Autonomic neuropathy**

15 1.8.6 Think about the possibility of contributory sympathetic nervous
16 system damage in adults with type 2 diabetes who lose the warning
17 signs of hypoglycaemia. **[2009, amended 2015]**

18 1.8.7 Think about the possibility of autonomic neuropathy affecting the
19 gut in adults with type 2 diabetes who have unexplained diarrhoea
20 that happens particularly at night. **[2009, amended 2015]**

21 1.8.8 For adults with type 2 diabetes and autonomic neuropathy who are
22 taking tricyclic drugs and antihypertensive drug treatments, be
23 aware of the increased likelihood of side effects such as orthostatic
24 hypotension. **[2009]**

25 1.8.9 For adults with type 2 diabetes who have unexplained
26 bladder-emptying problems, investigate the possibility of autonomic
27 neuropathy affecting the bladder. **[2009]**

1 1.8.10 In managing autonomic neuropathy symptoms, include specific
2 interventions indicated by the manifestations (for example, for
3 abnormal sweating or nocturnal diarrhoea). **[2009]**

4 **Diabetic foot problems**

5 1.8.11 For guidance on preventing and managing foot problems in adults
6 with type 2 diabetes, see the [NICE guideline on diabetic foot
7 problems](#). **[2015]**

8 **Diabetic kidney disease**

9 1.8.12 For guidance on managing kidney disease in adults with type 2
10 diabetes, see the [NICE guideline on chronic kidney disease in
11 adults](#). **[2015]**

12 **Erectile dysfunction**

13 1.8.13 Offer men with type 2 diabetes the opportunity to discuss erectile
14 dysfunction as part of their annual review. **[2015]**

15 1.8.14 Assess, educate and support men with type 2 diabetes who have
16 problematic erectile dysfunction, addressing contributory factors
17 such as cardiovascular disease as well as possible treatment
18 options. **[2015]**

19 1.8.15 Consider a phosphodiesterase-5 inhibitor to treat problematic
20 erectile dysfunction in men with type 2 diabetes. Initially choose the
21 drug with the lowest acquisition cost and take into account any
22 contraindications. **[2015]**

23 1.8.16 After discussion, refer men with type 2 diabetes to a service
24 offering other medical, surgical or psychological management of
25 erectile dysfunction if treatment (including a phosphodiesterase-5
26 inhibitor, as appropriate) has been unsuccessful. **[2015]**

1 **Eye disease**

2 1.8.17 When adults are diagnosed with type 2 diabetes, refer them
3 immediately to the local eye screening service. **[2009, amended**
4 **2020]**

5 1.8.18 Encourage adults to attend eye screening, and explain that it will
6 help them to keep their eyes healthy and help to prevent problems
7 with their vision. Explain that the screening service is effective at
8 identifying problems so that they can be treated early. **[2009]**

9 1.8.19 Arrange emergency review by an ophthalmologist for:

- 10
- 11 • sudden loss of vision
 - 12 • rubeosis iridis
 - 13 • pre-retinal or vitreous haemorrhage
 - retinal detachment. **[2009]**

14 1.8.20 Refer to an ophthalmologist in accordance with the National
15 Screening Committee criteria and timelines for any large sudden
16 unexplained drop in visual acuity. **[2009, amended 2020]**

17 **Terms used in this guideline**

18 **Consultant-led multidisciplinary team**

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

21 **Insulin glargine**

22 The recommendations in this guideline also apply to any current or future
23 biosimilar product of insulin glargine that has an appropriate marketing
24 authorisation that allows the use of the biosimilar in the same indication.

25 **High risk of developing cardiovascular disease**

26 Adults with type 2 diabetes who have:

- 27
- QRISK2 more than 10% in adults aged 40 and over **or**

- 1 • clinical judgement of an elevated lifetime risk of cardiovascular disease
2 (defined as the presence of 1 or more cardiovascular risk factor in
3 someone under 40).

4 Cardiovascular disease risk factors: hypertension, dyslipidaemia, smoking,
5 obesity, family history (in a first-degree relative) of premature cardiovascular
6 disease.

7 **Recommendations for research**

8 The Guideline Development Group has made the following recommendations
9 for research.

10 **Key recommendations for research**

11 **1 The effects of stopping and/or switching drug treatments to** 12 **control blood glucose levels**

13 In adults with type 2 diabetes, what are the effects of stopping and/or
14 switching drug treatments to control blood glucose levels, and what criteria
15 should inform the decision? **[2015]**

16 **2 Non-metformin-based drug treatment combinations to control** 17 **blood glucose levels**

18 In adults with type 2 diabetes, what treatment combinations (for example,
19 glucagon-like peptide-1 [GLP-1] mimetics and insulin combination therapy
20 with meglitinides) are most effective when initial drug treatment with
21 non-metformin monotherapy fails to adequately control blood glucose levels?
22 **[2015]**

23 **3 Drug treatment for when blood glucose levels are inadequately** 24 **controlled by 3 oral antidiabetic drugs and/or insulin combinations**

25 When **blood glucose levels are inadequately controlled by 3 oral antidiabetic**
26 **drugs and/or insulin combinations**, which blood glucose lowering therapies
27 should be used to control blood glucose levels? **[2015, amended 2021]**

1 **4 Self-monitoring of blood glucose levels**

2 What is the optimal frequency for self-monitoring of blood glucose in adults
3 with type 2 diabetes? [2015]

4 **5 Glucagon-like peptide-1 receptor agonists (GLP-1) and insulin
5 therapy**

6 What is the effectiveness and cost effectiveness of GLP-1 mimetics compared
7 with insulin therapy in adults with type 2 diabetes? [2021]

For a short explanation of why the committee made this recommendation and how it might affect practice, see the [rationale and impact section on treatment options if further interventions are needed](#).

Full details of the evidence and the committee's discussion are in [evidence review A: pharmacological therapies with cardiovascular and other benefits in people with type 2 diabetes](#).

8 **Other recommendations for research**

9 **Long-term outcomes associated with blood glucose lowering
10 agents**

11 In adults with type 2 diabetes, what are the long-term effects of blood glucose
12 lowering therapies such as dipeptidyl peptidase-4 (DPP-4) inhibitors, sodium–
13 glucose cotransporter-2 (SGLT2) inhibitors and meglitinides? [2015]

14 **Rationale and impact**

15 These sections briefly explain why the committee made the recommendations
16 and how they might affect practice.

17 NICE technology appraisals for SGLT2 inhibitors recommend the use of these
18 medicines only in specific populations and in certain circumstances. This
19 guideline update (2021) has looked at the clinical and cost-effectiveness
20 evidence for SGLT2 inhibitors in people with cardiovascular disease or at high
21 risk of developing cardiovascular disease and recommends SGLT2 inhibitors

1 in a wider population than the technology appraisals published before August
2 2021.

3 **First-line drug treatment**

4 [Recommendations 1.7.3 to 1.7.14](#)

5 **Why the committee made the recommendations**

6 The evidence from the clinical trials looking at cardiovascular benefits, the
7 network meta-analyses, and the economic modelling, showed that some
8 treatments were effective at improving cardiovascular outcomes and were
9 likely to be cost effective. All of these trials recruited people with established
10 cardiovascular disease, and some also included people with a high risk of
11 developing cardiovascular disease. However, for people without high
12 cardiovascular risk, the committee agreed there was more uncertainty
13 whether the same level of cardiovascular benefits seen in the high-risk groups
14 could be applied to a lower risk population. They decided that they could not
15 justify changing the recommendations for people at lower risk based on this
16 evidence. Therefore, they retained the 2015 recommendations outlining the
17 drug treatment options for people in the lower risk group.

18 The committee agreed it was important to assess people's cardiovascular
19 status and risk to help determine which treatments are suitable for them. They
20 used a definition for the established cardiovascular disease group (adults with
21 type 2 diabetes and congestive heart failure or established atherosclerotic
22 cardiovascular disease) that reflected the people included in all the clinical
23 trials and modelled as a subgroup in the economic model. To assess whether
24 people are at high risk of developing cardiovascular disease, the committee
25 recommended using the QRISK2 tool because this is recommended in the
26 [NICE guideline on cardiovascular disease: risk assessment and reduction,
27 including lipid modification](#) for adults with type 2 diabetes, and the factors
28 covered by this tool were similar to those used in the trials and economic
29 model to define this population. Lifetime cardiovascular risk may be
30 underestimated in people aged under 40 using this tool, so the committee also
31 included risk factors to consider for this age group. This definition was broadly

1 aligned to the subgroup of people with high cardiovascular risk without
2 established cardiovascular disease who were included in the model.

3 The evidence showed that SGLT2 inhibitors as a class of drugs were effective
4 at improving cardiovascular outcomes and were most likely to be cost
5 effective in combination with metformin, although the incremental cost-
6 effectiveness ratio (ICER) varied between drugs within the class. The
7 committee agreed there was more certainty of cardiovascular benefits in
8 adults with type 2 diabetes and congestive heart failure or established
9 atherosclerotic cardiovascular disease because they were participants in all of
10 the included trials, while people at a high risk of developing cardiovascular
11 disease were included in fewer trials. So, they recommended dual therapy
12 with an SGLT2 inhibitor in addition to metformin for both groups, but only as
13 an option to consider for people without established cardiovascular disease, to
14 reflect the lower certainty.

15 For people without a high risk of developing cardiovascular disease who do
16 not have congestive heart failure or established atherosclerotic cardiovascular
17 disease, metformin monotherapy remains the recommended first-line
18 treatment option, based on the 2015 recommendation.

19 The committee noted the importance of introducing the drugs sequentially
20 when starting first-line dual therapy. This enables any side effects and
21 intolerances from the first drug to be identified before the second drug is
22 introduced. In line with current practice, the committee recommended starting
23 with metformin and then, if metformin is tolerated, adding the SGLT2 inhibitor.
24 If metformin is not tolerated, then a trial with a modified-release form may be
25 considered (as per the 2015 recommendation) before the SGLT2 inhibitor is
26 added.

27 People who cannot tolerate metformin or for whom it is contraindicated were
28 not included as a separate group in the economic model because the
29 evidence was taken from trials that did not separate results by whether the
30 person was able to take metformin or not. Most people in these trials were
31 expected to be able to take metformin. The committee agreed with the

1 assumption that people who cannot tolerate metformin or for whom it is
2 contraindicated would be offered the next most effective and cost-effective
3 treatment options after metformin. In the economic model scenario when
4 another drug was used in place of metformin for people with established
5 cardiovascular disease or at high risk of developing cardiovascular disease,
6 SGLT2 inhibitors were the class of drugs that were most likely to be cost
7 effective. They therefore prioritised this class of drugs for these people. As
8 before, there was greater certainty in the results for people with established
9 cardiovascular disease compared with those at high risk of developing
10 cardiovascular disease.

11 The committee noted some particularly important safety considerations to take
12 into account before an adult with type 2 diabetes starts on an SGLT2 inhibitor.
13 The committee highlighted these because the SGLT2 inhibitors are
14 comparatively new drugs and clinical experience with their use is low. In
15 particular, in the committee's experience there have been multiple instances
16 of avoidable diabetic ketoacidosis (DKA) resulting in hospital admission.
17 Checking that the person is not following a very low carbohydrate or ketogenic
18 diet when they are prescribed an SGLT2 inhibitor should help reduce the
19 number of people who experience DKA and thereby reduce unnecessary
20 hospital admissions. However, the committee noted that these diets are often
21 used in remission treatment for type 2 diabetes and that treatment with
22 SGLT2 inhibitors should not be a barrier to accessing such programmes.

23 Secondly, the manufacturers of SGLT2 inhibitors recommend that these drugs
24 should be avoided in pregnancy and breastfeeding because in animal studies
25 they have been shown to be toxic in pregnancy and present in breast milk.
26 The committee highlighted in the recommendation to check for this to reduce
27 the potential for harm from these drugs to babies before and after birth. The
28 cross reference to the NICE guideline on diabetes in pregnancy should help
29 ensure that women with type 2 diabetes are supported to avoid unplanned
30 pregnancies while taking these drugs, or to plan for a safe future pregnancy.

1 Finally, the committee highlighted the need for renal monitoring because
2 SGLT2 inhibitors can have adverse effects on renal function. Because of the
3 relatively recent introduction of SGLT2 inhibitors, the committee were
4 concerned that drug-induced renal damage could become widespread if
5 monitoring is not carried out appropriately. They did not specify how often this
6 should occur, because it should depend on individual clinical factors and
7 baseline renal function. In addition, SGLT2 inhibitors have a diuretic effect
8 which can lead to volume depletion (typically dehydration and lower blood
9 pressure) in some people and increase the risk of DKA. This may affect
10 people with certain clinical characteristics in particular, such as people who
11 are frail, older adults (aged 65 or over) or people at increased risk of
12 dehydration.

13 The committee were aware that adults with type 2 diabetes who are
14 overweight or obese may wish to try a ketogenic diet to reverse or reduce the
15 symptoms or severity, or induce remission of their diabetes. However, the
16 committee agreed, based on their experience, that there may be an increased
17 risk of DKA associated with SGLT2 inhibitors and such diets. It is important to
18 tell people about these risks and to advise them to discuss any planned
19 change to a very low carbohydrate or ketogenic diet with their healthcare
20 professional first. Additionally, the committee agreed that prescribers should
21 advise adults with type 2 diabetes not to take their SGLT2 inhibitor if they
22 become unwell with symptoms that might lead to dehydration, such as fever,
23 diarrhoea and vomiting, as this can lead to DKA.

24 **How the recommendations might affect practice**

25 The recommendations to offer SGLT2 inhibitors with metformin to people with
26 type 2 diabetes and congestive heart failure or established atherosclerotic
27 cardiovascular disease at first-line treatment or if they are already taking
28 metformin monotherapy are expected to lead to a change in practice and
29 increase the numbers of people taking SGLT2 inhibitors at the beginning of
30 their treatment. This is also expected to be the case for people with a high risk
31 of developing cardiovascular disease, as this category is expected to cover a
32 large proportion of the people with type 2 diabetes. In current practice, these

1 people would not be offered combination therapy with an SGLT2 until
2 additional treatment is needed to control their HbA1c to below their
3 individually agreed threshold for intervention, and then only if they met the
4 criteria in the relevant NICE technology appraisals for being prescribed an
5 SGLT2 inhibitor. Overall, this recommendation is expected to greatly increase
6 the numbers of people taking SGLT2 inhibitors and is likely to have a
7 substantial resource impact.

8 The numbers of adults with type 2 diabetes and congestive heart failure or
9 established atherosclerotic cardiovascular disease or a high risk of developing
10 cardiovascular disease who cannot tolerate metformin, or for whom metformin
11 is contraindicated, are expected to be relatively low. The new
12 recommendations are likely to see a change in practice as more people start
13 taking an SGLT2 inhibitor, and this will likely be associated with a resource
14 impact.

15 The recommendations about how to begin combination therapy, factors to
16 check before a person starts on an SGLT2 inhibitor, additional monitoring, and
17 topics to cover in a conversation with the person, are not expected to
18 significantly increase consultation time or be a change in practice because
19 these should already form part of the prescribing process and routine
20 monitoring. However, the expected increase in numbers of adults with type 2
21 diabetes taking SGLT2 inhibitors is likely to increase renal function testing,
22 which will increase resource use. This is not expected to be a large increase
23 because some monitoring already occurs, and the costs may be offset by a
24 reduction in monitoring associated with other treatments. Ensuring that people
25 are aware of the risks of DKA when taking SGLT2 inhibitors on a very low
26 carbohydrate or ketogenic diet may lead to a resource saving by reducing
27 avoidable hospital admissions for DKA.

28 [Return to recommendations](#)

29 **Reviewing drug treatments**

30 [Recommendations 1.7.15 to 1.7.16](#)

1 **Why the committee made the recommendations**

2 The committee agreed that when changes to treatment are being considered
3 it is important to review existing treatment options first. Stopping medications
4 that have not worked (for example, in terms of controlling blood glucose or
5 weight loss) and optimising current treatments may remove the need to
6 prescribe additional drugs. However, some drugs, such as SGLT2 inhibitors,
7 may be continued because they provide additional cardiovascular protective
8 benefits. In particular, there might be reasons, such as problems with
9 adherence or adverse effects, that might make existing treatments less
10 effective or ineffective. Addressing these might mean that adding a new drug
11 is unnecessary. The list of factors to think about as part of optimisation is not
12 exhaustive but includes those that the committee thought were particularly
13 important.

14 Reviews should also take into account a person's current clinical
15 circumstances (as detailed in [recommendation 1.7.1](#) on choosing drug
16 treatments). This will help ensure that appropriate treatment options are
17 considered if the person's clinical situation has changed: for example, if it has
18 improved because of weight loss or if they have developed congestive heart
19 failure or atherosclerotic cardiovascular disease.

20 Based on the evidence and the economic model, the benefits of SGLT2
21 inhibitors were not confined to first-line treatment for people with elevated
22 cardiovascular risk or congestive heart failure or established atherosclerotic
23 cardiovascular disease. To ensure that people who are already on drug
24 therapy for type 2 diabetes can have an SGLT2 inhibitor if their level of
25 cardiovascular risk is sufficiently high or they have congestive heart failure or
26 established atherosclerotic cardiovascular disease, the committee included a
27 separate recommendation on SGLT2 inhibitors for these people.

28 This recommendation also takes into account that adults with type 2 diabetes
29 may develop these conditions (or an increase in their risk) over time. If that
30 happens, an SGLT2 inhibitor could then be of benefit to them. The committee
31 agreed that it was very important to highlight that it may be more appropriate

1 to replace an existing therapy with an SGLT2 inhibitor than to add to it,
2 depending on the person's circumstances. This is because they were aware
3 that treatment optimisation as detailed in [recommendation 1.7.15](#) is not
4 always carried out in practice.

5 **How the recommendations might affect practice**

6 The recommendation about reviewing drug treatment is not expected to be a
7 change in practice or to need substantial additional resources because these
8 conversations should already take place. However, the wider use of SGLT2
9 inhibitors in people who are already being treated for type 2 diabetes and who
10 have or develop high cardiovascular risk or congestive heart failure or
11 established atherosclerotic cardiovascular disease is expected to lead to an
12 increase in resource use.

13 [Return to recommendations](#)

14 **Treatment options if further interventions are needed**

15 [Recommendations 1.7.17 to 1.7.24](#)

16 **Why the committee made the recommendations**

17 The committee agreed that for later stages of treatment separate
18 recommendations were not needed for people at high risk of developing
19 cardiovascular disease or with congestive heart failure or established
20 atherosclerotic cardiovascular disease. This was for several reasons. Firstly,
21 the evidence and the economic model continued to show that an SGLT2
22 inhibitor was likely to be the most cost-effective option for these people.
23 Secondly, the recommendations they had made on first-line treatment using
24 an SGLT2 inhibitor (either with metformin, or alone if metformin is
25 contraindicated or not tolerated) and for switching or adding this drug at later
26 stages meant that these people would be able to access an SGLT2 inhibitor
27 without adding this consideration to the existing 2015 recommendations.
28 Finally, the alternative treatment options for people with and without increased
29 cardiovascular risk remained the same for later treatment stages. Therefore,
30 the committee agreed to retain the existing recommendations for treatment

1 options if further interventions are needed, without making any changes based
2 on cardiovascular risk.

3 To simplify the treatment pathway, the committee merged recommendations
4 for people in whom metformin is contraindicated or not tolerated into the
5 existing 2015 recommendations where possible, and added the NICE
6 technology appraisals as bullet points to the relevant existing
7 recommendations.

8 The evidence that was reviewed in this update was limited to the
9 cardiovascular benefits of GLP-1 mimetics and the committee agreed that this
10 was only generalisable to people with high risk of developing cardiovascular
11 disease or with congestive heart failure or established atherosclerotic
12 cardiovascular disease. GLP-1 mimetic therapy was not cost effective at any
13 stage of the economic modelling in relation to cardiovascular benefits. The
14 committee therefore recommended that the use of GLP-1 mimetics solely to
15 reduce cardiovascular risk could not be justified.

16 The committee did not look at clinical and cost-effectiveness evidence for the
17 use of GLP-1 mimetics to control blood glucose levels. As a result, the
18 committee were unable to update the 2015 GLP-1 mimetic recommendations.
19 However, the committee were concerned that, as written, the 2015
20 recommendation on GLP1-mimetics would mean that people taking newer
21 drugs with proven cardiovascular benefit, such as SGLT2 inhibitors, would
22 have to switch to a combination of metformin, a sulfonylurea and a GLP-1
23 mimetic. They agreed that this might be clinically inappropriate and not in
24 keeping with current clinical practice, so they amended recommendation
25 [1.7.22](#) to remove the requirement for this specific combination of treatment
26 options. The rest of the recommendation and the other recommendations for
27 GLP-1 mimetics were out of scope for this update, so the criteria for accessing
28 a GLP-1 mimetic remain unchanged. These recommendations set tight limits
29 on who should be offered a GLP-1 mimetic, based on the lack of cost
30 effectiveness of this treatment for most people in the 2015 guideline.

1 The committee included a [research recommendation](#) to compare the
2 effectiveness and cost effectiveness of GLP-1 mimetics and insulin. They
3 agreed that adults with type 2 diabetes may prefer to take GLP-1 mimetics
4 instead of insulin as they are weekly rather than daily injections, and because
5 of the association of GLP-1 mimetics with weight loss. In contrast, insulins are
6 associated with weight gain, need blood glucose monitoring and may lead to
7 restrictions on activities of daily living such as driving. The current review and
8 economic model did not look at this comparison and so there is uncertainty
9 whether GLP-1 mimetics would be cost-effective options at this point in the
10 pathway for adults with type 2 diabetes.

11 **How the recommendations might affect practice**

12 Since no new drug options have been added to later stages of treatment,
13 these recommendations are not expected to lead to an increase in resource
14 impact over that detailed above for initiating treatment with metformin and an
15 SGLT2 inhibitor, or an SGLT2 inhibitor alone, or for people who are already
16 on drug therapy when an SGLT2 inhibitor is or becomes appropriate based on
17 their cardiovascular risk.

18 The recommendation not to offer GLP-1 mimetic therapy solely for
19 cardiovascular risk reduction may lead to fewer people with high
20 cardiovascular risk taking these drugs at earlier stages of the treatment
21 pathway. However, removing the previous restriction limiting the use of GLP-1
22 mimetics to combination therapy with metformin and a sulfonylurea may
23 increase the use of GLP-1 mimetics at later stages of the treatment pathway
24 by making additional combinations of triple therapy that include GLP-1
25 mimetics available to eligible people. However, these drugs are already widely
26 used in some areas and this change may bring the guideline into line with
27 current practice.

28 [Return to recommendations](#)

1 **Context**

2 Type 2 diabetes is a chronic metabolic condition characterised by insulin
3 resistance (that is, the body's inability to effectively use insulin) and
4 insufficient pancreatic insulin production, resulting in high blood glucose levels
5 (hyperglycaemia). Type 2 diabetes is commonly associated with obesity,
6 physical inactivity, raised blood pressure, disturbed blood lipid levels and a
7 tendency to develop thrombosis, and therefore is recognised to have an
8 increased cardiovascular risk. It is associated with long-term microvascular
9 and macrovascular complications, together with reduced quality of life and life
10 expectancy.

11 In 2013, over 3.2 million adults were diagnosed with diabetes, with prevalence
12 rates of 6% and 6.7% in England and Wales respectively. It is estimated that
13 about 90% of adults currently diagnosed with diabetes have type 2 diabetes.
14 Type 2 diabetes is more common in people of African, African-Caribbean and
15 South Asian family origin. It can occur in all age groups and is increasingly
16 being diagnosed in children.

17 Multiple vascular risk factors and wide-ranging complications make diabetes
18 care complex and time consuming, and many areas of healthcare services
19 must be involved for optimal management. Necessary lifestyle changes, the
20 complexities and possible side effects of therapy make patient education and
21 self-management important aspects of diabetes care. Diabetes care is
22 estimated to account for at least 5% of UK healthcare expenditure, and up to
23 10% of NHS expenditure.

24 This guideline contains recommendations for managing type 2 diabetes in
25 adults, and focuses on patient education, dietary advice, managing
26 cardiovascular risk, managing blood glucose levels, and identifying and
27 managing long-term complications. The guideline does not cover diagnosis,
28 secondary diabetes, type 1 diabetes in adults, diabetes in pregnancy and
29 diabetes in children and young people.

1 **Reasons for the 2015 update**

2 Since the publication of the 2009 guideline, availability of new evidence and
3 several key developments have prompted an update in the following areas:
4 managing blood glucose levels, antiplatelet therapy and erectile dysfunction.
5 In particular, reasons included safety concerns surrounding some blood
6 glucose lowering medicines, new evidence on new dipeptidyl peptidase-4
7 (DPP-4) inhibitors, sodium–glucose cotransporter-2 (SGLT2) inhibitors and
8 glucagon-like peptide-1 (GLP-1) receptor agonists, new indications and
9 licensed combinations for licensed class members and the potential impact of
10 drugs coming off patent on health-economic issues. In addition, new evidence
11 and safety issues relating to the off-label use of antiplatelet therapy (aspirin
12 and clopidogrel) in the primary prevention of cardiovascular disease motivated
13 an update of this review.

14 **Reasons for the 2021 update**

15 Since the publication of the 2015 guideline a key development has been the
16 publication of new evidence from cardiovascular outcomes trials, which have
17 looked at DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists and a
18 sulfonylurea and thiazolidinedione, and how they affect major adverse
19 cardiovascular outcomes such as cardiovascular mortality, myocardial
20 infarction and stroke.

21 **Finding more information and committee details**

22 To find NICE guidance on related topics, including guidance in development,
23 see the [NICE webpage on diabetes](#).

24 For details of the guideline committee see the [committee member list](#).

25 **Update information**

26 **September 2021:** This guideline is an update of NICE guideline NG28
27 (published December 2015) and will replace it.

1 We have reviewed the evidence on drug treatment for adults with type 2
2 diabetes.

3 Recommendations are marked **[2021]** if the evidence has been reviewed.

4 **Recommendations that have been deleted, or changed**
5 **without an evidence review**

6 We propose to delete some recommendations from the 2015 guideline. [Table](#)
7 [1](#) sets out these recommendations and includes details of replacement
8 recommendations. If there is no replacement recommendation then an
9 explanation for the proposed deletion is given.

10 For recommendations shaded in grey and ending **[2015, amended 2021]**, we
11 have made changes that could affect the intent without reviewing the
12 evidence. Yellow shading is used to highlight these changes, and reasons for
13 the changes are given in [table 2](#).

14 For recommendations shaded in grey and ending **[2015], [2009], [2009,**
15 **amended 2015]** or **[2009, amended 2020]** we have not reviewed the
16 evidence. In some cases, minor changes have been made – for example, to
17 update links, or to bring the language and style up to date – without changing
18 the intent of the recommendation. Minor changes are listed in [table 3](#).

19 See also the [previous NICE guideline and supporting documents](#).

1 **Table 1 Recommendations that have been deleted**

Recommendation in 2015 guideline	Comment
1.6.22 In adults with type 2 diabetes, review the dose of metformin if the estimated glomerular filtration rate (eGFR) is below 45 ml/minute/1.73 m ² : <ul style="list-style-type: none"> • Stop metformin if the eGFR is below 30 ml/minute/1.73 m². • 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/1.73 m². [2015] 	This recommendation no longer accurately reflected the SPCs, so it was replaced by a general cross reference to MHRA safety information and to checking the BNF and SPCs.
1.6.24 In adults with type 2 diabetes, do not offer or continue pioglitazone if they have any of the following: <ul style="list-style-type: none"> • heart failure or history of heart failure • hepatic impairment • diabetic ketoacidosis • current, or a history of, bladder cancer • uninvestigated macroscopic haematuria. [2015] 	This recommendation is covered by the SPCs. As part of a decision to simplify the treatment pathway, a general cross reference was included to MHRA safety information and to checking the BNF and SPCs.

2

3 **Table 2 Amended recommendation wording (change to intent) without**
4 **an evidence review**

Recommendation in 2015 guideline	Recommendation in current guideline	Reason for change
1.1.1 Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preferences, comorbidities, risks from polypharmacy, and their ability to benefit from long-term interventions because of reduced life expectancy. Such an approach is especially important in the context of multimorbidity. Reassess the person's needs and circumstances at each review and think	1.1.1 Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preferences, comorbidities, risks from polypharmacy, and their likelihood of benefiting from long-term interventions . Such an approach is especially important in the context of multimorbidity.	The recommendation has been amended to take account of the likelihood of benefit seen in the cardiovascular outcome trials. The final sentence of the recommendation has been moved to a new (1.1.21.7.15) recommendation below.

<p>about whether to stop any medicines that are not effective.</p>	<p>1.1.2 Reassess the person's needs and circumstances at each review and think about whether to stop any medicines that are not effective.</p>	
<p>1.6.5 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.</p>	<p>1.6.5 Discuss and agree with adults with type 2 diabetes an individual HbA1c target (see figure 1). Encourage them to reach their target and maintain it unless any resulting adverse effects (including hypoglycaemia), or their efforts to achieve their target, impair their quality of life.</p>	<p>A cross reference to the new figure about weighing up your target HcA1c has been added.</p>
<p>1.6.9 Consider relaxing the target HbA1c level (see recommendations 1.6.7 and 1.6.8) on a case-by-case basis, with particular consideration for people who are older or frail, for adults with type 2 diabetes:</p> <ul style="list-style-type: none"> • 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 	<p>1.6.9 Consider relaxing the target HbA1c level (see recommendations 1.6.7 and 1.6.8 and NICE's patient decision aid in appendix A) on a case by case basis and in discussion with adults with type 2 diabetes, with particular consideration for people who are older or frail, if:</p> <ul style="list-style-type: none"> • they are unlikely to achieve longer term risk reduction benefits, for example, people with a reduced life expectancy • tight blood glucose control would put them at high risk if they developed hypoglycaemia, for example, they are at risk of falling, they have impaired awareness of hypoglycaemia, or they drive or operate machinery as part of their job • intensive management would not be appropriate, for example if they have significant comorbidities 	<p>A cross reference to the new figure about weighing up your target HcA1c has been added.</p>

<p>example, people with significant comorbidities</p>		
<p>1.6.17 For adults with type 2 diabetes, discuss the benefits and risks of drug treatment, and the options available. Base the choice of drug treatments on:</p> <ul style="list-style-type: none"> • the effectiveness of the drug treatments in terms of metabolic response • safety (see Medicines and Healthcare products Regulatory Agency guidance) and tolerability of the drug treatments • 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). 	<p>1.7.1 Discuss with adults with type 2 diabetes the benefits and risks of drug treatment and the options available. Base the choice of drug treatments on:</p> <ul style="list-style-type: none"> • the person's individual clinical circumstances, for example, comorbidities, contraindications and risks from polypharmacy • the person's individual preferences and needs • the effectiveness of the drug treatments in terms of metabolic response and cardiovascular protection • safety (see Medicines and Healthcare products Regulatory Agency guidance) and tolerability of the drug treatment • monitoring requirements • the licensed indications or combinations available • cost (if 2 drugs in the same class are appropriate, choose the option with the lowest acquisition cost). <p>See also the NICE guideline on shared decision making and the section on safety of medicines for diabetes before and during pregnancy in the NICE guideline on diabetes in pregnancy.</p>	<p>Cardiovascular protection has been added as a consideration when choosing a drug because of evidence of cardiovascular benefit seen in the clinical evidence for some drug treatments. Contraindications was added to the list of clinical factors because the use of certain treatments may be harmful for people with certain conditions. Monitoring requirements vary between drugs and more intensive monitoring requirements may negatively impact on quality of life. The bullet order was updated in line with the principles in the shared decision making guideline to make the recommendation more person-centred by emphasising the need for the decision about drug choice to be guided by the needs (clinical and otherwise) and preferences of the person. The cross references were added to support shared decision making about the choice of drug and to ensure that any considerations relating to pregnancy or the possibility of pregnancy are also taken into account at this time.</p>

<p>1.6.23 In adults with type 2 diabetes, if metformin is contraindicated or not tolerated, consider initial drug treatment with:</p> <ul style="list-style-type: none"> • a dipeptidyl peptidase-4 (DPP-4) inhibitor or • pioglitazone or • a sulfonylurea. <p>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.</p>	<p>1.7.10 For first-line drug treatment in adults with type 2 diabetes, if metformin is contraindicated or not tolerated and if they are not in either of the groups in recommendation 1.7.9, consider:</p> <ul style="list-style-type: none"> • a DPP 4 inhibitor or • pioglitazone or • a sulfonylurea or • an SGLT2 inhibitor for people who meet the criteria in NICE technology appraisal guidance 390, or TA572 <p>1.7.11 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 as dual therapy.</p>	<p>‘Initial drug treatment’ has been changed to ‘first-line treatment’ in line with plain English and NICE style.</p> <p>The recommendation was amended to reflect the new treatment pathway for adults with established or at high risk of developing cardiovascular disease and to make it clear this recommendation applies to people without high risk of cardiovascular disease.</p> <p>The information about the NICE technology appraisals for SGLT2 inhibitors that was formerly covered in the text below the recommendation has been included as a new bullet to make it clearer that they may be treatment options at this point in the treatment pathway.</p> <p>The additional paragraph on repaglinide has been made into a separate recommendation for clarity. The guideline no longer uses the term ‘first intensification’ so this has been replaced with ‘dual therapy’.</p>
<p>1.6.25 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:</p> <ul style="list-style-type: none"> • metformin and a DPP-4 inhibitor or • metformin and pioglitazone or 	<p>1.7.18 For adults with type 2 diabetes, if monotherapy has not continued to control HbA1c to below the person’s individually agreed threshold for further intervention, consider adding:</p> <ul style="list-style-type: none"> • a DPP 4 inhibitor or • pioglitazone or • a sulfonylurea or 	<p>Amended to reflect that people may be taking monotherapy other than metformin at this stage in the pathway (if it is contraindicated for example).</p> <p>Reference to intensification has been removed throughout the guideline to make the treatment pathway easier to follow. The dual</p>

<ul style="list-style-type: none"> metformin and a sulfonylurea. 	<ul style="list-style-type: none"> an SGLT2 inhibitor for people who meet the criteria in NICE technology appraisal guidance 315, TA572, TA288, or TA336 	<p>therapy combinations have been replaced by the drugs that could be added at this stage to simplify the recommendation.</p> <p>The information about the NICE technology appraisals for SGLT2 inhibitors that was formerly covered in the text below the recommendation has been included as a new bullet.</p>
<p>1.6.26 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 with:</p> <ul style="list-style-type: none"> a DPP-4 inhibitor and pioglitazone or a DPP-4 inhibitor and a sulfonylurea or pioglitazone and a sulfonylurea. <p>Be aware that the drugs in dual therapy should be introduced in a stepwise manner, checking for tolerability and effectiveness of each drug.</p>	<p>This recommendation has been merged with the recommendation above (1.7.18)</p>	<p>Amended to simplify the treatment pathway because the additional treatment options are the same for people who can and cannot take metformin at this stage.</p> <p>The additional paragraph recommending stepwise introduction and tolerability and effectiveness check is now a separate recommendation (1.7.17).</p>
<p>1.6.27 In adults with type 2 diabetes, if dual therapy with metformin and another oral drug (see recommendation 1.6.25) has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider either:</p> <ul style="list-style-type: none"> triple therapy with: 	<p>1.7.19 For adults with type 2 diabetes, if dual therapy with metformin and another oral drug has not continued to control HbA1c to below the person's individually agreed threshold for further intervention consider either:</p> <ul style="list-style-type: none"> triple therapy by adding a DPP 4 inhibitor, pioglitazone 	<p>Reference to intensification has been removed throughout the guideline to make the treatment pathway easier to follow.</p> <p>The triple therapy combinations have been replaced by the drugs that could be added at this stage to simplify the recommendation.</p>

<ul style="list-style-type: none"> – metformin, a DPP-4 inhibitor and a sulfonylurea or – metformin, pioglitazone and a sulfonylurea or • starting insulin-based treatment (see recommendations 1.6.32 to 1.6.34). 	<p>or a sulfonylurea or an SGLT2 inhibitor for people who meet the criteria in NICE technology appraisal guidance 315, TA418, TA336, or TA583) or</p> <ul style="list-style-type: none"> • starting insulin-based treatment (see the section on insulin-based treatments) 	<p>The information about NICE technology appraisals for SGLT2 inhibitors that was formerly covered in the text below the recommendation has been included as a new bullet.</p>
<p>1.6.28 If triple therapy with metformin and 2 other oral drugs (see recommendation 1.6.27) is not effective, not tolerated or contraindicated, consider combination therapy with metformin, a sulfonylurea and a glucagon-like peptide-1 (GLP-1) mimetic for adults with type 2 diabetes who:</p> <ul style="list-style-type: none"> • have a body mass index (BMI) of 35 kg/m² 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/m² and: <ul style="list-style-type: none"> – for whom insulin therapy would have significant occupational implications or – weight loss would benefit other significant obesity-related comorbidities. 	<p>1.7.22 If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider triple therapy including a GLP-1 mimetic for adults with type 2 diabetes who:</p> <ul style="list-style-type: none"> • have a BMI of 35 kg/m² 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/m² and: <ul style="list-style-type: none"> – for whom insulin therapy would have significant occupational implications or – weight loss would benefit other significant obesity-related comorbidities. 	<p>Amended to remove the requirement for a specific combination of therapy in order to use GLP-1 mimetics. This was carried out to reflect that people may be taking different treatments (including SGLT2 inhibitors) at this stage in the treatment pathway based on the new 2021 recommendations on the use of SGLT2 inhibitors for people with high cardiovascular risk and to be more reflective of current practice.</p>
<p>1.6.30 In adults with type 2 diabetes, if metformin is contraindicated or not tolerated, and if dual therapy with 2 oral drugs (see recommendation</p>	<p>1.7.20 In adults with type 2 diabetes, if metformin is contraindicated or not tolerated and dual therapy with 2 oral drugs has not</p>	<p>Reference to intensification has been removed throughout the guideline to make the</p>

<p>1.6.26) has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider insulin-based treatment (see recommendations 1.6.32–1.6.34).</p>	<p>continued to control HbA1c to below the person's individually agreed threshold for intervention, consider insulin-based treatment (see the section on insulin-based treatments).</p>	<p>treatment pathway easier to follow. The cross reference to earlier recommendations has been removed to make this recommendation easier to read.</p>
<p>Research recommendation 3: When third intensification of treatment is indicated, which blood glucose lowering therapies should be used to control blood glucose levels?</p>	<p>Research recommendation 3: When blood glucose levels are inadequately controlled by 3 oral antidiabetic drugs and/or insulin combinations, which blood glucose lowering therapies should be used to control blood glucose levels?</p>	<p>Reference to intensification has been removed throughout the guideline to make the pathway easier to follow. This has been replaced by the explanation of what the third intensification was.</p>

1

1 **Table 3 Minor changes to recommendation wording (no change to**
 2 **intent)**

Recommendation numbers in current guideline	Comment
All recommendations except those labelled [2021]	Recommendations have been edited into the direct style (in line with current NICE style for recommendations in guidelines) where possible. Yellow highlighting has not been applied to these changes.
Recommendations 1.2.1, 1.2.2, 1.2.4 to 1.2.7, 1.3.5 to 1.3.10, 1.4, 1.5.1, 1.5.2, 1.6.1, 1.6.2, 1.6.6 to 1.6.9, 1.6.12 to 1.6.14, 1.7.1, 1.7.2, 1.7.11, 1.7.17, 1.7.25 to 1.7.27, 1.7.31, 1.8.1, 1.8.3, 1.8.4, 1.8.8, 1.8.9, 1.8.16,.	The language in these recommendations has been updated in places for simplicity and clarity or to make the population clearer, and some recommendations have been split to make them shorter and more succinct. Some wording has also been updated to be more person-centred and reflect shared decision making. Yellow highlighting has not been applied to these changes.
'Initial treatment'/'initiation'	Throughout the guideline this has been changed to 'first-line' for plain English and NICE style.
1.3.3	The language in this recommendation has been simplified and restructured to be clearer and simpler.
1.6.5	'Involve adults... in decisions' has been changed to 'Discuss and agree with adults' to update the language in line with the principles of shared decision making.
1.8.17	GP was removed from the recommendation because the committee agreed that this action could be carried out by any primary care professional, so the recommendation was simplified to only include the action.

3

4 **December 2020:** We have amended recommendations 1.7.17 and 1.7.20 to
 5 bring them in line with the diabetic eye screening programme. The evidence
 6 for these recommendations has not been reviewed, and they are marked
 7 **[2009, amended 2020]**.

8 **August 2019:** The recommendations in section 1.4 on diagnosing and
 9 managing hypertension have been removed because diagnosis, treatment

1 and monitoring of hypertension is broadly the same for people with type 2
2 diabetes as for other people (see the [NICE guideline on hypertension in](#)
3 [adults](#)). When a different approach is needed for people with type 2 diabetes,
4 this is specified in the hypertension guideline.

5 **May 2017:** Text on sodium–glucose cotransporter-2 (SGLT2) inhibitors was
6 added to the section on initial drug treatment. The algorithm for blood glucose
7 lowering therapy in adults with type 2 diabetes was also updated to revise
8 footnote b with links to relevant NICE guidance on SGLT2 inhibitors, and new
9 information on SGLT2 inhibitors was also added to the box on action to take if
10 metformin is contraindicated or not tolerated.

11 **December 2016:** The text after recommendation 1.6.31 and the algorithm for
12 blood glucose lowering therapy were updated to refer to NICE technology
13 appraisal guidance on dapagliflozin in triple therapy for treating type 2
14 diabetes (TA418).

15 **December 2015:** We updated and replaced NICE guideline CG87 (published
16 May 2009) and NICE technology appraisal guidance 203 and 248. We made a
17 change without an evidence review. The recommendation on the treatment of
18 gastroparesis was replaced by recommendations from the [NICE guideline on](#)
19 [type 1 diabetes](#). This change is labelled **[2015]**.

20 **Minor changes since publication**

21 **December 2019:** Relationships to the [NICE guideline on hypertension](#) were
22 clarified, and a link was added to the decision aid on choice of medicine to
23 control blood glucose. We added a link to the patient decision aid and user
24 guide about taking a second medicine to control blood glucose.

25 **June 2018:** Recommendation 1.3.11 was added to provide a link to NICE's
26 advice on bariatric surgery.

27 **January 2018:** Notes were added with links to MHRA warnings about
28 sodium–glucose cotransporter-2 (SGLT2) inhibitors.

1 Appendix A Patient decision aid



Type 2 diabetes: agreeing my blood glucose (HbA1c) target

Patient decision aid

2

3 What is the best blood glucose (HbA1c) target for me?

4 If you have type 2 diabetes you will have higher levels of glucose (sugar) in
5 your blood. Your blood glucose levels are usually measured by an HbA1c
6 blood test. Your HbA1c level shows your average blood glucose over the past
7 2 to 3 months.

8 You can help to manage your blood glucose levels with diet and changes to
9 your lifestyle, such as keeping a healthy weight. But most people also need to
10 take medicines to manage their blood glucose.

11 NICE recommends that you and your diabetes team should agree a target
12 HbA1c that you will aim for with their support. We've written this decision aid
13 to help you work out together what that target should be. You can use the
14 diagram on the last page to help.

15 When you are agreeing the target, it's important to think about what else is
16 happening in your life and what matters most to you. **It is important that you**
17 **make a decision that you feel is right for you.** Once you've agreed a target
18 HbA1c, every so often it's a good idea to think about whether this is still the
19 best target for you. This could be at your annual review, or sooner if you wish.

20 Nearly everyone with type 2 diabetes finds their HbA1c increases over time,
21 even with treatment. That's why treatments may need to be changed as part
22 of your ongoing care.

23 Blood glucose and long-term health

24 In the long term, people who have a higher HbA1c are at higher risk of having
25 problems with their blood vessels and heart. These might include angina, a
26 heart attack or a stroke. They also have an increased risk of conditions
27 affecting the eyes and vision, the feet, nerves and kidneys. All of these could
28 lead to complications that could seriously harm the person's quality of life.

1 But not everyone gets these problems, and there is a lot you can do to reduce
2 your risk. As well as managing your blood glucose levels, these include:

- 3 • stopping smoking (if you smoke)
- 4 • keeping a healthy weight
- 5 • staying active

6 and for some people:

- 7 • managing your blood pressure (usually with medicines) if this is high
- 8 • taking a statin to manage your cholesterol if this is high.

9 Your diabetes team can explain more about these and how you can get help
10 with them. NICE has produced other decision aids about managing blood
11 pressure and taking a statin.

12 **What are the possible benefits from managing my blood** 13 **glucose?**

14 High blood glucose levels can cause symptoms such as feeling very thirsty,
15 needing to pass urine a lot and feeling more tired than usual. Managing your
16 blood glucose can stop these things from happening and improve your quality
17 of life.

18 For reducing the risk of long-term health problems, the evidence is unclear
19 about how much extra benefit comes from aiming for a lower target HbA1c
20 compared with aiming for a slightly more relaxed target. Discuss with your
21 diabetes team how much benefit you might expect, taking into account your
22 age, how long you have had diabetes and whether you already have some of
23 the health problems that can come with diabetes.

24 Diabetes specialists agree that managing your blood glucose will reduce the
25 risk of health problems in the long term. However, it's not possible to say for
26 sure what will happen to any individual person.

27 **What are the possible challenges in managing my blood** 28 **glucose?**

29 There might be times when your blood glucose level goes too low – this is
30 called hypoglycaemia (or 'hypo' for short). The lower the target HbA1c you
31 aim for, the more likely you are to get hypos. Most hypos are mild and do not
32 cause much trouble, but some can cause people to feel dizzy or faint and
33 even to pass out. If this happens, they might need help from someone else to

1 treat the hypo. **There are special rules for some drivers who have**
2 **diabetes – talk to your diabetes team to see if they affect you.**

3 The lower you want to keep your blood glucose level, the more medicines you
4 are likely to need to take. This also means you are more likely to get side
5 effects. But not everyone will get side effects and they may not trouble you if
6 they do happen. It is usually possible to change your medicines to ones that
7 suit you better.

1 Your target HbA1c: weighing it up

Make a mark on each of the lines to show how you feel about these statements. The more you agree with the statement on the left, the further to the left you should put your mark. The more you agree with the statement on the right, the further to the right you should put your mark. You and your diabetes team can use this to help decide the best target HbA1c for you.

Thinking about things like driving, having severe hypos would not be a problem for me*



Thinking about things like driving, having severe hypos would be a big problem for me*

I'm not concerned about the chance of getting side effects from medicines



Getting side effects from medicines would be a big problem for me

I'm willing to take more medicines if I need to



I do not want to take any more medicines

I do not have any health issues apart from my diabetes



I have lots of health issues as well as my diabetes

Thinking about my age and my health overall, my quality of life in the long term is important to me



Thinking about my age and my health overall, my quality of life in the shorter-term is more important to me



*Hypos might also be a problem for you for other reasons, such as if you operate machinery, if you are at risk of falling, or if you find it difficult to recognise the warning symptoms of a hypo.

2

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2 ISBN: 978-1-4731-1477-7