

Issue date: May 2009

# **Type 2 diabetes**

## **The management of type 2 diabetes**

**This guideline partially updates  
NICE clinical guideline 66 and replaces it**

### **March 2010**

Recommendations 1.14.2.3, 1.14.2.4, 1.14.2.5 and 1.14.2.6 in this guideline have been updated and replaced by 'Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specialist settings' (NICE clinical guideline 96), available from [www.nice.org.uk/guidance/CG96](http://www.nice.org.uk/guidance/CG96)

### **September 2010**

In September 2010 the European Medicines Agency (EMA), the European Union (EU) body responsible for monitoring the safety of medicines, recommended the suspension of the marketing authorisation for rosiglitazone (Avandia, Avandamet and Avaglim) from GlaxoSmithKline. The EMA has concluded that the benefits of rosiglitazone no longer outweigh its risks and the marketing authorisation should be suspended across the EU.

The EMA has advised that patients who are currently taking rosiglitazone-containing medicines should make an appointment with their doctor at a convenient time to discuss suitable alternative treatments. Patients are advised not to stop their treatment without speaking to their doctor. NICE does not recommend the use of drugs without marketing authorisation. Therefore, as a result of the EMA's decision, NICE has temporarily withdrawn its recommendations on the use of rosiglitazone in this guideline.

## **NICE clinical guideline 87**

Developed by the National Collaborating Centre for Chronic Conditions and the Centre for Clinical Practice at NICE

## **NICE clinical guideline 87**

### **Type 2 diabetes: the management of type 2 diabetes**

#### **Ordering information**

You can download the following documents from [www.nice.org.uk/CG87](http://www.nice.org.uk/CG87)

- The NICE guideline (this document) – all the recommendations.
- A quick reference guide – a summary of the recommendations for healthcare professionals.
- ‘Understanding NICE guidance’ – a summary for patients and carers.
- The full guidelines (NICE short clinical guideline 87 and CG66) – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

For printed copies of the quick reference guide or ‘Understanding NICE guidance’, phone NICE publications on 0845 003 7783 or email [publications@nice.org.uk](mailto:publications@nice.org.uk) and quote:

- N1863 (quick reference guide)
- N1864 (‘Understanding NICE guidance’).

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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This clinical guideline is a partial update of NICE clinical guideline 66 and replaces it. NICE clinical guideline 66 updated NICE clinical guidelines E, F, G and H (2002) and updated and replaced the recommendations on type 2 diabetes in NICE technology appraisal guidance 53 (2002), 60 and 63 (2003).

The recommendations in sections 1.6 and 1.7.2 have been updated by the short clinical guideline 'Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes', and are new **[new 2009]** or unchanged. This short guideline addresses the licensed indications of drugs as of September 2008. The recommendations do not apply to drugs not yet available in the UK and exclude liraglutide, which did not receive UK marketing authorisation for type 2 diabetes during the development of this guideline. Recommendations are consistent with safety information from the European Medicines Agency and the Medicines and Healthcare products Regulatory Agency.

## Introduction

Type 2 diabetes is commonly associated with raised blood pressure, a disturbance of blood lipid levels and a tendency to develop thrombosis. It is notable for the increased cardiovascular risk that it carries: coronary artery disease (leading to heart attacks, angina); peripheral artery disease (leg claudication, gangrene); and carotid artery disease (strokes, dementia). The specific ('microvascular') complications of diabetes include eye damage (blindness), kidney damage (sometimes requiring dialysis or transplantation) and nerve damage (resulting in amputation, painful symptoms, erectile dysfunction, other problems). This picture of multiple vascular risk factors and wide-ranging complications means that the management of type 2 diabetes draws on many areas of healthcare management. As a result, diabetes care is typically complex and time-consuming. The necessary lifestyle changes, the complexities of management and the side effects of therapy make self-monitoring and education for people with diabetes central parts of management.

### Definition

The guideline recommendations were developed using the World Health Organization (WHO) definition of diabetes, which requires a degree of high plasma glucose levels sufficient to put the individual at risk of the microvascular complications of diabetes. This definition was re-confirmed by WHO in 2006<sup>1</sup> but, like earlier versions, it does not contain a specific definition for type 2 diabetes. A person is normally thought to have type 2 diabetes if he or she does not have type 1 diabetes (rapid onset, often in childhood, insulin-dependent, ketoacidosis if neglected), monogenetic diabetes or other medical conditions or treatment suggestive of secondary diabetes. Diagnosis is not addressed in this guideline.

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<sup>1</sup>International Diabetes Federation (2006) Definition and diagnosis of diabetes mellitus and immediate hyperglycemia: report of a WHO/IDF consultation. Geneva: World Health Organization.

## **Patient-centred care**

This guideline offers best practice advice on the care of people with type 2 diabetes. It does not address care in or before pregnancy, or care by specialist services for specific advanced organ damage (cardiac, renal, eye, vascular, stroke and other services).

Management of diabetes typically involves a considerable element of self-care, and advice should, therefore, be aligned with the perceived needs and preferences of people with diabetes, and carers. People with type 2 diabetes should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – ‘Reference guide to consent for examination or treatment’ (2001) (available from [www.dh.gov.uk](http://www.dh.gov.uk)). Healthcare professionals should also follow a code of practice accompanying the Mental Capacity Act (summary available from [www.publicguardian.gov.uk](http://www.publicguardian.gov.uk)).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient’s needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

## Key priorities for implementation

- Offer structured education to every person and/or their carer at and around the time of diagnosis, with annual reinforcement and review. Inform people and their carers that structured education is an integral part of diabetes care.
- Provide individualised and ongoing nutritional advice from a healthcare professional with specific expertise and competencies in nutrition.
- When setting a target glycosylated haemoglobin (HbA<sub>1c</sub>):
  - involve the person in decisions about their individual HbA<sub>1c</sub> target level, which may be above that of 6.5% set for people with type 2 diabetes in general
  - encourage the person to maintain their individual target unless the resulting side effects (including hypoglycaemia) or their efforts to achieve this impair their quality of life
  - offer therapy (lifestyle and medication) to help achieve and maintain the HbA<sub>1c</sub> target level
  - inform a person with a higher HbA<sub>1c</sub> that any reduction in HbA<sub>1c</sub> towards the agreed target is advantageous to future health
  - avoid pursuing highly intensive management to levels of less than 6.5%.
- Offer self-monitoring of plasma glucose to a person newly diagnosed with type 2 diabetes only as an integral part of his or her self-management education. Discuss its purpose and agree how it should be interpreted and acted upon.
- When starting insulin therapy, use a structured programme employing active insulin dose titration that encompasses:
  - structured education
  - continuing telephone support
  - frequent self-monitoring
  - dose titration to target
  - dietary understanding
  - management of hypoglycaemia
  - management of acute changes in plasma glucose control
  - support from an appropriately trained and experienced healthcare professional.

# 1 Guidance

The following guidance is based on the best available evidence. The full guidelines ([www.nice.org.uk/CG87](http://www.nice.org.uk/CG87)) give details of the methods and the evidence used to develop the guidance.

## 1.1 *Patient education*<sup>2</sup>

- 1.1.1 Offer structured education to every person and/or their carer at and around the time of diagnosis, with annual reinforcement and review. Inform people and their carers that structured education is an integral part of diabetes care.
- 1.1.2 Select a patient-education programme that meets the criteria laid down by the Department of Health and Diabetes UK Patient Education Working Group<sup>3</sup>.
- Any programme should be evidence-based and suit the needs of the individual. The programme should have specific aims and learning objectives, and should support development of self-management attitudes, beliefs, knowledge and skills for the learner, their family and carers.
  - The programme should have a structured curriculum that is theory driven and evidence-based, resource-effective, has supporting materials, and is written down.
  - The programme should be delivered by trained educators who have an understanding of education theory appropriate to the age and needs of the programme learners, and are trained and competent in delivery of the principles and content of the programme they are offering.

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<sup>2</sup> The recommendations in this section replace 'Guidance on the use of patient-education models for diabetes' (NICE technology appraisal guidance 60).

<sup>3</sup> Structured patient education in diabetes: report from the patient education working group. Available from: [www.dh.gov.uk](http://www.dh.gov.uk)

- The programme itself should be quality assured, and be reviewed by trained, competent, independent assessors who assess it against key criteria to ensure sustained consistency.
  - The outcomes from the programme should be regularly audited.
- 1.1.3 Ensure the patient-education programme provides the necessary resources to support the educators, and that educators are properly trained and given time to develop and maintain their skills.
- 1.1.4 Offer group education programmes as the preferred option. Provide an alternative of equal standard for a person unable or unwilling to participate in group education.
- 1.1.5 Ensure the patient-education programmes available meet the cultural, linguistic, cognitive and literacy needs in the locality.
- 1.1.6 Ensure all members of the diabetes healthcare team are familiar with the programmes of patient education available locally, that these programmes are integrated with the rest of the care pathway, and that people with diabetes and their carers have the opportunity to contribute to the design and provision of local programmes.

## **1.2 *Lifestyle management/non-pharmacological management***

Neither the management of obesity nor smoking cessation is specifically addressed in this guideline. Follow other NICE guidance in these areas (see section 6 for further details).

### **1.2.1 Dietary advice**

- 1.2.1.1 Provide individualised and ongoing nutritional advice from a healthcare professional with specific expertise and competencies in nutrition.
- 1.2.1.2 Provide dietary advice in a form sensitive to the individual's needs, culture and beliefs, being sensitive to their willingness to change and the effects on their quality of life.

- 1.2.1.3 Emphasise advice on healthy balanced eating that is applicable to the general population when providing advice to people with type 2 diabetes. Encourage high-fibre, low-glycaemic-index sources of carbohydrate in the diet, such as fruit, vegetables, wholegrains and pulses; include low-fat dairy products and oily fish; and control the intake of foods containing saturated and trans fatty acids).
- 1.2.1.4 Integrate dietary advice with a personalised diabetes management plan, including other aspects of lifestyle modification, such as increasing physical activity and losing weight.
- 1.2.1.5 Target, for people who are overweight, an initial body weight loss of 5–10%, while remembering that lesser degrees of weight loss may still be of benefit and that larger degrees of weight loss in the longer term will have advantageous metabolic impact.
- 1.2.1.6 Individualise recommendations for carbohydrate and alcohol intake, and meal patterns. Reducing the risk of hypoglycaemia should be a particular aim for a person using insulin or an insulin secretagogue.
- 1.2.1.7 Advise individuals that limited substitution of sucrose-containing foods for other carbohydrate in the meal plan is allowable, but that care should be taken to avoid excess energy intake.
- 1.2.1.8 Discourage the use of foods marketed specifically for people with diabetes.
- 1.2.1.9 When patients are admitted to hospital as inpatients or to any other institutions, implement a meal-planning system that provides consistency in the carbohydrate content of meals and snacks.

## **1.2.2 Management of depression**

- 1.2.2.1 Follow the recommendations in 'Depression: management of depression in primary and secondary care clinical guideline' (NICE clinical guideline 23).

### **1.3 Glucose control levels**

- 1.3.1 When setting a target glycated haemoglobin (HbA<sub>1c</sub>):
- involve the person in decisions about their individual HbA<sub>1c</sub> target level, which may be above that of 6.5% set for people with type 2 diabetes in general
  - encourage the person to maintain their individual target unless the resulting side effects (including hypoglycaemia) or their efforts to achieve this impair their quality of life
  - offer therapy (lifestyle and medication) to help achieve and maintain the HbA<sub>1c</sub> target level
  - inform a person with a higher HbA<sub>1c</sub> that any reduction in HbA<sub>1c</sub> towards the agreed target is advantageous to future health
  - avoid pursuing highly intensive management to levels of less than 6.5%.
- 1.3.2 Measure the individual's HbA<sub>1c</sub> levels at:
- 2–6-monthly intervals (tailored to individual needs) until the blood glucose level is stable on unchanging therapy; use a measurement made at an interval of less than 3 months as an indicator of direction of change, rather than as a new steady state
  - 6-monthly intervals once the blood glucose level and blood glucose-lowering therapy are stable.
- 1.3.3 If HbA<sub>1c</sub> levels remain above target levels, but pre-meal self-monitoring levels remain well controlled (< 7.0 mmol/litre), consider self-monitoring to detect postprandial hyperglycaemia (> 8.5 mmol/litre) and manage to below this level if detected (see sections 1.5–1.7).
- 1.3.4 Measure HbA<sub>1c</sub> using high-precision methods and report results in units aligned with those used in the DCCT trial<sup>4</sup> (or as

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<sup>4</sup> Little RR, Rohlfing CL, Wiedmeyer HM, et al (2001) The National Glycohemoglobin Standardization Program (NGSP): a five-year progress report. *Clinical Chemistry* 47: 1985–1992

recommended by national agreement after publication of this guideline).

- 1.3.5 When HbA<sub>1c</sub> monitoring is invalid (because of disturbed erythrocyte turnover or abnormal haemoglobin type), estimate trends in blood glucose control using one of the following:
- fructosamine estimation
  - quality-controlled plasma glucose profiles
  - total glycated haemoglobin estimation (if abnormal haemoglobins).
- 1.3.6 Investigate unexplained discrepancies between HbA<sub>1c</sub> and other glucose measurements. Seek advice from a team with specialist expertise in diabetes or clinical biochemistry.

## **1.4 Self-monitoring of plasma glucose**

- 1.4.1 Offer self-monitoring of plasma glucose to a person newly diagnosed with type 2 diabetes only as an integral part of his or her self-management education. Discuss its purpose and agree how it should be interpreted and acted upon.
- 1.4.2 Self-monitoring of plasma glucose should be available:
- to those on insulin treatment
  - to those on oral glucose-lowering medications to provide information on hypoglycaemia
  - to assess changes in glucose control resulting from medications and lifestyle changes
  - to monitor changes during intercurrent illness
  - to ensure safety during activities, including driving.
- 1.4.3 Assess at least annually and in a structured way:
- self-monitoring skills
  - the quality and appropriate frequency of testing
  - the use made of the results obtained
  - the impact on quality of life

- the continued benefit
- the equipment used.

1.4.4 If self-monitoring is appropriate but blood glucose monitoring is unacceptable to the individual, discuss the use of urine glucose monitoring.

## **1.5 Oral glucose control therapies (1): metformin, insulin secretagogues and acarbose**

### **1.5.1 Metformin**

- 1.5.1.1 Start metformin treatment in a person who is overweight or obese (tailoring the assessment of body-weight-associated risk according to ethnic group<sup>5</sup>) and whose blood glucose is inadequately controlled (see 1.3.1) by lifestyle interventions (nutrition and exercise) alone.
- 1.5.1.2 Consider metformin as an option for first-line glucose-lowering therapy for a person who is not overweight.
- 1.5.1.3 Continue with metformin if blood glucose control remains or becomes inadequate (see 1.3.1) and another oral glucose-lowering medication (usually a sulfonylurea) is added.
- 1.5.1.4 Step up metformin therapy gradually over weeks to minimise risk of gastro-intestinal (GI) side effects. Consider a trial of extended-absorption metformin tablets where GI tolerability prevents continuation of metformin therapy.
- 1.5.1.5 Review the dose of metformin if the serum creatinine exceeds 130 micromol/litre or the estimated glomerular filtration rate (eGFR) is below 45 ml/minute/1.73-m<sup>2</sup>.
- Stop the metformin if the serum creatinine exceeds 150 micromol/litre or the eGFR is below 30 ml/minute/1.73-m<sup>2</sup>.

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<sup>5</sup> See 'Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children' (NICE clinical guideline 43) ([www.nice.org.uk/CG43](http://www.nice.org.uk/CG43)).

- 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-m<sup>2</sup>.

1.5.1.6 The benefits of metformin therapy should be discussed with a person with mild to moderate liver dysfunction or cardiac impairment so that:

- due consideration can be given to the cardiovascular-protective effects of the drug
- an informed decision can be made on whether to continue or stop the metformin.

## **1.5.2 Insulin secretagogues**

1.5.2.1 Consider a sulfonylurea as an option for first-line glucose-lowering therapy if:

- the person is not overweight
- the person does not tolerate metformin (or it is contraindicated)
- or**
- a rapid response to therapy is required because of hyperglycaemic symptoms.

1.5.2.2 Add a sulfonylurea as second-line therapy when blood glucose control remains or becomes inadequate (see 1.3.1) with metformin.

1.5.2.3 Continue with a sulfonylurea if blood glucose control remains or becomes inadequate (see 1.3.1) and another oral glucose-lowering medication is added.

1.5.2.4 Prescribe a sulfonylurea with a low acquisition cost (but not glibenclamide) when an insulin secretagogue is indicated (see 1.5.2.1 and 1.5.2.2).

1.5.2.5 When drug concordance is a problem, offer a once-daily, long-acting sulfonylurea.

1.5.2.6 Educate a person being treated with an insulin secretagogue, particularly if renally impaired, about the risk of hypoglycaemia.

### **1.5.3 Rapid-acting insulin secretagogues**

1.5.3.1 Consider offering a rapid-acting insulin secretagogue to a person with an erratic lifestyle.

### **1.5.4 Acarbose**

1.5.4.1 Consider acarbose for a person unable to use other oral glucose-lowering medications.

## **1.6 Oral glucose control therapies (2): other oral agents and exenatide**

The recommendations in this section were updated by the short clinical guideline 'Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes' ([www.nice.org.uk/CG87shortguideline](http://www.nice.org.uk/CG87shortguideline)). The guideline gives details of the methods and the evidence used to develop the recommendations.

### **1.6.1 DPP-4 inhibitors (sitagliptin, vildagliptin)**

1.6.1.1 Consider adding a DPP-4 inhibitor (sitagliptin, vildagliptin) instead of a sulfonylurea as second-line therapy to first-line metformin when control of blood glucose remains or becomes inadequate ( $\text{HbA}_{1c} \geq 6.5\%$ , or other higher level agreed with the individual) if:

- the person is at significant risk of hypoglycaemia or its consequences (for example, older people and people in certain jobs [for example, those working at heights or with heavy machinery] or people in certain social circumstances [for example, those living alone]), or
- the person does not tolerate a sulfonylurea or a sulfonylurea is contraindicated. **[new 2009]**

1.6.1.2 Consider adding a DPP-4 inhibitor (sitagliptin, vildagliptin) as second-line therapy to first-line sulfonylurea monotherapy when

control of blood glucose remains or becomes inadequate ( $\text{HbA}_{1c} \geq 6.5\%$ , or other higher level agreed with the individual) if:

- the person does not tolerate metformin, or metformin is contraindicated. **[new 2009]**

1.6.1.3 Consider adding sitagliptin<sup>6</sup> as third-line therapy to first-line metformin and a second-line sulfonylurea when control of blood glucose remains or becomes inadequate ( $\text{HbA}_{1c} \geq 7.5\%$  or other higher level agreed with the individual) and insulin is unacceptable or inappropriate<sup>7</sup>. **[new 2009]**

1.6.1.4 Only continue DPP-4 inhibitor therapy (sitagliptin, vildagliptin) if the person has had a beneficial metabolic response (a reduction of at least 0.5 percentage points in  $\text{HbA}_{1c}$  in 6 months). **[new 2009]**

1.6.1.5 Discuss the potential benefits and risks of treatment with a DPP-4 inhibitor (sitagliptin, vildagliptin) with the person to enable them to make an informed decision.

A DPP-4 inhibitor (sitagliptin, vildagliptin) may be preferable to a thiazolidinedione (pioglitazone, rosiglitazone) if:

- further weight gain would cause or exacerbate significant problems associated with a high body weight, or
- a thiazolidinedione (pioglitazone, rosiglitazone) is contraindicated, or
- the person has previously had a poor response to, or did not tolerate, a thiazolidinedione (pioglitazone, rosiglitazone).

There may be some people for whom either a DPP-4 inhibitor (sitagliptin, vildagliptin) or a thiazolidinedione (pioglitazone,

<sup>6</sup> At the time of publication, sitagliptin was the only DPP-4 inhibitor with UK marketing authorisation for use in this combination.

<sup>7</sup> Because of employment, social or recreational issues related to putative hypoglycaemia, injection anxieties, other personal issues or obesity.

rosiglitazone) may be suitable and, in this case, the choice of treatment should be based on patient preference. **[new 2009]**

## 1.6.2 Thiazolidinediones (pioglitazone, rosiglitazone)<sup>8</sup>

1.6.2.1 Consider adding a thiazolidinedione (pioglitazone, rosiglitazone) instead of a sulfonylurea as second-line therapy to first-line metformin when control of blood glucose remains or becomes inadequate ( $\text{HbA}_{1c} \geq 6.5\%$ , or other higher level agreed with the individual) if:

- the person is at significant risk of hypoglycaemia or its consequences (for example, older people and people in certain jobs [for example, those working at heights or with heavy machinery] or people in certain social circumstances [for example, those living alone]), or
- a person does not tolerate a sulfonylurea or a sulfonylurea is contraindicated. **[new 2009]**

1.6.2.2 Consider adding a thiazolidinedione (pioglitazone, rosiglitazone) as second-line therapy to first-line sulfonylurea monotherapy when control of blood glucose remains or becomes inadequate ( $\text{HbA}_{1c} \geq 6.5\%$ , or other higher level agreed with the individual) if:

- the person does not tolerate metformin or metformin is contraindicated. **[new 2009]**

1.6.2.3 Consider adding a thiazolidinedione (pioglitazone, rosiglitazone) as third-line therapy to first-line metformin and a second-line sulfonylurea when control of blood glucose remains or becomes inadequate ( $\text{HbA}_{1c} \geq 7.5\%$ , or other higher level agreed with the individual) and insulin is unacceptable or inappropriate<sup>9</sup>. **[new 2009]**

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<sup>8</sup> The recommendations in this section replace 'Guidance on the use of glitazones for the treatment of type 2 diabetes' (NICE technology appraisal guidance 63).

<sup>9</sup> Because of employment, social or recreational issues related to putative hypoglycaemia, injection anxieties, other personal issues or obesity.

- 1.6.2.4 Do not commence or continue a thiazolidinedione (pioglitazone, rosiglitazone) in people who have heart failure, or who are at higher risk of fracture. **[new 2009]**
- 1.6.2.5 When selecting a thiazolidinedione (pioglitazone, rosiglitazone), take into account up-to-date advice from the relevant regulatory bodies (the European Medicines Agency and the Medicines and Healthcare products Regulatory Agency), cost, safety and prescribing issues (see 1.6.2.8). **[new 2009]**
- 1.6.2.6 Only continue thiazolidinedione therapy (pioglitazone, rosiglitazone) if the person has had a beneficial metabolic response (a reduction of at least 0.5 percentage points in HbA<sub>1c</sub> in 6 months). **[new 2009]**
- 1.6.2.7 Consider combining pioglitazone with insulin therapy<sup>10</sup> for a person:
- who has previously had a marked glucose-lowering response to thiazolidinedione therapy (pioglitazone, rosiglitazone), or
  - who is on high-dose insulin therapy and whose blood glucose is inadequately controlled. **[new 2009]**
- 1.6.2.8 Discuss the potential benefits and risks of treatment with a thiazolidinedione (pioglitazone, rosiglitazone) with the person to enable them to make an informed decision.
- A thiazolidinedione (pioglitazone, rosiglitazone) may be preferable to a DPP-4 inhibitor (sitagliptin, vildagliptin) if:
- the person has marked insulin insensitivity, or
  - a DPP-4 inhibitor (sitagliptin, vildagliptin) is contraindicated, or
  - the person has previously had a poor response to, or did not tolerate, a DPP-4 inhibitor (sitagliptin, vildagliptin).
- There may be some people for whom either a thiazolidinedione (pioglitazone, rosiglitazone) or a DPP-4 inhibitor (sitagliptin,

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<sup>10</sup> At the time of publication pioglitazone was the only thiazolidinedione with UK marketing authorisation for use with insulin.

vildagliptin) may be suitable and, in this case, the choice of treatment should be based on patient preference. **[new 2009]**

### **1.6.3 GLP-1 mimetic (exenatide)**

1.6.3.1 Consider adding a GLP-1 mimetic (exenatide) as third-line therapy to first-line metformin and a second-line sulfonylurea when control of blood glucose remains or becomes inadequate ( $\text{HbA}_{1c} \geq 7.5\%$ , or other higher level agreed with the individual), and the person has:

- a body mass index (BMI)  $\geq 35.0 \text{ kg/m}^2$  in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight, or
- a BMI  $< 35.0 \text{ kg/m}^2$ , and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities. **[new 2009]**

1.6.3.2 Only continue GLP-1 mimetic (exenatide) therapy if the person has had a beneficial metabolic response (a reduction of at least 1.0 percentage point in  $\text{HbA}_{1c}$  and a weight loss of at least 3% of initial body weight at 6 months). **[new 2009]**

1.6.3.3 Discuss the potential benefits and risks of treatment with a GLP-1 mimetic (exenatide) with the person to enable them to make an informed decision. **[new 2009]**

## **1.7 Glucose control: insulin therapy**

### **1.7.1 Oral agent combination therapy with insulin**

1.7.1.1 When starting basal insulin therapy:

- continue with metformin and the sulfonylurea (and acarbose, if used)
- review the use of the sulfonylurea if hypoglycaemia occurs.

- 1.7.1.2 When starting pre-mixed insulin therapy (or mealtime plus basal insulin regimens):
- continue with metformin
  - continue the sulfonylurea initially, but review and discontinue if hypoglycaemia occurs.

## 1.7.2 Insulin therapy

The recommendations in this section were updated by the short clinical guideline 'Type 2 diabetes newer agents for blood glucose control in type 2 diabetes' ([www.nice.org.uk/CG87shortguideline](http://www.nice.org.uk/CG87shortguideline)). The guideline gives details of the methods and the evidence used to develop the recommendations.

- 1.7.2.1 Discuss the benefits and risks of insulin therapy when control of blood glucose remains or becomes inadequate ( $\text{HbA}_{1c} \geq 7.5\%$  or other higher level agreed with the individual) with other measures. Start insulin therapy if the person agrees. **[new 2009]**
- 1.7.2.2 For a person on dual therapy who is markedly hyperglycaemic, consider starting insulin therapy in preference to adding other drugs to control blood glucose unless there is strong justification<sup>11</sup> not to. **[new 2009]**
- 1.7.2.3 When starting insulin therapy, use a structured programme employing active insulin dose titration that encompasses:
- structured education
  - continuing telephone support
  - frequent self-monitoring
  - dose titration to target
  - dietary understanding
  - management of hypoglycaemia
  - management of acute changes in plasma glucose control

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<sup>11</sup> Because of employment, social or recreational issues related to putative hypoglycaemia, injection anxieties, other personal issues or obesity.

- support from an appropriately trained and experienced healthcare professional.

#### 1.7.2.4 Initiate insulin therapy from a choice of a number of insulin types and regimens.

- Begin with human NPH insulin injected at bed-time or twice daily according to need.
- Consider, as an alternative, using a long-acting insulin analogue (insulin detemir, insulin glargine) if:
  - ~ the person needs assistance from a carer or healthcare professional to inject insulin, and use of a long-acting insulin analogue (insulin detemir, insulin glargine) would reduce the frequency of injections from twice to once daily, or
  - ~ the person's lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes, or
  - ~ the person would otherwise need twice-daily NPH insulin injections in combination with oral glucose-lowering drugs, or
  - ~ the person cannot use the device to inject NPH insulin.
- Consider twice-daily pre-mixed (biphasic) human insulin (particularly if  $HbA_{1c} \geq 9.0\%$ ). A once-daily regimen may be an option.
- Consider pre-mixed preparations that include short-acting insulin analogues, rather than pre-mixed preparations that include short-acting human insulin preparations, if:
  - ~ a person prefers injecting insulin immediately before a meal, or
  - ~ hypoglycaemia is a problem, or
  - ~ blood glucose levels rise markedly after meals. **[new 2009]**

#### 1.7.2.5 Consider switching to a long-acting insulin analogue (insulin detemir, insulin glargine) from NPH insulin in people:

- who do not reach their target HbA<sub>1c</sub> because of significant hypoglycaemia, or
- who experience significant hypoglycaemia on NPH insulin irrespective of the level of HbA<sub>1c</sub> reached, or
- who cannot use the device needed to inject NPH insulin but who could administer their own insulin safely and accurately if a switch to a long-acting insulin analogue were made, or
- who need help from a carer or healthcare professional to administer insulin injections and for whom switching to a long-acting insulin analogue would reduce the number of daily injections. **[new 2009]**

1.7.2.6 Monitor a person on a basal insulin regimen (NPH insulin or a long-acting insulin analogue [insulin detemir, insulin glargine]) for the need for short-acting insulin before meals (or a pre-mixed insulin preparation). **[new 2009]**

1.7.2.7 Monitor a person who is using pre-mixed insulin once or twice daily for the need for a further injection of short-acting insulin before meals or for a change to a regimen of mealtime plus basal insulin, based on NPH insulin or long-acting insulin analogues (insulin detemir, insulin glargine), if blood glucose control remains inadequate. **[new 2009]**

### **1.7.3 Insulin delivery devices**

1.7.3.1 Offer education to a person who requires insulin about using an injection device (usually a pen injector and cartridge or a disposable pen) that they and/or their carer find easy to use.

1.7.3.2 Appropriate local arrangements should be in place for the disposal of sharps.

1.7.3.3 If a person has a manual or visual disability and requires insulin, offer a device or adaptation that:

- takes into account his or her individual needs

- he or she can use successfully.

## **1.8 Blood pressure therapy**

- 1.8.1 Measure blood pressure at least annually in a person without previously diagnosed hypertension or renal disease. Offer and reinforce preventive lifestyle advice.
- 1.8.2 For a person on antihypertensive therapy at diagnosis of diabetes, review control of blood pressure and medications used, and make changes only where there is poor control or where current medications are not appropriate because of microvascular complications or metabolic problems.
- 1.8.3 Repeat blood pressure (BP) measurements within:
- 1 month if BP is higher than 150/90 mmHg
  - 2 months if BP is higher than 140/80 mmHg
  - 2 months if BP is higher than 130/80 mmHg and there is kidney, eye or cerebrovascular damage.
- Offer lifestyle advice (diet and exercise) at the same time.
- 1.8.4 Offer lifestyle advice (see dietary recommendations in section 1.2.1 of this guideline and the lifestyle recommendations in section 1.2 of 'Hypertension: management of hypertension in adults in primary care' [NICE clinical guideline 34]) if blood pressure is confirmed as being consistently above 140/80 mmHg (or above 130/80 mmHg if there is kidney, eye or cerebrovascular damage).
- 1.8.5 Add medications if lifestyle advice does not reduce blood pressure to below 140/80 mmHg (below 130/80 mmHg if there is kidney, eye or cerebrovascular damage).
- 1.8.6 Monitor blood pressure 1–2-monthly, and intensify therapy if on medications until blood pressure is consistently below 140/80 mmHg (below 130/80 mmHg if there is kidney, eye or cerebrovascular disease).

- 1.8.7 First-line blood-pressure-lowering therapy should be a once-daily, generic angiotensin-converting enzyme (ACE) inhibitor. Exceptions to this are people of African-Caribbean descent or women for whom there is a possibility of becoming pregnant (see 1.8.8 and 1.8.9).
- 1.8.8 First-line blood-pressure-lowering therapy for a person of African-Caribbean descent should be an ACE inhibitor plus either a diuretic or a generic calcium-channel antagonist (calcium-channel blocker).
- 1.8.9 A calcium-channel blocker should be the first-line blood-pressure-lowering therapy for a woman for whom, after an informed discussion, it is agreed there is a possibility of her becoming pregnant.
- 1.8.10 For a person with continuing intolerance to an ACE inhibitor (other than renal deterioration or hyperkalaemia), substitute an angiotensin II-receptor antagonist for the ACE inhibitor.
- 1.8.11 If the person's blood pressure is not reduced to the individually agreed target with first-line therapy, add a calcium-channel blocker or a diuretic (usually bendroflumethiazide, 2.5 mg daily). Add the other drug (that is, the calcium-channel blocker or diuretic) if the target is not reached with dual therapy.
- 1.8.12 If the person's blood pressure is not reduced to the individually agreed target with triple therapy (see 1.8.11), add an alpha-blocker, a beta-blocker or a potassium-sparing diuretic (the last with caution if the individual is already taking an ACE inhibitor or an angiotensin II-receptor antagonist).
- 1.8.13 Monitor the blood pressure of a person who has attained and consistently remained at his or her blood pressure target every 4–6 months, and check for possible adverse effects of

antihypertensive therapy – including the risks from unnecessarily low blood pressure.

## **1.9 Cardiovascular risk estimation**

- 1.9.1 Consider a person to be at high premature cardiovascular risk for his or her age unless he or she:
- is not overweight, tailoring this with an assessment of body-weight-associated risk according to ethnic group<sup>12</sup>
  - is normotensive (< 140/80 mmHg in the absence of antihypertensive therapy)
  - does not have microalbuminuria
  - does not smoke
  - does not have a high-risk lipid profile
  - has no history of cardiovascular disease **and**
  - has no family history of cardiovascular disease.
- 1.9.2 If the person is considered not to be at high cardiovascular risk, estimate cardiovascular risk annually using the UK Prospective Diabetes Study (UKPDS) risk engine (see [www.dtu.ox.ac.uk/index.php?maindoc=/riskengine/](http://www.dtu.ox.ac.uk/index.php?maindoc=/riskengine/)).
- 1.9.3 Consider using cardiovascular risk estimates from the UKPDS risk engine (see 1.9.2) for educational purposes when discussing cardiovascular complications with the individual.
- 1.9.4 Perform a full lipid profile (including high-density lipoprotein [HDL] cholesterol and triglyceride estimations) when assessing cardiovascular risk after diagnosis and annually, and before starting lipid-modifying therapy.

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<sup>12</sup> See 'Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children (NICE clinical guideline 43). ([www.nice.org.uk/CG043](http://www.nice.org.uk/CG043))

## **1.10 Management of blood lipid levels**

### **1.10.1 Statins and ezetimibe**

- 1.10.1.1 Review cardiovascular risk status annually by assessment of cardiovascular risk factors, including features of the metabolic syndrome and waist circumference, and change in personal or family cardiovascular history.
- 1.10.1.2 For a person who is 40 years old or over:
- initiate therapy with generic simvastatin (to 40 mg) or a statin of similar efficacy and cost unless the cardiovascular risk from non-hyperglycaemia-related factors is low (see 1.9.1 )
  - if the cardiovascular risk from non-hyperglycaemia-related factors is low, assess cardiovascular risk using the UKPDS risk engine (see 1.9.2) and initiate simvastatin therapy (to 40 mg), or a statin of similar efficacy and cost, if the cardiovascular risk exceeds 20% over 10 years.
- 1.10.1.3 For a person who is under 40 years old, consider initiating generic simvastatin therapy (to 40 mg), or a statin of similar efficacy and cost, where the cardiovascular risk factor profile appears particularly poor (multiple features of the metabolic syndrome, presence of conventional risk factors, microalbuminuria, at-risk ethnic group, or strong family history of premature cardiovascular disease).
- 1.10.1.4 Once a person has been started on cholesterol-lowering therapy, assess his or her lipid profile (together with other modifiable risk factors and any new diagnosis of cardiovascular disease) 1–3 months after starting treatment, and annually thereafter. In those not on cholesterol-lowering therapy, reassess cardiovascular risk annually and consider initiating a statin (see 1.10.1.2 and 1.10.1.3).

- 1.10.1.5 Increase the dose of simvastatin, in anyone initiated on simvastatin in line with the above recommendations, to 80 mg daily unless total cholesterol level is below 4.0 mmol/litre or low-density lipoprotein [LDL] cholesterol level is below 2.0 mmol/litre.
- 1.10.1.6 Consider intensifying cholesterol-lowering therapy (with a more effective statin or ezetimibe in line with NICE guidance)<sup>13</sup> if there is existing or newly diagnosed cardiovascular disease, or if there is an increased albumin excretion rate, to achieve a total cholesterol level below 4.0 mmol/litre (and HDL cholesterol not exceeding 1.4 mmol/litre) or an LDL cholesterol level below 2.0 mmol/litre.
- 1.10.1.7 If there is a possibility of a woman becoming pregnant, do not use statins unless the issues have been discussed with the woman and agreement has been reached.

## **1.10.2 Fibrates**

- 1.10.2.1 If there is a history of elevated serum triglycerides, perform a full fasting lipid profile (including HDL cholesterol and triglyceride estimations) when assessing cardiovascular risk annually.
- 1.10.2.2 Assess possible secondary causes of high serum triglyceride levels, including poor blood glucose control (others include hypothyroidism, renal impairment and liver inflammation, particularly from alcohol). If a secondary cause is identified, manage according to need.
- 1.10.2.3 Prescribe a fibrate (fenofibrate as first-line) if triglyceride levels remain above 4.5 mmol/litre despite attention to other causes. In some circumstances, this will be before a statin has been started because of acute need (that is, risk of pancreatitis) and because of the undesirability of initiating two drugs at the same time.

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<sup>13</sup> 'Statins for the prevention of cardiovascular events' (NICE technology appraisal guidance 94); 'Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia' (NICE technology appraisal guidance 132).

1.10.2.4 If cardiovascular risk is high (as is usual in people with type 2 diabetes), consider adding a fibrate to statin therapy if triglyceride levels remain in the range 2.3–4.5 mmol/litre despite statin therapy.

### **1.10.3 Nicotinic acid**

1.10.3.1 Do not use nicotinic acid preparations and derivatives routinely for people with type 2 diabetes. They may have a role in a few people who are intolerant of other therapies and have more extreme disorders of blood lipid metabolism, when managed by those with specialist expertise in this area.

### **1.10.4 Omega-3 fish oils**

1.10.4.1 Do not prescribe fish oil preparations for the primary prevention of cardiovascular disease in people with type 2 diabetes. This recommendation does not apply to people with hypertriglyceridaemia receiving advice from a healthcare professional with special expertise in blood lipid management.

1.10.4.2 Consider a trial of highly concentrated, licensed omega-3 fish oils for refractory hypertriglyceridaemia if lifestyle measures and fibrate therapy have failed.

## **1.11 *Anti-thrombotic therapy***

1.11.1 Offer low-dose aspirin, 75 mg daily, to a person who is 50 years old or over, if blood pressure is below 145/90 mmHg.

1.11.2 Offer low-dose aspirin, 75 mg daily, to a person who is under 50 years old and has significant other cardiovascular risk factors (features of the metabolic syndrome, strong early family history of cardiovascular disease, smoking, hypertension, extant cardiovascular disease, microalbuminuria).

1.11.3 Clopidogrel should be used instead of aspirin only in those with clear aspirin intolerance (except in the context of acute

cardiovascular events and procedures). Follow the recommendations in 'Clopidogrel and modified-release dipyridamole in the prevention of occlusive vascular events' (NICE technology appraisal guidance 90).

## **1.12 Kidney damage**

- 1.12.1 Ask all people with or without detected nephropathy to bring in a first-pass morning urine specimen once a year. In the absence of proteinuria/urinary tract infection (UTI), send this for laboratory estimation of albumin:creatinine ratio. Request a specimen on a subsequent visit if UTI prevents analysis.
- 1.12.2 Make the measurement on a spot sample if a first-pass sample is not provided (and repeat on a first-pass specimen if abnormal) or make a formal arrangement for a first-pass specimen to be provided.
- 1.12.3 Measure serum creatinine and estimate the glomerular filtration rate (using the method-abbreviated modification of diet in renal disease [MDRD] four-variable equation) annually at the time of albumin:creatinine ratio estimation.
- 1.12.4 Repeat the test if an abnormal albumin:creatinine ratio is obtained (in the absence of proteinuria/UTI) at each of the next two clinic visits but within a maximum of 3–4 months. Take the result to be confirming microalbuminuria if a further specimen (out of two more) is also abnormal (> 2.5 mg/mmol for men, > 3.5 mg/mmol for women).
- 1.12.5 Suspect renal disease other than diabetic nephropathy and consider further investigation or referral when the albumin:creatinine ratio (ACR) is raised and **any** of the following apply:
- there is no significant or progressive retinopathy
  - blood pressure is particularly high or resistant to treatment

- the person previously had a documented normal ACR and develops heavy proteinuria (ACR > 100 mg/mmol)
- significant haematuria is present
- the glomerular filtration rate has worsened rapidly
- the person is systemically ill.

1.12.6 Discuss the significance of a finding of abnormal albumin excretion rate, and its trend over time, with the individual concerned.

1.12.7 Start ACE inhibitors with the usual precautions and titrate to full dose in all individuals with confirmed raised albumin excretion rate (> 2.5 mg/mmol for men, > 3.5 mg/mmol for women).

1.12.8 Have an informed discussion before starting an ACE inhibitor in a woman for whom there is a possibility of pregnancy, assessing the relative risks and benefits of the use of the ACE inhibitor.

1.12.9 Substitute an angiotensin II-receptor antagonist for an ACE inhibitor for a person with an abnormal albumin:creatinine ratio if an ACE inhibitor is poorly tolerated.

1.12.10 For a person with an abnormal albumin:creatinine ratio, maintain blood pressure below 130/80 mmHg.

1.12.11 Agree referral criteria for specialist renal care between local diabetes specialists and nephrologists.

### **1.13 Eye damage**

1.13.1 Arrange or perform eye screening at or around the time of diagnosis. Arrange repeat of structured eye surveillance annually.

1.13.2 Explain the reasons for, and success of, eye surveillance systems to the individual and ensure attendance is not reduced by ignorance of need or fear of outcome.

1.13.3 Use mydriasis with tropicamide when photographing the retina, after prior informed agreement following discussion of the

advantages and disadvantages. Discussions should include precautions for driving.

- 1.13.4 Use a quality-assured digital retinal photography programme using appropriately trained staff.
- 1.13.5 Perform visual acuity testing as a routine part of eye surveillance programmes.
- 1.13.6 Repeat structured eye surveillance according to the findings by:
  - routine review in 1 year, or
  - earlier review, or
  - referral to an ophthalmologist.
- 1.13.7 Arrange emergency review by an ophthalmologist for:
  - sudden loss of vision
  - rubeosis iridis
  - pre-retinal or vitreous haemorrhage
  - retinal detachment.
- 1.13.8 Arrange rapid review by an ophthalmologist for new vessel formation.
- 1.13.9 Refer to an ophthalmologist in accordance with the National Screening Committee criteria and timelines if any of these features is present:
  - referable maculopathy:
    - exudate or retinal thickening within one disc diameter of the centre of the fovea
    - circinate or group of exudates within the macula (the macula is defined here as a circle centred on the fovea, with a diameter the distance between the temporal border of the optic disc and the fovea)
    - any microaneurysm or haemorrhage within one disc diameter of the centre of the fovea, only if associated with deterioration of best visual acuity to 6/12 or worse

- referable pre-proliferative retinopathy (if cotton wool spots are present, look carefully for the following features, but cotton wool spots themselves do not define pre-proliferative retinopathy):
  - any venous beading
  - any venous loop or reduplication
  - any intraretinal microvascular abnormalities
  - multiple deep, round or blot haemorrhages
- any unexplained drop in visual acuity.

## **1.14 Nerve damage**

1.14.1 For the management of foot problems relating to type 2 diabetes, follow recommendations in 'Type 2 diabetes: prevention and management of foot problems' (NICE clinical guideline 10).

### **1.14.2 Diabetic neuropathic pain management**

- 1.14.2.1 Make a formal enquiry annually about the development of neuropathic symptoms causing distress.
- Discuss the cause and prognosis (including possible medium-term remission) of troublesome neuropathic symptoms, if present (bearing in mind alternative diagnoses).
  - Agree appropriate therapeutic options and review understanding at each clinical contact.
- 1.14.2.2 Be alert to the psychological consequences of chronic, painful diabetic neuropathy and offer psychological support according to the needs of the individual.
- ~~1.14.2.3 Use a tricyclic drug to treat neuropathic discomfort (start with low doses, titrated as tolerated) if standard analgesic measures have not worked, timing the medication to be taken before the time of~~

~~day when the symptoms are troublesome; advise that this is a trial of therapy<sup>14</sup>.~~

~~1.14.2.4 Offer a trial of duloxetine, gabapentin or pregabalin if a trial of tricyclic drug does not provide effective pain relief. The choice of drug should be determined by current drug prices. Trials of these therapies should be stopped if the maximally tolerated drug dose is ineffective. If side effects limit effective dose titration, try another one of the drugs<sup>14</sup>.~~

~~1.14.2.5 Consider a trial of opiate analgesia if severe chronic pain persists despite trials of other measures. If there is inadequate relief of the pain associated with diabetic neuropathic symptoms, seek the assistance of a chronic pain management service following a discussion with the person concerned<sup>14</sup>.~~

~~1.14.2.6 If drug management of diabetic neuropathic pain has been successful, consider reducing the dose and stopping therapy following discussion and agreement with the individual<sup>14</sup>.~~

1.14.2.7 If neuropathic symptoms cannot be controlled adequately, it may be helpful to further discuss:

- the reasons for the problem
- the likelihood of remission in the medium term
- the role of improved blood glucose control.

### **1.14.3 Gastroparesis**

1.14.3.1 Consider the diagnosis of gastroparesis in an adult with erratic blood glucose control or unexplained gastric bloating or vomiting, taking into consideration possible alternative diagnoses.

1.14.3.2 Consider a trial of metoclopramide, domperidone or erythromycin for an adult with gastroparesis.

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<sup>14</sup> Updated and replaced by 'Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specialist settings' (NICE clinical guideline 96), available from [www.nice.org.uk/guidance/CG96](http://www.nice.org.uk/guidance/CG96)

1.14.3.3 If gastroparesis is suspected, consider referral to specialist services if:

- the differential diagnosis is in doubt, or
- persistent or severe vomiting occurs.

#### **1.14.4 Erectile dysfunction**

1.14.4.1 Review the issue of erectile dysfunction with men annually.

1.14.4.2 Provide assessment and education for men with erectile dysfunction to address contributory factors and treatment options.

1.14.4.3 Offer a phosphodiesterase-5 inhibitor (choosing the drug with the lowest acquisition cost), in the absence of contraindications, if erectile dysfunction is a problem.

1.14.4.4 Following discussion, refer to a service offering other medical, surgical, or psychological management of erectile dysfunction if phosphodiesterase-5 inhibitors have been unsuccessful.

#### **1.14.5 Other aspects of autonomic neuropathy**

1.14.5.1 Consider the possibility of contributory sympathetic nervous system damage for a person who loses the warning signs of hypoglycaemia.

1.14.5.2 Consider the possibility of autonomic neuropathy affecting the gut in an adult with unexplained diarrhoea, particularly at night.

1.14.5.3 When using tricyclic drugs and antihypertensive medications in people with autonomic neuropathy, be aware of the increased likelihood of side effects such as orthostatic hypotension.

1.14.5.4 Investigate a person with unexplained bladder-emptying problems for the possibility of autonomic neuropathy affecting the bladder.

1.14.5.5 Include in the management of autonomic neuropathy symptoms the specific interventions indicated by the manifestations (for example, for abnormal sweating or nocturnal diarrhoea).

## 2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scopes for this guideline are available from [www.nice.org.uk/CG66](http://www.nice.org.uk/CG66) and [www.nice.org.uk/CG87](http://www.nice.org.uk/CG87)

The application of the guideline to children has not been excluded. However, we were not able to specifically search for paediatric literature due to the volume of work involved. Healthcare professionals need to use their clinical judgement when applying this guideline to children. For further assistance with applying this guideline to children, refer to the 'British national formulary for children' (BNFC) 2007.

### **How this guideline was developed**

NICE commissioned the National Collaborating Centre for Chronic Conditions to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B). The Centre for Clinical Practice at NICE developed or updated the recommendations in sections 1.6 and 1.7.2 in line with the NICE short clinical guideline process. The members of the Guideline Development Group for this short guideline are also given in appendix A. Members of the independent Guideline Review Panel that oversaw the development of the short guideline are given in appendix B.

There is more information about how NICE clinical guidelines are developed on the NICE website ([www.nice.org.uk/guidelinesprocess](http://www.nice.org.uk/guidelinesprocess)). A booklet: 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' (fourth edition, published 2009), is available from NICE publications (phone 0845 003 7783 or email [publications@nice.org.uk](mailto:publications@nice.org.uk) and quote reference N1739).

### **3 Implementation**

NICE has developed tools to help organisations implement this guidance (see [www.nice.org.uk/CG87](http://www.nice.org.uk/CG87)).

### **4 Research recommendations**

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

#### **4.1 *Glucose control: oral glucose-lowering therapy***

Metformin: confirmatory studies of the advantage in terms of cardiovascular outcome studies.

##### **Why this is important**

The UKPDS study confirmed that metformin offered cardiovascular protection. However, the extent of the relative risk reduction was unexpectedly large and needs formal testing in a further study. This is critical to the positioning of metformin in the treatment cascade.

#### **4.2 *Glucose control: oral glucose-lowering therapy***

Studies of the role of sulfonylureas when starting a pre-mixed insulin preparation.

##### **Why this is important**

Both pre-mixed insulins and sulfonylureas are effective glucose-lowering agents throughout the day, but can cause hypoglycaemia. When starting insulin, continuing sulfonylureas prevents deterioration of glucose control during insulin dose titration and reduces the requirement for insulin. However, it is not clear that these advantages are not offset by an increased risk of hypoglycaemia.

#### **4.3 *Self-monitoring of plasma glucose***

Longer-term studies of the role of self-monitoring as part of an integrated package with patient education and therapies used to target.

### **Why this is important**

Studies of self-monitoring, in people not using insulin, continue to fail to address the complicated issue of its integration into patient education and self-management behaviours. Self-monitoring can be moderately expensive and a significant burden if not used appropriately. While it is accepted that study designs are difficult in this area, the positive results from large observational studies need further support.

## **4.4 *Blood-pressure-lowering medications***

The use of ACE inhibitors and angiotensin II-receptor antagonists in combination in early diabetic nephropathy.

### **Why this is important**

Both of these classes of renin–angiotensin system blockers are effective in reducing the rate of progression of diabetic kidney damage. However, there are acute risks of side effects associated with both classes of drug. As these risks are similar, it is not clear whether the expected combined benefit from ACE inhibitors and angiotensin II-receptor antagonists would outweigh the combined risks.

## **4.5 *Diabetic neuropathic pain management***

Comparison studies on tricyclic drugs, duloxetine, gabapentin and pregabalin.

### **Why this is important**

While all these drugs are partially effective in the control of neuropathic pain, they differ in cost and side-effect profile. This makes the recommendations of treatment cascade uncertain to some extent. There is a need for comparative studies between these drugs and, in particular, of the newer agents with the tricyclic drugs.

The Guideline Development Group that developed the recommendations in sections 1.6 and 1.7.2 on newer agents for blood glucose control made the following recommendations for research.

#### **4.6      *Effectiveness and safety of GLP-1 mimetics***

Studies of the effectiveness and safety of GLP-1 mimetics (with and without insulin) in the long-term management of blood glucose.

##### **Why this is important**

There is a lack of long-term evidence (12 months or longer) on the clinical and cost effectiveness of GLP-1 mimetics compared with standard UK practice or other newer agents. There is also limited evidence on the effect of replacing insulin with a GLP-1 mimetic and it is not clear whether some subgroups would benefit from this more than others. GLP-1 mimetics do not currently have UK marketing authorisation for use with insulin, but there is anecdotal evidence that this combination is being used. More evidence is needed on safety and effectiveness.

#### **4.7      *Effectiveness of DPP-4 inhibitors***

Studies of the clinical and cost effectiveness of DPP-4 inhibitors in the long-term management of blood glucose.

##### **Why this is important**

There is a lack of long-term evidence (12 months or longer) on the clinical and cost effectiveness of DPP-4 inhibitors compared with standard UK practice or other newer agents. It is not clear whether there are any subgroups in which DPP-4 inhibitors are more clinically and cost effective.

#### **4.8      *Adherence with different complexities of treatment regimen***

Studies of how adherence varies with complexity of treatment regimen.

##### **Why this is important**

Adherence to treatment is important for clinical (blood glucose control) and patient (health-related quality of life) outcomes. There are currently few data on how the complexity of treatment regimen affects adherence.

## **4.9 Health-related quality of life**

Studies to investigate how the initiation and titration of long-acting insulin affects health-related quality of life, the changes associated with hypoglycaemia and the direct affect of weight loss or avoiding weight gain.

### **Why this is important**

Health-related quality of life is an important determinant of adherence to treatment.

## **5 Other versions of this guideline**

### **5.1 Full guidelines**

The full guideline, 'Type 2 diabetes (update): national clinical guideline for management in primary and secondary care' contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Chronic Conditions and is available from [www.rcplondon.ac.uk/pubs/brochure.aspx?e=247](http://www.rcplondon.ac.uk/pubs/brochure.aspx?e=247) and our website ([www.nice.org.uk/CG66fullguideline](http://www.nice.org.uk/CG66fullguideline)). The short clinical guideline 'Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes' contains details of the methods and evidence used to develop the recommendations in 1.6 and 1.7.2. This is also available from our website ([www.nice.org.uk/CG87shortguideline](http://www.nice.org.uk/CG87shortguideline)).

### **5.2 Quick reference guide**

A quick reference guide for healthcare professionals is available from [www.nice.org.uk/CG87quickrefguide](http://www.nice.org.uk/CG87quickrefguide)

For printed copies, phone NICE publications on 0845 003 7783 or email [publications@nice.org.uk](mailto:publications@nice.org.uk) (quote reference number N1863).

### **5.3 'Understanding NICE guidance'**

Information for patients and carers ('Understanding NICE guidance') is available from [www.nice.org.uk/CG87publicinfo](http://www.nice.org.uk/CG87publicinfo)

For printed copies, phone NICE publications on 0845 003 7783 or email [publications@nice.org.uk](mailto:publications@nice.org.uk) (quote reference number N1864).

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about type 2 diabetes.

## **6 Related NICE guidance**

### **Published**

- Chronic kidney disease. NICE clinical guideline 73 (2008). Available from [www.nice.org.uk/CG73](http://www.nice.org.uk/CG73)
- Lipid modification. NICE clinical guideline 67 (2008). Available from [www.nice.org.uk/CG67](http://www.nice.org.uk/CG67)
- Diabetes in pregnancy. NICE clinical guideline 63 (2008). Available from [www.nice.org.uk/CG63](http://www.nice.org.uk/CG63)
- Smoking cessation services in primary care, pharmacies, local authorities and workplaces, particularly for manual working groups, pregnant women and hard to reach communities. NICE public health guidance 10 (2008). Available from [www.nice.org.uk/PH10](http://www.nice.org.uk/PH10)
- Promoting and creating built or natural environments that encourage and support physical activity. NICE public health guidance 8 (2008). Available from [www.nice.org.uk/PH8](http://www.nice.org.uk/PH8)
- Ezetimibe for the treatment of primary (heterozygous-familial and non-familial) hypercholesterolaemia. NICE technology appraisal guidance 132 (2007). Available from [www.nice.org.uk/TA132](http://www.nice.org.uk/TA132)
- Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health intervention guidance 1 (2006). Available from [www.nice.org.uk/PH1](http://www.nice.org.uk/PH1)
- Four commonly used methods to increase physical activity: brief interventions in primary care, exercise referral schemes, pedometers and community-based exercise programmes for walking and cycling. NICE public health intervention guidance 2 (2006). Available from [www.nice.org.uk/PH2](http://www.nice.org.uk/PH2)

- Hypertension (partial update of NICE clinical guideline 18). NICE clinical guideline 34 (2006). Available from [www.nice.org.uk/CG34](http://www.nice.org.uk/CG34)
- Obesity. NICE clinical guideline 43 (2006). Available from [www.nice.org.uk/CG43](http://www.nice.org.uk/CG43)
- Statins for the prevention of cardiovascular events. NICE technology appraisal guidance 94 (2006). Available from [www.nice.org.uk/TA94](http://www.nice.org.uk/TA94)
- Clopidogrel and modified-release dipyridamole in the prevention of occlusive vascular events. NICE technology appraisal guidance 90 (2005). Available from [www.nice.org.uk/TA90](http://www.nice.org.uk/TA90)
- Depression. NICE clinical guideline 23 (2004, amended 2007). Available from [www.nice.org.uk/CG23](http://www.nice.org.uk/CG23)
- Type 1 diabetes. NICE clinical guideline 15 (2004). Available from [www.nice.org.uk/CG15](http://www.nice.org.uk/CG15)
- Type 2 diabetes: prevention and management of foot problems. NICE clinical guideline 10 (2004). Available from [www.nice.org.uk/CG10](http://www.nice.org.uk/CG10)

### **Under development**

NICE is developing the following guidance (details available from [www.nice.org.uk](http://www.nice.org.uk)):

- Prevention of type 2 diabetes. NICE public health guidance. Publication expected June 2011.

## **7 Updating the guideline**

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

## **Appendix A: The Guideline Development Groups**

### ***The Guideline Development Group for NICE clinical guideline***

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**Mrs Lina Bakhshi**

Information Scientist, NCC-CC

**Ms Margaret Bannister**

Nurse Consultant in Diabetes Care

**Mrs Katherine Cullen**

Health Economist, NCC-CC, and Research Fellow, Queen Mary University of London

**Professor Melanie Davies**

Professor of Diabetes Medicine, University of Leicester

**Dr Jose Diaz**

Health Services Research Fellow in Guideline Development, NCC-CC

**Mrs Barbara Elster**

Patient and Carer Representative, Essex

**Dr Roger Gadsby**

General Practitioner and Senior Lecturer in Primary Care, Warwickshire

**Dr Anupam Garrib**

Health Services Research Fellow in Guideline Development, NCC-CC

**Ms Irene Gummerson**

Primary Care Pharmacist, Yorkshire

**Dr Martin Hadley-Brown**

General Practitioner (trainer), University of Cambridge

**Professor Philip Home (Clinical Adviser to the GDG)**

Professor of Diabetes Medicine, Newcastle University

**Mrs Kathryn Leivesley**

Practice Nurse, North Manchester Primary Care Trust

**Professor Jonathan Mant (Chair)**

Professor of Primary Care Stroke Research, University of Birmingham

**Mrs Emma Marcus**

Clinical Specialist Diabetes Dietitian, Hinckley and Bosworth Primary Care Trust

**Mr Leo Nherera**

Health Economist, National Collaborating Centre for Women's and Children's Health

**Ms Roberta Richey**

Health Services Research Fellow in Guideline Development, NCC-CC

**Mr John Roberts**

Patient and Carer Representative, Merseyside

**Dr Mark Savage**

Consultant Physician, North Manchester General Hospital

**Dr Stuart Smellie**

Consultant Chemical Pathologist, Bishop Auckland General Hospital

**Ms Nicole Stack**

Guideline Development Project Manager, NCC-CC

**Ms Claire Turner**

Guideline Development Project Manager, NCC-CC

**Ms Susan Varney**

Health Services Research Fellow in Guideline Development, NCC-CC

**Dr Jiten Vora**

Consultant Physician Endocrinologist, Royal Liverpool and Broadgreen University Hospitals

***The following experts were invited to attend specific meetings and to advise the Guideline Development Group:***

**Dr Julian Barth**

Consultant Chemical Pathologist, Leeds NHS Trust (attended one meeting as a deputy for Dr Stuart Smellie)

**Dr Indranil Dasgupta**

Consultant Physician and Nephrologist, Birmingham Heartlands Hospital

**Dr Michael Feher**

Consultant Physician, Chelsea Westminster Hospital (attended one meeting as a deputy for Dr Mark Savage)

**Dr Charles Fox**

Consultant Physician, Northampton General Trust (attended one meeting as a deputy for Professor Melanie Davies)

**Natasha Jacques**

Principal Pharmacist, Solihull Hospital (attended one meeting as a deputy for Ms Irene Gummerson)

**Dr Eric Kilpatrick**

Consultant Chemical Pathologist, University of Hull (attended one meeting as a deputy for Dr Stuart Smellie)

**Dr Ian Lawrence**

Consultant Diabetologist, University of Leicester (attended one meeting as a deputy for Professor Melanie Davies and Dr Jiten Vora)

**Professor Sally Marshall**

Professor of Diabetes, Newcastle University

**Professor David Wood**

Professor of Cardiovascular Medicine, Imperial College London

***The Guideline Development Group for the short clinical guideline (recommendations in 1.6 and 1.7.2)***

**Amanda Adler (Chair)**

Consultant Physician with an interest in diabetes, Addenbrooke's Hospital, Cambridge

**Claudette Allerdycce**

Principal Locality Pharmacist, Croydon Primary Care Trust

**Tony Doherty**

Diabetes Nurse Specialist and Service Improvement Officer, Diabetes UK (Scotland)

**Andrew Farmer**

University Lecturer in General Practice, University of Oxford

**Niru Goenka**

Consultant Physician with an interest in diabetes/endocrinology, Countess of Chester NHS Foundation Trust

**Martin Hadley-Brown**

General Practitioner, Thetford, Norfolk; Clinical Teacher at University of Cambridge Clinical School of Medicine

**Philip Home**

Professor of Diabetes Medicine and Consultant Physician in Diabetes and Metabolic Medicine, Newcastle Primary Care Trust

**Philip Ivory**

Patient/carer representative

**Yvonne Johns**

Patient/carer representative

**Ian Lewin**

Consultant Physician with an interest in diabetes/endocrinology, North Devon District Hospital

**Alistair McGuire**

Head of Social Policy, London School of Economics

**Julie Wood**

Diabetes Nurse Specialist, Diabetes and Renal Programme Manager, Kirklees Primary Care Trust

***The following people were not full members of the GDG but were co-opted onto the group as expert advisers.***

**Anthony Barnett**

Professor of Medicine, University of Birmingham and Heart of England NHS Foundation Trust

**Andrew Krentz**

Consultant in Diabetes and Endocrinology, Southampton University Hospitals

***The following person contributed expertise.***

**Alistair Gray**

Director of the Health Economics Research Centre, Division of Public Health and Primary Care, University of Oxford

***The following people, who are employees of NICE, made up the technical team working on the short guideline.***

**Tim Stokes**

Associate Director

**Beth Shaw**

Technical Adviser

**Francis Ruiz**

Technical Adviser in Health Economics

**Michael Heath**

Project Manager

**Lynda Ayiku**

Information Specialist

**Nicole Elliott**

Commissioning Manager

**Emma Banks**

Coordinator

## **Appendix B: The Guideline Review Panel**

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, lay, public health and industry.

### ***Members of the Guideline Review Panel for NICE clinical guideline 66***

**Dr Robert Walker (Chair)**

General Practitioner, Cumbria

**Dr Mark Hill**

Head of Medical Affairs, Novartis Pharmaceuticals UK

**Dr John Harley**

Clinical Governance and Prescribing Lead, North Tees Primary Care Trust

**Ailsa Donnelly**

Lay member

### ***Members of the Guideline Review Panel for the short clinical guideline (recommendations in 1.6 and 1.7.2)***

**Robert Walker (Chair)**

General Practitioner, Workington

**John Harley**

Clinical Governance and Prescribing Lead and General Practitioner, North Tees Primary Care Trust

**Ailsa Donnelly**

Lay member

## **Appendix C: The algorithms**

The quick reference guide can be found at

<http://guidance.nice.org.uk/CG87/QuickRefGuide/pdf/English>