

# Type 2 diabetes mellitus: medicines optimisation priorities

Key therapeutic topic

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[nice.org.uk/guidance/ktt12](https://www.nice.org.uk/guidance/ktt12)

## Key points

- The NICE guideline on [type 2 diabetes in adults](#) recommends adopting an individualised approach to diabetes care.
- The NICE guideline recommends that self-monitoring of blood glucose levels for adults with type 2 diabetes should not routinely be offered. See the guideline for details on when self-monitoring is appropriate.
- Diabetes features in the [NHS Long Term Plan](#) published in January 2019.
- Options for local implementation:
  - Involve people with type 2 diabetes in decisions about their individual glycated haemoglobin (HbA1c) target, and reassess their individual needs and circumstances at each review. Consider stopping any medicines that are not effective.
  - Consider carefully, with an individualised approach, the benefits and risks of controlling blood glucose and the use of blood glucose lowering medicines. Review and, if appropriate, optimise prescribing to ensure that it is in line with NICE guidance taking into account the person's preferences, comorbidities, risks from polypharmacy, and their life expectancy and consequent chances of benefiting from long-term interventions.
  - When choosing and reviewing medicines, take into account the person's individual

- – clinical circumstances, preferences and needs; the medicines' efficacy (based on metabolic response), safety and tolerability; and the licensed indications or combinations available. Consider also the cost of medicines: the NICE guideline recommends choosing medicines with the lowest acquisition cost if 2 in the same class are appropriate.

## Evidence context

The NICE guideline on [type 2 diabetes in adults](#) recommends adopting an individualised approach to diabetes care, which takes into account personal preferences, comorbidities, risks from polypharmacy, and the ability to benefit from long-term interventions because of reduced life expectancy. Such an approach is especially important in the context of multimorbidity. See also the medicines optimisation: key therapeutic topic on [multimorbidity and polypharmacy](#) for further information on reviewing polypharmacy and de-prescribing.

The guideline recommends that the person's needs and circumstances should be reassessed at each review and consideration given to stopping any medicines that are not effective. Controlling blood glucose levels requires a careful balance between the intensity of the treatment regimen and avoiding hypoglycaemia. This key therapeutic topic focusses on blood glucose management; however, the NICE guideline also has recommendations on patient education, dietary advice, blood pressure management, antiplatelet therapy and management of complications. Recommendations on the management of blood lipids in people with type 2 diabetes are given in the NICE guideline on [cardiovascular disease: risk assessment and reduction, including lipid modification](#). All these components should be given due consideration in the care of people with type 2 diabetes.

The NICE Pathway on [diabetes](#) brings together everything NICE has said on diabetes in an interactive flowchart. NICE has also published a quality standard on [diabetes in adults](#), which provides a concise set of prioritised statements designed to drive measurable quality improvements within this area. In September 2016, the Care Quality Commission published [My diabetes, my care](#), a community diabetes care review that considers how well care services work together to deliver high-quality diabetes care. The review makes a number of recommendations for how health and social care commissioners, providers and professionals could work together to improve diabetes care and prevention.

## *Target blood glucose levels*

The NICE guideline on [type 2 diabetes in adults](#) recommends that people with type 2 diabetes should be involved in decisions about their individual glycated haemoglobin (HbA1c) target and be supported to achieve and maintain this. For adults with type 2 diabetes that is managed either by

lifestyle and diet, or by lifestyle and diet combined with a single drug not associated with hypoglycaemia, the guideline recommends supporting the person to aim for an HbA1c level of 48 mmol/mol (6.5%). For adults taking a drug associated with hypoglycaemia, the recommended aim is an HbA1c level of 53 mmol/mol (7.0%). If HbA1c levels are not adequately controlled by a single drug and rise to 58 mmol/mol (7.5%) or higher, advice about diet, lifestyle and adherence to drug treatment should be reinforced, the person should be supported to aim for an HbA1c level of 53 mmol/mol (7.0%) and drug treatment should be intensified (taking into account principles of individualised care). When intensification of drug treatment is needed the guideline recommends that additional treatments should be introduced in a stepwise manner, checking for tolerability and effectiveness of each drug.

The target HbA1c level can be relaxed on a case-by-case basis, with particular consideration for people who are older or frail, those with a reduced life expectancy, those for whom tight blood glucose control poses a high risk of the consequences of hypoglycaemia, and those for whom intensive management would not be appropriate, such as people with significant comorbidities. The NICE [patient decision aid](#) for adults with type 2 diabetes can support the implementation of the guideline recommendations on the individualised agreement of HbA1c targets.

The [Quality and Outcomes Framework](#) allocates points for achieving 3 levels of glucose control in people with type 2 diabetes: HbA1c of 75 mmol/mol (9%) or less, 64 mmol/mol (8%) or less and 59 mmol/mol (7.5%) or less.

## What are the benefits and risks of controlling blood glucose?

The NICE guideline included a review question comparing intensive glycaemic control with conventional glycaemic control in people with type 2 diabetes (see the [full guideline](#) for details). This used a Cochrane review ([Hemmingsen et al. 2013](#)) as the primary source of evidence because it included all relevant randomised controlled trials (RCTs). The Cochrane review included 28 RCTs in 34,912 people with type 2 diabetes; the NICE guideline excluded 8 RCTs in which intensive and conventional glycaemic control groups had significant baseline differences in adjunctive treatment for cardiovascular risk factors.

Compared with conventional control, the NICE guideline found that intensive glycaemic control did not statistically significantly reduce death from any cause ([relative risk \[RR\]](#) 0.98, 95% [confidence interval \[CI\]](#) 0.88 to 1.09; 16 RCTs, n=6,504) or death from cardiovascular causes (RR 1.15, 95% CI 0.98 to 1.35; 14 RCTs, n=6,356). No statistically significant effect of targeting intensive glycaemic control was found on the composite of macrovascular complications.

Intensive glycaemic control did reduce the risk of the composite of microvascular complications (RR 0.75, 95% CI 0.61 to 0.92; 3 RCTs, n=4,376), but no statistically significant reductions in risk were seen for the individual end points of nephropathy, progression to end-stage renal disease or retinopathy.

Intensive glycaemic control increased the risk of severe hypoglycaemia (RR 2.23, 95% CI 1.22 to 4.08; 13 RCTs, n=5,452) and mild hypoglycaemia (RR 1.85, 95% CI 1.53 to 2.25; 12 RCTs, n=6,320). The guideline development group agreed overall that there was evidence to support the setting of target values, but considered it important to ensure that a person's risk of hypoglycaemia is evaluated when setting appropriate target levels.

### *Self-monitoring of blood glucose*

The NICE guideline on [type 2 diabetes in adults](#) recommends that self-monitoring of blood glucose levels for adults with type 2 diabetes should not routinely be offered unless:

- the person is on insulin treatment or
- there is evidence of hypoglycaemic episodes or
- the person is on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery or
- the person is pregnant, or is planning to become pregnant (see the NICE guideline on [diabetes in pregnancy](#) for more information).

Healthcare professionals should also take the Driver and Vehicle Licensing Agency (DVLA) guidance [Assessing fitness to drive guide](#) into account when offering self-monitoring of blood glucose levels to people with type 2 diabetes and advise them about their own particular requirements.

The guideline development group discussed the evidence for self-monitoring of blood glucose and concluded that overall, while a statistically significant difference was observed in HbA1c levels in favour of self-monitoring, this was not clinically meaningful and was unlikely to be cost-effective. The reduction in HbA1c levels with self-monitoring was 2 mmol/mol (0.22%), which was less than 5 mmol/mol (0.5%), the agreed threshold for minimal important difference.

The guideline recommends considering short-term self-monitoring of blood glucose levels in adults with type 2 diabetes (and reviewing treatment as necessary) when starting treatment with oral or intravenous corticosteroids or to confirm suspected hypoglycaemia. It is also recommended for

healthcare professionals to be aware that adults with type 2 diabetes who have acute intercurrent illness are at risk of worsening hyperglycaemia, and reviewing treatment as necessary.

The guideline recommends that if adults with type 2 diabetes are self-monitoring their blood glucose levels this should be assessed in a structured way at least annually, assessing various issues including the impact on the person's quality of life and the continued benefit of self-monitoring.

## *Blood glucose lowering therapy*

Recommendations on blood glucose lowering therapy are given in the NICE guideline on [type 2 diabetes in adults](#). These are summarised in the current [algorithm for blood glucose lowering therapy in adults with type 2 diabetes](#).

The NICE guideline recommends that the choice of medicine for managing blood glucose levels should be made following a discussion with the individual person about the benefits and risks of drug treatment, and the options available. The guideline recommends an individualised approach to treatment choice taking into account the person's individual preferences and needs, and their individual clinical circumstances, for example, comorbidities and risks from polypharmacy. Choice should also take into account the medicine's efficacy (based on metabolic response), safety and tolerability; and the licensed indications or combinations available. Cost should be taken into account and the guideline recommends choosing medicines with the lowest acquisition cost if more than 1 in the same class are appropriate. NICE's [patient decision aid](#) for adults with type 2 diabetes can support the implementation of the guideline recommendations on the pharmacological management of blood glucose.

## **Efficacy**

Although all blood glucose lowering medicines are effective (at a population level) in reducing HbA1c levels, clinical outcome data, particularly around cardiovascular outcomes, are limited. Improvements in surrogate markers (including HbA1c levels) do not automatically confer benefits on mortality or morbidity, and risks may only become apparent over time when medicines are used widely in a diverse population.

Metformin, sulfonylureas and insulin have outcome data from the [UK Prospective Diabetes Study \(UKPDS\)](#). In July 2017, NICE [reviewed the evidence](#) on the effectiveness and impact of medicines used to manage diabetes in people with a high risk of cardiovascular disease. The committee agreed that there was limited evidence from large trials focusing on cardiovascular outcomes, other macrovascular outcomes, and microvascular outcomes in type 2 diabetes and that, historically, the

focus has been on glucose control. The committee agreed that, of all the antidiabetic drugs and combination of drugs, healthcare professionals and patients do not know which drug or combination of drug is best at improving macrovascular and microvascular outcomes.

NICE found that there was insufficient evidence to make further recommendations because trials had only reported on some sodium-glucose cotransporter 2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) mimetics, with trials of others still ongoing at that time. Since then the following trials have been completed and published:

- EXSCEL, evaluating the GLP-1 mimetic exenatide ([Holman et al. September 2017](#))
- HARMONY Outcomes, evaluating the GLP-1 mimetic albiglutide ([Hernandez et al. October 2018](#))
- DECLARE-TIMI58, evaluating the SGLT-2 inhibitor dapagliflozin ([Wiviott et al. January 2019](#)).

At the time of publication of this key therapeutic topic (March 2019), [REWIND](#), evaluating the GLP-1 mimetic dulaglutide, had been completed but had not yet been published.

The GLP-1 mimetic liraglutide was the subject of NICE technology appraisal guidance published in 2010. This recommended not offering the 1.8 mg dose. However the technology appraisal guidance was replaced by the NICE guideline on [type 2 diabetes in adults](#), which makes recommendations about GLP-1 mimetics, SGLT-2 inhibitors and sulfonylureas at a class level and does not make recommendations about doses.

The [LEADER](#) study (Marso et al. 2016) evaluated the cardiovascular effects of liraglutide 1.8 mg as an add-on to standard care in people with type 2 diabetes who had established cardiovascular disease or were at high risk of developing it, with a median follow-up of 3.5 years. LEADER was considered in the 2017 [evidence review](#) of medicines in diabetes. The committee noted that the trial found a clinically meaningful reduction of nephropathy, cardiovascular mortality and mortality from all causes in participants treated with liraglutide compared with placebo (for more information about LEADER, see NICE's medicines evidence commentary on [type 2 diabetes: liraglutide reduces cardiovascular risk in people at high risk of having a cardiovascular event](#)).

The committee discussed that the beneficial effect of liraglutide on cardiovascular mortality and mortality from all causes could be because of the higher dose that was used in the trial, and this may not be applicable to the 1.2 mg dose usually prescribed in clinical practice. Additionally, the LEADER trial had no restrictions on body mass index (BMI), and a higher dose may be more beneficial in reducing cardiovascular disease risk in people with a higher BMI. The committee noted

that previous NICE recommendations based on GLP-1 mimetics considered liraglutide at a dose of 1.2 mg and that the LEADER trial is not sufficient evidence by itself to recommend a dosage of 1.8 mg. Additionally, it was noted that a brand of liraglutide, Saxenda, is licensed at a maintenance dose of 3.0 mg for weight reduction in adults with a BMI of 30 kg/m<sup>2</sup> or more or from 27 to 30 kg/m<sup>2</sup> in the presence of at least 1 weight-related comorbidity, such as type 2 diabetes. The committee noted that liraglutide at the higher dose of 3.0 mg may have cardiovascular benefits in a population of overweight or obese people with type 2 diabetes, but there is a lack of research in this area.

The recommendations in the NICE guideline on [type 2 diabetes in adults](#) remain unchanged. As new trial evidence becomes available NICE will consider the need to update this guidance. For further information, see the [evidence reviews](#) on SGLT-2 inhibitors and GLP-1 mimetics.

## Safety

The MHRA has issued several [Drug Safety Updates](#) highlighting safety concerns with blood glucose lowering medicines, including:

- [SGLT-2 inhibitors: reports of Fournier's gangrene \(necrotising fasciitis of the genitalia or perineum\)](#) (February 2019)
- [SGLT-2 inhibitors: updated advice on increased risk of lower-limb amputation \(mainly toes\)](#) (March 2017)
- [SGLT-2 inhibitors: updated advice on the risk of diabetic ketoacidosis](#) (April 2016)
- [Dipeptidylpeptidase-4 inhibitors: risk of acute pancreatitis](#) (September 2012)
- [Pioglitazone: risk of bladder cancer](#) (August 2011)
- [Insulin combined with pioglitazone: risk of cardiac failure](#) (January 2011)
- [Exenatide \(Byetta ▼\): risk of severe pancreatitis and renal failure](#) (March 2009).

These safety concerns are cross referenced in the NICE guideline on [type 2 diabetes in adults](#) and have been incorporated into the [summaries of product characteristics](#).

Another possible side effect of blood glucose lowering medicines is hypoglycaemia, and controlling blood glucose needs a careful balance between the intensity of the treatment regimen and avoiding hypoglycaemia. Many of the summaries of product characteristics for blood glucose lowering medicines warn about the increased risk of hypoglycaemia when combining treatments, particularly with a sulfonylurea or insulin, and a lower dose of insulin or a sulfonylurea may be

needed.

Several new insulin products have been launched in recent years and the European Medicines Agency issued a [risk minimisation strategy for high-strength and fixed-combination insulin products](#) in October 2015. In the [April 2015 edition of Drug Safety Update](#), the MHRA issued advice to health professionals to minimise the risk of medication errors with recently launched high strength, fixed combination and biosimilar insulin products. See the medicines optimisation: key therapeutic topic on [safer insulin prescribing](#) for more information.

The recommendations for insulin in the NICE guideline on [type 2 diabetes in adults](#) also apply to any current and future biosimilar product(s) of insulin that have an appropriate marketing authorisation that allows the use of the biosimilar(s) in the same indication. For more information on the insulin glargine biosimilar, Abasaglar, see NICE's evidence summary on [diabetes mellitus type 1 and type 2: insulin glargine biosimilar \(Abasaglar\)](#).

### *Practice examples and shared learning*

There are NICE [shared learning case studies](#) relating to type 2 diabetes, showing how NICE guidance and standards have been put into practice by some NHS organisations. These include:

- [Supporting the management of type 2 diabetes with pharmacist-led reviews and implementing NICE recommended nine key care processes.](#)
- [PITstop training and the use of NICE guidance and the type 2 diabetes treatment pathway.](#)

### **Prescribing data, metrics or supporting resources**

The selection of metrics to support key therapeutic topics is overseen by the NHS England Medicines Optimisation Intelligence Group, and work is ongoing in this area. At this point, the following prescribing data and metrics have been identified by this group to support this topic.

The NHS Digital report [Prescribing for diabetes, England: 2007/08 to 2017/18](#) found that in the financial year 2017/18 there were 53.4 million items prescribed for diabetes at a total net ingredient cost of £1,012.4 million. This represents an additional 22.6 million items (73% relative increase) and an additional £421.7 million (71% relative increase) compared with 2007/08. The prescribing of 'other antidiabetic drugs' (which includes the newer blood glucose lowering drugs) has increased considerably in recent years. The number of items prescribed increased by 250% (6.7 million) from 2007/08 to 2017/18 with a growth in net ingredient cost of 224% (£250.2 million).



The net ingredient cost of all insulin therapy in primary care in 2017/18 was £350.5 million; a growth of 31% from 2007/08. In the financial year 2017/18, 1.5 million items of insulin glargine were prescribed at a cost of £82 million, 700,000 items of insulin detemir were prescribed at a cost of £41 million and 160,000 items of insulin degludec at a cost of £10 million. This compared with 600,000 items of NPH (isophane) insulin at a cost of £19 million.

A medicines optimisation key therapeutic topic (MO KTT) [prescribing comparator](#) is available on long-acting insulin analogues.

Several diabetes metrics related to this key therapeutic topic are also included in the [Medicines optimisation dashboard](#), which brings together a range of medicines-related metrics from across sectors. These are:

- Diabetes Mellitus (DM009) % achieving upper threshold or above, which is the percentage of practices in a clinical commissioning group (CCG) that achieve upper threshold or above (92% or more inclusive of exceptions) for quality and outcomes framework indicator DM009.
- Diabetes Mellitus (DM009) % underlying achievement, which is the percentage underlying achievement at CCG level for QOF indicator DM009 inclusive of exceptions.
- Emergency diabetes admissions, which is the number of emergency attendances for diabetes per 100 patients on the practice QOF diabetes disease register.

The medicines optimisation dashboard helps NHS organisations to understand how well their local populations are being supported to optimise medicines use and inform local planning. The dashboard allows NHS organisations to highlight variation in local practice and provoke discussion on the appropriateness of local care. It is not intended as a performance measurement tool and there are no targets.

## Update information

**March 2019:** This topic was retained for the 2019 update of medicines optimisation: key therapeutic topics. The evidence context has been updated in the light of new guidance and important new evidence where appropriate.

## About this key therapeutic topic

This document summarises the evidence base on this key therapeutic topic that has been identified to support medicines optimisation. **It is not formal NICE guidance.**

For information about the process used to develop the key therapeutic topics, see the [integrated process statement](#).

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