Reporting Organisation

Appendix B: Scopes for NICE clinical guideline update 2015, NICE clinical guideline 87 & NICE clinical guideline 66

Commissioned by the National Institute for Health and Clinical Excellence

Part 1. Scope for the clinical guideline update (2015)

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE - SCOPE

1 Guideline title

Type 2 diabetes: management of type 2 diabetes in adults

1.1 Short title

Type 2 diabetes in adults

2 The remit

This is an update of Type 2 diabetes (NICE clinical guideline 66) and Type 2 diabetes: newer agents (NICE clinical guideline 87). See section 4.3.1 for details of which sections will be updated. We will also carry out an editorial review of all the recommendations to ensure that they comply with NICE's duties under equality legislation.

This is the scope for 1 of 4 NICE clinical guidelines being developed that address diabetes care. Included below is a summary of the content for each guideline and of the NICE steering committee.

Guideline 1 – Diabetes in children and young people (developed by the National Collaborating Centre for Women's and Children's Health)

This guideline will update Type 1 diabetes in children, young people (NICE clinical guideline 15). It will cover the diagnosis and management of type 1 and type 2 diabetes in children and young people (younger than 18 years). It will include: structured education programmes, behavioural interventions to improve adherence, glucose monitoring strategies, ketone monitoring, insulin regimens for type 1 diabetes and metformin monotherapy for type 2 diabetes.

Guideline 2 – Diabetes in pregnancy (developed by the National Collaborating Centre for Women's and Children's Health)

This guideline will update Diabetes in pregnancy (NICE clinical guideline 63). It will cover women of reproductive age who have pre existing diabetes or who develop diabetes during pregnancy and it will also cover their newborn babies. It will include: target glucose ranges in the preconception period and during pregnancy, glucose monitoring strategies during pregnancy, screening, diagnosis and treatment of gestational diabetes, and postnatal testing for type 2 diabetes.

Guideline 3 – Type 1 diabetes in adults (developed by the National Clinical Guideline Centre)

This guideline will update Type 1 diabetes in children, young people and adults (NICE clinical guideline 15). It will cover adults (18 years or older) with type 1 diabetes. It will include: tests to differentiate type 1 diabetes from type 2 diabetes, structured education programmes, clinical monitoring of glucose control, insulin regimens, ketone monitoring, dietary advice on carbohydrate counting and glycaemic index, and treatment and monitoring of specific complications.

Guideline 4 –Type 2 diabetes in adults (developed by the Internal Clinical Guidelines Programme, Centre for Clinical Practice, NICE)

This guideline will update Type 2 diabetes (NICE clinical guideline 66) and Type 2 diabetes: newer agents (NICE clinical guideline 87). It will cover adults (18 years or older) with type 2 diabetes. It will include: pharmacological management of blood glucose levels, target values for blood glucose

control, self-monitoring of blood glucose levels for blood glucose control, antithrombotic therapy and drug therapy for erectile dysfunction.

NICE steering committee

NICE has set up a steering committee to oversee the production of these clinical guidelines. The group, which includes the Guideline Development Groups' chairs, together with staff from the 3 guidance-producing centres and NICE, will identify and act on any gaps or overlaps across the different guidance topics to ensure that the final guidelines are complementary and consistent. It is intended that the guidance-producing centres will share systematic reviews and cross-refer to recommendations in the other guidelines where appropriate. This update is being undertaken as part of the guideline review cycle.

3 Clinical need for the guideline

3.1 Epidemiology

Type 2 diabetes is a condition of insufficient insulin production often exacerbated by insulin resistance, the primary treatment for which is weight loss and exercise. Pharmacological measures to increase insulin sensitivity or to increase insulin release can be added to lifestyle interventions, but insulin therapy may eventually be needed by the majority of people as their insulin secretion declines. Like type 1 diabetes, type 2 diabetes has a significant impact on lifestyle in the short term, and is associated with major long-term complications and reduced life expectancy. There are 2.9 million people known to be diagnosed with diabetes in the UK, with an average prevalence of approximately 4.45%. Currently, it is thought that more than 1 in 20 of the UK population has diagnosed or undiagnosed diabetes and incidence rates are increasing. Approximately 90% of adults currently diagnosed with diabetes have type 2 diabetes.

Type 2 diabetes mainly develops in people aged over 40 years, although it is usually diagnosed earlier in people of South Asian, Chinese, African or African Caribbean family origin. It can occur in all age groups and is increasingly being diagnosed in children. People who are overweight or obese, have inactive lifestyles or have a family history of diabetes are at risk. It is more prevalent in less-affluent populations and in people of South Asian, Chinese, African or African Caribbean family origin.

Type 2 diabetes can lead to acute metabolic disturbances such as hyperglycaemia (high blood glucose). If prolonged, hyperglycaemia can cause irreversible complications. These can include microvascular complications such as diabetic retinopathy (eye damage), nephropathy (kidney damage) and neuropathy (nerve damage), and macrovascular complications such as cardiovascular disease (for example, coronary heart disease, cerebrovascular disease and peripheral vascular disease). The UK Prospective Diabetes Study (UKPDS) found that approximately 50% of people newly diagnosed with type 2 diabetes already have complications. The study recognised the need for early diagnosis and screening for people in high-risk groups.

People receiving pharmacological therapy for type 2 diabetes may also be susceptible to hypoglycaemia (low blood glucose). Increasing age and longer duration of diabetes may be associated with an increased risk of hypoglycaemia. Hypoglycaemic episodes range from mild to severe and the most serious episodes can be life threatening.

It is estimated that approximately 10% of NHS expenditure goes on diabetes care. The presence of diabetic complications can lead to a 5-fold increase in a patient's NHS costs and people with diabetes can experience prolonged stays in hospital. Life-expectancy for people with type 2 diabetes is reduced by an average of 5 to 7 years, and the impact on quality of life can be considerable.

3.2 Current practice

Initial management of type 2 diabetes typically involves lifestyle interventions, although as the condition progresses glucose lowering therapies may be needed to control blood glucose levels. Many people start on metformin therapy, but some people may require alternative or additional glucose-lowering therapies. Many people may progress to insulin therapy as their insulin secretion declines. Regular monitoring of blood glucose levels can help people with diabetes to manage their risk of developing complications. The current NICE recommended target for blood glucose control in people with type 2 diabetes is haemoglobin A1c (HbA1c) of 6.5% (48 mmol/mol is now used in clinical practice). However, specific targets may be individualised to meet people's needs, taking into consideration their risk of hypoglycaemia, cardiovascular risk and other comorbidities.

Good management of blood pressure (including the use of angiotensin-converting enzyme [ACE] inhibitors, calcium-channel blockers and diuretics) and the management of blood lipid levels (including the use of statins and fibrates) can help to prevent or delay the onset of microvascular or macrovascular complications.

The 2011 review of NICE clinical guidelines 66 and 87 identified new evidence in a number of areas and recommended that the guidelines should be updated. In particular, new evidence was found relating to the pharmacological management of blood glucose. This includes newly licensed combinations, as well as safety concerns about some classes of glucose-lowering therapies. The effect of drugs coming off patent may also have an impact on health-economic issues. There are new members of the dipeptidyl peptidase 4 (DPP-4) inhibitor class of drugs and new indications for licensed class members. New evidence has also arisen relating to the use of aspirin in the primary prevention of cardiovascular disease.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, ‘Further information’).

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

1. Adults (aged 18 years and older) with type 2 diabetes.
2. Specific patient sub-groups for whom the management of type 2 diabetes may vary. These may include (but are not restricted to):
    a. adults aged 65 years and older
    b. people with renal impairment
    c. people in specific ethnic groups
    d. people in specific cardiovascular risk groups.

4.1.2 Groups that will not be covered

1. Children and young people with type 1 or type 2 diabetes (this will be addressed in a separate guideline).
2. Adults (aged 18 years and older) with type 1 diabetes (this will be addressed in a separate guideline).

3. Diabetes in pregnancy (this will be addressed in a separate guideline).

4.2 Healthcare setting

All settings in which NHS care is received or commissioned.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

4.3.2 Areas from the original guidelines that will be updated by an evidence review

1. Pharmacological management of blood glucose levels. The following blood glucose-lowering therapies will be examined as part of treatment strategies involving monotherapy, dual therapy and triple therapy [a]:

- DPP-4 inhibitors:
  - sitagliptin, vildagliptin, linagliptin and saxagliptin
- glucagon-like peptide-1 (GLP-1) receptor agonists:
  - exenatide (conventional formula and prolonged release), lixisenatide and liraglutide
- thiazolidinediones (peroxisome proliferator-activated receptor gamma [PPAR-γ] agonists):
  - pioglitazone
- sulfonylureas
- metformin
- insulin
- acarbose
- meglitinides.

2. Target values for blood glucose control:

- HbA1c
- fasting blood glucose
- post-prandial blood glucose.

3. Self monitoring of blood glucose levels (finger pricks). This will include:

- Targets
- Frequency of monitoring
- Timing
- Site of testing

4. Antithrombotic therapy:

- Clopidogrel and aspirin for the primary prevention of cardiovascular disease.

5. Drug therapy for erectile dysfunction:

- Phosphodiesterase 5 (PDE-5) inhibitors
- Testosterone therapy
- Alprostdil.

a The following drugs were not previously included in the original guidelines but will be covered in this update: DPP-4 inhibitors (linagliptin and saxagliptin); GLP-1 receptor agonist (lixisenatide).

4.3 Clinical issues that will not be covered

4.4 Areas from the original guidelines that will not be updated by an evidence review

1. Patient education (including structured education).
2. Dietary advice.
3. Management of depression.
4. Screening for diabetic retinopathy.
5. Pharmacological management of blood glucose levels:

- sodium glucose cotransporter 2 (SGLT-2) inhibitors. It is intended that these drugs will be covered by NICE technology appraisals guidance. The clinical guideline intends to use these drugs as comparators but will not make new recommendations on their use
- rosiglitazone (original recommendations removed following European Medicines Agency [EMA] safety warning, September 2010)
- alogliptin (full license not anticipated to be in time for inclusion within the guideline)

6. Blood pressure control (including target values and pharmacological management).

4.5 Areas from the original guidelines that will be removed

No areas from the original guidelines will be removed.

4.6 Areas not covered by the original guidelines or the update

1. Diagnosis of type 2 diabetes.
2. Primary prevention of type 2 diabetes.
3. Ketone testing of blood glucose and urine
4. The management of hypoglycaemia, unless this is as a consequence of pharmacological interventions for hyperglycaemia.
5. The diagnosis and management of diabetic retinopathy.
6. Peripheral arterial disease comprising peripheral vascular disease (PVD) and peripheral sensory neuropathy (PSN).
7. Surgical interventions: the use and effectiveness of bariatric surgery for the management of type 2 diabetes (this is covered in Obesity [NICE clinical guideline 43]).

The following NICE guidance will be cross-referred to

8. Identification of arterial risk, interventions to reduce risk (with the exception of aspirin) and blood pressure management:

- Hypertension. NICE clinical guideline 127 (2011).
- Lipid modification. NICE clinical guideline 67 (2007). An update of clinical guideline 67 is in progress.
- Statins for the prevention of cardiovascular events. NICE technology appraisal 94 (2006).

9. Insulin pumps:

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

10. Kidney disease:

- Chronic kidney disease. NICE clinical guideline 73 (2008). An update of clinical guideline 73 is in progress.

11. Diabetic foot problems:

- Diabetic foot problems - inpatient management. NICE clinical guideline 119 (2011).

- Type 2 diabetes - footcare. NICE clinical guideline 10 (2004).

12. Painful neuropathy:

- Neuropathic pain. NICE clinical guideline 96 (2010). An update of clinical guideline 96 is in progress.
- Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. NICE technology appraisal 159 (2008).

13. Monitoring and management of special situations including eating disorders, depression, or other psychological problems:

- Anxiety. NICE clinical guideline 113 (2011).
- Depression with a chronic physical health problem. NICE clinical guideline 91 (2009).
- Depression in adults (update). NICE clinical guideline 90 (2009).
- Nutrition support in adults. NICE clinical guideline 32 (2006).
- Eating disorders. NICE clinical guideline 9 (2004).

4.4 Main outcomes

1. Changes in blood glucose levels (including HbA1c).
2. Changes in weight or body mass index (BMI).
3. Frequency and severity of hypoglycaemic episodes.
4. Adverse events.
5. The development of microvascular and macrovascular complications.
6. Changes in lipid levels and blood pressure[b].
7. Mortality.
8. Quality of life.
9. Resource use and cost.

4.5 Review questions

4.5.1 Pharmacological management of blood glucose levels

- Whichpharmacological blood glucose-lowering therapies should be used as monotherapy to control blood glucose levels in people with type 2 diabetes?
- Which pharmacological blood glucose-lowering therapies should be used as part of dual therapy to control blood glucose levels in people with type 2 diabetes?
- Which pharmacological blood glucose-lowering therapies should be used as part of triple therapy to control blood glucose levels in people with type 2 diabetes?
- What are the long-term effects of pharmacological interventions to control blood glucose levels in people with type 2 diabetes, including adverse events and impact on development of microvascular and macrovascular complications?

4.5.2 Target values for glucose control

- What are the optimal target values for HbA1c, fasting blood glucose and post-prandial blood glucose in people with type 2 diabetes?

b Treatment strategies that have the primary aim of controlling blood pressure and/or lipid levels are excluded from consideration in this update (see 4.3.2 f and g) however, any effect that included treatments have on blood pressure and/or lipid levels is an outcome of interest.

4.5.13 Self monitoring of plasma glucose

- Should self monitoring be used to manage blood glucose levels in people with type 2 diabetes?

4.5.14 Antithrombotic therapy

- Should aspirin and/or clopidogrel be used for primary prevention of cardiovascular disease in people with type 2 diabetes?

4.5.15 Erectile dysfunction

- What pharmacological treatment should be used to manage erectile dysfunction in men with type 2 diabetes?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.7 Status

4.7.1 Scope

This is the final version of the scope.

4.7.2 Timing

The development of the guideline recommendations will begin in October 2012.

5 Related NICE guidance

Comment [s1]: Add hyperlinks

5.1 Published guidance

5.1.1 NICE guidance to be updated

Depending on the evidence, this guideline might update and replace parts of the following NICE guidance:

- Type 2 diabetes: newer agents. NICE clinical guideline 87 (2009).
- Type 2 diabetes. NICE clinical guideline 66 (2008).
- TA248 (exenatide prolonged-release) and TA203 (liraglutide).

5.1.2 NICE guidance to be incorporated

This guideline will incorporate the following NICE guidance subject to a technology appraisal review proposal agreement:

- Dapagliflozin in combination therapy for the treatment of type 2 diabetes (ID427)
- Canagliflozin for type 2 diabetes mellitus (ID554)

5.1.3 Other related NICE guidance

- Lower limb peripheral arterial disease. NICE clinical guideline 147 (2012).
- Preventing type 2 diabetes: risk identification and interventions for individuals at high risk. NICE public health guidance 38 (2012).
- Patient experience in adult NHS services. NICE clinical guideline 138 (2012).
- Hyperglycaemia in acute coronary syndromes. NICE clinical guideline 130 (2011).
- Ranibizumab for the treatment of diabetic macular oedema. NICE technology appraisal guidance 237 (2011).
- Preventing type 2 diabetes: population and community-level interventions in high-risk groups and the general population. NICE public health guidance 35 (2011).
- Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events. NICE technology appraisal guidance 210 (2010).
- Depression with a chronic physical health problem. NICE clinical guideline 91 (2009).
- Depression in adults. NICE clinical guideline 90 (2009).
- Medicines adherence. NICE clinical guideline 76 (2009).
- Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus. NICE technology appraisal guidance 151 (2008).
- Smoking cessation services. NICE public health guidance 10 (2008).
- Obesity. NICE clinical guideline 43 (2006).
- Nutrition support in adults. NICE clinical guideline 32 (2006).
- Four commonly used methods to increase physical activity. NICE public health guidance 2 (2006).
- Type 1 diabetes. NICE clinical guideline 15 (2004).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Fluocinolone acetonide intravitreal implant for the treatment of diabetic macular oedema. NICE technology appraisal guidance. Publication expected November 2012.
- Obesity – working with local communities. NICE public health guidance. Publication expected 2013.
- Type 1 diabetes (update). NICE clinical guideline. Publication expected 2014.
- Diabetes in children (update). NICE clinical guideline. Publication expected 2014.
- Diabetes in pregnancy. NICE clinical guideline. Publication expected 2014.
- Chronic kidney disease (update). NICE clinical guideline. Publication expected 2014.
- Lipid modification (update). NICE clinical guideline. Publication expected 2014.
- Buccal insulin for the management of type 1 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.
- Pegaptanib sodium for the treatment of diabetic macular oedema. NICE technology appraisal guidance. Publication date to be confirmed.
- Ranibizumab for the treatment of macular oedema caused by retinal vein occlusion. NICE technology appraisal guidance. Publication date to be confirmed.
- Canagliflozin for the treatment of type 2 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.
- Dapaglifozin for the treatment of type 2 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.

- Empagliflozin for type 2 diabetes. NICE technology appraisal guidance. Publication date to be confirmed.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual'.

Information on the progress of the guideline will also be available from the NICE website.

Part 2. Scope for clinical guideline 87

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SHORT CLINICAL GUIDELINE – SCOPE

1 Guideline title

Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes

1.1 Short title

Type 2 diabetes newer agents

2 Background

The Department of Health has asked the National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') to develop a short clinical guideline on 'newer agents for blood glucose control in type 2 diabetes' for use in the NHS in England and Wales. This will be a rapid update of the relevant section of the NICE clinical guideline 'Type 2 diabetes: the management of type 2 diabetes (update)'. The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

The Institute's clinical guidelines support the implementation of National Service Frameworks (NSFs) in those aspects of care for which a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisal guidance published by NICE after an NSF has been issued will have the effect of updating the Framework.

NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

3 Clinical need for the guideline

Type 2 diabetes is a chronic metabolic disorder caused by insulin insensitivity and a failure of pancreatic insulin and glucagon secretion to compensate for this. It can be associated with acute metabolic disturbances such as hyperglycaemia (high blood glucose). If prolonged, hyperglycaemia can cause microvascular and macrovascular damage. Good management of blood-glucose levels, blood pressure and lipid levels is known to delay or prevent the long-term complications of diabetes. Current practice is that treatment should aim to achieve a glycated haemoglobin (HbA1c) level of 6.5%, or 7.5% for those at risk of severe hypoglycaemia, although it is acknowledged that such targets may not be achieved in everyone.

The prevalence of diabetes is around 3.7% in England and 4.21% in Wales; diabetes affects more than 2.09 million people in England and Wales. More than 85% of these people have type 2 diabetes, and it is accepted that there are also many people who have undiagnosed type 2 diabetes. It has been estimated that diabetes may be responsible for at least 5% of

healthcare expenditure in the UK, and up to 10% of hospital budgets are used for the care of people with diabetes. Type 2 diabetes usually occurs in people older than 40; however, it can appear earlier in life, particularly in people of South Asian or African-Caribbean origin.

Although lifestyle interventions (diet and exercise) are the first-line treatments for the management of type 2 diabetes, in most cases the condition is progressive and people will usually need to take oral glucose-lowering drugs. Metformin is widely-used as first-line oral therapy, with sulphonylurea as an 'add on' second-line therapy if glycaemic control remains poor, but clinical practice varies according to patient attributes (such as body weight and insulin sensitivity). Current NICE guidance (NICE technology appraisal guidance 63) is that glitazones (thiazolidinediones) are not recommended as second-line therapy for most people. Because type 2 diabetes tends to progress, as a result of the continuing failure of insulin secretion, many patients eventually need to take insulin. Insulin therapy may be given in a number of different forms, for example intermediate-acting insulin (NPH insulin) or biphasic insulin (premix) or basal bolus regimens.

In recent years new drugs have been developed for blood glucose control. These include the long-acting insulin analogues (insulin glargine and insulin detemir), incretin mimetics (exenatide and liraglutide) and incretin enhancers (sitagliptin and vildagliptin). So far only insulin glargine has been the subject of NICE guidance (NICE technology appraisal guidance 53). There is an urgent need for guidance that determines the role of all of these agents and their place in the care pathway of blood glucose control for people with type 2 diabetes. The place of thiazolidinediones (rosiglitazone and pioglitazone) within this pathway also needs to be addressed, including their positioning relative to the newer agents, and there are recent safety concerns specifically in relation to rosiglitazone to be addressed regarding the risk of cardiovascular adverse events.

The NICE clinical guideline 'Type 2 diabetes: the management of type 2 diabetes (update)' is scheduled for publication in May 2008. It makes recommendations on the use of thiazolidinediones (rosiglitazone and pioglitazone), an incretin mimetic (exenatide) and a long-acting insulin analogue (insulin glargine). These recommendations will be reviewed and updated by this short guideline.

4 The guideline

The guideline development process is described in detail in four publications that are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development. 'Background and overview of the short guidelines programme' and 'The short guideline process – consultation document' describe short clinical guidelines and how they are developed.

This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

1. Adults (18 and older) diagnosed with type 2 diabetes.
2. Specific patient subgroups (for example, based on cardiovascular risk or ethnicity) for whom the impact of these agents might differ.

4.1.2 Groups that will not be covered

1. People with type 2 diabetes who are younger than 18 years.
2. Pregnant women with type 2 diabetes or gestational diabetes.

4.2 Healthcare setting

Primary and secondary care.

4.3 Clinical management

4.3.1 Areas covered by the guideline

1. The newer agents for the control of blood glucose in type 2 diabetes that are detailed in 4.3.1 e–n. The relevant comparators for these interventions are:
   - oral glucose-lowering medications (metformin or sulphonylurea) used alone or in combination
   - intermediate-acting, long-acting or biphasic (premix) insulins.
2. Comparison of the newer agents with each other, if relevant evidence is available.
3. Use of these newer agents and their positioning within the care pathway of glucose control in patients with type 2 diabetes.
4. Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

Incretin enhancers (DPP-4 inhibitors)

5. Sitagliptin (Januvia, Merck Sharp & Dohme). Sitagliptin has UK marketing authorisation for use in patients with type 2 diabetes mellitus as oral therapy to improve glycaemic control in combination with:
   - metformin if diet and exercise plus metformin do not provide adequate glycaemic control
   - a sulphonylurea, in patients with insufficient glycaemic control despite the maximum tolerated dose of a sulphonylurea and for whom metformin is inappropriate because of contraindications or intolerance
   - a sulphonylurea and metformin, in patients with insufficient glycaemic control
   - a thiazolidinedione, in patients with insufficient glycaemic control and for whom the use of a thiazolidinedione is appropriate.
6. Vildagliptin (Galvus, Novartis). Vildagliptin has UK marketing authorisation for use in the treatment of type 2 diabetes mellitus as dual oral therapy in combination with:
   - metformin, in patients with insufficient glycaemic control despite the maximum tolerated dose of monotherapy with metformin
   - a sulphonylurea, in patients with insufficient glycaemic control despite the maximum tolerated dose of a sulphonylurea and for whom metformin is inappropriate because of contraindications or intolerance
   - a thiazolidinedione, in patients with insufficient glycaemic control and for whom the use of a thiazolidinedione is appropriate.

Incretin mimetics (GLP-1 analogues)

Exenatide (Byetta, Eli Lilly and Company). Exenatide currently has UK marketing authorisation for the treatment of type 2 diabetes mellitus in combination with metformin

and/or sulphonylureas in people who have insufficient glycaemic control on the maximum tolerated doses of these oral therapies. It is administered as a subcutaneous injection.

Liraglutide (NN2211, Novo Nordisk). Liraglutide does not yet have UK marketing authorisation. It has been studied in phase III trials in patients with type 2 diabetes who have been treated with oral glucose-lowering medications (metformin and a sulphonylurea). These studies have examined the use of liraglutide as monotherapy and as combination with metformin, sulphonylureas, metformin and a sulphonylurea, and metformin and a thiazolidinedione. Liraglutide has also been studied in combination with a sulphonylurea, and in combination with a thiazolidinedione. Liraglutide will be considered according to its anticipated licensed indication. Guidance on this intervention will be issued only if it achieves UK marketing authorisation for use in type 2 diabetes.

Thiazolidinediones

Pioglitazone (Actos, Takeda). Pioglitazone is administered orally and has UK marketing authorisation for use:

- as monotherapy in people (particularly those who are overweight) who have insufficient glycaemic control from diet and exercise, and for whom metformin is inappropriate because of contraindications of intolerance
- as dual oral therapy in combination with metformin in people (particularly those who are overweight) with insufficient glycaemic control despite the maximum tolerated dose of monotherapy with metformin
- as dual oral therapy in combination with a sulphonylurea, only in people who show intolerance to metformin or for whom metformin is contraindicated, and who have insufficient glycaemic control despite the maximum tolerated dose of monotherapy with a sulphonylurea
- as triple therapy in combination with metformin and a sulphonylurea, in people (particularly those who are overweight) with insufficient glycaemic control despite dual oral therapy
- in combination with insulin in people with type 2 diabetes with insufficient glycaemic control on insulin for whom metformin is inappropriate because of contraindications or intolerance.

Pioglitazone/metformin combination (Competact, Takeda). This combination product is administered orally and is indicated for the treatment of type 2 diabetes, particularly in people who are overweight, and who are unable to achieve sufficient glycaemic control at the maximum tolerated dose of oral metformin alone.

Rosiglitazone (Avandia, GlaxoSmithKline UK). Rosiglitazone is indicated for the treatment of type 2 diabetes and has UK marketing authorisation for use:

- as oral monotherapy in people (particularly those who are overweight) who have insufficient glycaemic control from diet and exercise for whom metformin is inappropriate because of contraindications or intolerance
- as dual oral therapy in combination with metformin in people (particularly those who are overweight) with insufficient glycaemic control despite the maximum tolerated dose of monotherapy with metformin
- as dual oral therapy in combination with a sulphonylurea, only in people who show intolerance to metformin or for whom metformin is contraindicated, and who have insufficient glycaemic control despite the maximum tolerated dose of monotherapy with a sulphonylurea
- as triple therapy in combination with metformin and a sulphonylurea, in people (particularly those who are overweight) with insufficient glycaemic control despite dual oral therapy.

Rosiglitazone/metformin combination (Avandamet, GlaxoSmithKline UK). This combination has UK marketing authorisation for oral use in people for whom the maximum tolerated dose of oral metformin alone does not provide sufficient glycaemic control. It also has UK marketing authorisation for use as triple oral therapy with a sulphonylurea in people with insufficient glycaemic control despite dual oral therapy with the maximum tolerated dose of metformin and a sulphonylurea.

Long-acting recombinant human insulin analogues

Insulin detemir (Levemir, Novo Nordisk). Insulin detemir is indicated for the treatment of diabetes mellitus, including use with oral hypoglycaemia agents. It is administered via subcutaneous injection.

Insulin glargine (Lantus, Sanofi Aventis). Insulin glargine is indicated for the treatment of diabetes mellitus, including use with oral hypoglycaemia agents. It is administered via subcutaneous injection.

4.3.2 Areas not covered by the guideline

1. Diagnosis of type 2 diabetes.
2. Treatments other than the ones listed in 4.3.1 e–n.

4.4 Outcome measures

1. Efficacy and tolerability of the newer agents for blood glucose control, and their impact on the control of type 2 diabetes including:
   - changes in blood glucose control
   - changes in HbA1c levels
   - frequency and severity of hypoglycaemic episodes
   - changes in weight control and body mass index.
2. Impact of the newer agents for blood glucose control on the development of complications associated with type 2 diabetes:
   - microvascular – retinopathy, nephropathy
   - macrovascular – heart disease, stroke, peripheral vascular disease.
3. Any adverse events reported that are considered to be associated with the specified newer agents for blood glucose control.
4. Resource use.
5. Health-related quality of life.
6. Mortality.

4.5 Economic aspects

Costs will be considered from an NHS and Personal Social Services perspective.

4.6 Status

4.6.1 Scope

This is the final version of the scope.

4.6.12 Related NICE guidance

This short guideline will update the NICE standard clinical guideline 'Type 2 diabetes: the management of type 2 diabetes (update)', which will in turn update the following NICE guidance:

- Guidance on the use of long-acting insulin analogues for the treatment of diabetes – .insulin glargine. NICE technology appraisal guidance 53 (2002).
- Guidance on the use of glitazones for the treatment of type 2 diabetes. NICE technology appraisal guidance 63 (2003).

NICE is also developing the following related guidance:

- Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period. NICE clinical guideline. Publication expected March 2008.
- Continuous subcutaneous insulin for the treatment of diabetes (review). NICE technology appraisal guidance. Publication expected May 2008.

4.6.13 Guideline

The development of the guideline recommendations will begin in May 2008.

5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'Guideline development methods: information for national collaborating centres and guideline developers'
- 'Background and overview of the short guidelines programme'
- 'The short guideline process – consultation document'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesprocess). Information on the progress of the guideline will also be available from the website.

Part 3. Scope for clinical guideline 66

2 SCOPE

1 Guideline title

4 Type 2 diabetes: the management of Type 2 diabetes (update).

1.1 Short title

6 Type 2 diabetes (update).

2 Background

8 The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has
9 commissioned the National Collaborating Centre for Chronic Conditions to review
10 recent evidence on the management of Type 2 diabetes, and update the existing guidelines:
11 'Clinical guidelines for Type 2 diabetes: diabetic renal disease: prevention and early
12 management'; 'Diabetic retinopathy: early management and screening'; 'Management of
13 blood glucose'; 'Blood pressure management'; and 'Lipids management' (Royal College of
14 General Practitioners, 2002) for use in the NHS in England and Wales. The updated
15 guideline will provide recommendations for good practice that are based on the best
16 available evidence of clinical and cost effectiveness. This guideline will be relevant only to
17 people with Type 2 diabetes, as guidance on the management of Type 1 diabetes is
18 available from the NICE guideline: 'Type 1 diabetes in adults: National clinical guideline for
19 diagnosis and management in primary and secondary care' (2004), developed by the
20 National Collaborating Centre for Chronic Conditions.

21 The Institute's clinical guidelines will support the implementation of National Service
22 Frameworks (NSFs) in those aspects of care where a Framework has been published. The
23 statements in each NSF reflect the evidence that was used at the time the Framework was
24 prepared. The clinical guidelines and technology appraisals published by the Institute after
25 an NSF has been issued will have the effect of updating the Framework.

26 NICE clinical guidelines support the role of healthcare professionals in providing care in
27 partnership with patients, taking account of their individual needs and preferences, and
28 ensuring that patients (and their carers and families, where appropriate) can make informed
29 decisions about their care and treatment.

3 Clinical need for the guideline

31 Type 2 diabetes is a common and chronic disease with a high risk of a number of serious
32 complications. About 1.6 million people in England and Wales are currently diagnosed with
33 diabetes. Type 2 diabetes accounts for more than 85% of these cases and many more
34 people may have Type 2 diabetes that is as yet undiagnosed. It has been estimated that
35 diabetes may be responsible for at least 5% of healthcare expenditure in the UK and up to
36 10% of hospital budgets are used for the care of people with diabetes.

37 Good management of blood-glucose levels, blood pressure and lipid levels is known to
38 prevent or delay the long-term complications of diabetes such as renal (kidney) disease,
39 retinopathy (eye problems), cardiovascular events (for example, heart attack or stroke) and
40 limb amputation.

Early detection of complications to enable their secondary prevention is important, as is effective management of late complications when they occur.

4 The guideline

The guideline development process is described in detail in two publications which are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered:

People with diagnosed Type 2 diabetes.

4.1.2 Groups that will not be covered:

Pregnant women with problems related to Type 2 diabetes, or gestational diabetes. A separate guideline on diabetes in pregnancy is availabe (date of publication: March 2008).

4.2 Healthcare setting

The guideline will cover the care of Type 2 diabetes in primary, secondary or tertiary care sectors, but will exclude specialist tertiary procedures in areas such as vascular surgery, renal medicine, cardiology and ophthalmology.

This is an NHS guideline; although it will also be relevant to practice within residential and nursing homes (care homes), social services and the voluntary sector, it will not make recommendations about services exclusive to these sectors.

4.3 Clinical management

The guideline will include recommendations on the following areas:

1. Clinical and self-monitoring (including target values) for:
    a. lipid levels
    b. blood pressure
    c. glucose levels.
2. Pharmacological treatments including those for:
    a. reducing blood pressure
    b. correcting abnormal blood-fat profile (dyslipidaemia)
    c. controlling blood glucose
    d. preventing vascular disease.

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only where clearly supported by evidence, use outside a licensed

indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

3. Non-pharmacological management, including:
   a. diet
   b. self-management education and empowerment, including use of care plans and emergency self-management.
4. The guideline will address the early detection, ongoing management (but not in tertiary care) or referral to specialist services, for the following complications:
   a. retinopathy including maculopathy
   b. renal disease
   c. aspects of autonomic neuropathy and painful neuropathy (including erectile dysfunction)
   d. depression.
5. The guideline will use the internationally accepted diagnostic criteria for Type 2 diabetes. The evidence base on diagnosis will not be reviewed as part of the guideline development.
6. The guideline will be sensitive to the specific issues affecting, and the clinical needs of, different ethnic groups.
7. Complementary therapies may be considered, if they are already in use in the NHS and there is evidence to support their effectiveness.
8. The guideline will not cover:
   a. prevention and management of foot problems (there is already updated guidance in this area: 'Type 2 diabetes: prevention and management of foot problems'. NICE clinical guideline no. 10)
   b. primary prevention of Type 2 diabetes or screening
   c. those problems which do not arise primarily from diabetes in particular patient groups who may also have diabetes.

4.4 Status

4.4.1 Scope

This is the final scope.

1. The guideline will incorporate the following NICE technology appraisal:
   a. inhaled insulin for the treatment of diabetes (Types 1 and 2) (date of publication: December 2006).
2. The guideline will update the following NICE technology appraisals, but only in relation to Type 2 diabetes:
   a. Guidance on the use of long-acting insulin analogues for the treatment of diabetes – insulin glargine. NICE technology appraisal guidance no. 53 (2002)
3. Guidance on the use of patient-education models for diabetes. NICE technology appraisal guidance no. 60 (2003)
   a. Guidance on the use of glitazones for the treatment of Type 2 diabetes. NICE technology appraisal guidance no. 63 (2003).
4. Related NICE public health guidance:
   a. Physical activity guidance for the Highways Agency, Local Authorities, primary care, pharmacists, health visitors and community nurses, schools, workplaces, the leisure and fitness industry and sports clubs. Public health programme guidance (date of publication: September 2007)

b. Smoking cessation services, including the use of pharmacotherapies, in primary care, pharmacies, local authorities and workplaces, with particular reference to manual working groups, pregnant smokers and hard to reach communities. Public health programme guidance (date of publication: February 2008).

5. Related NICE clinical guidelines:
   a. Cardiovascular risk assessment: the modification of blood lipids for the primary and secondary prevention of cardiovascular disease (expected date of publication:May 2008)
   b. Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period (date of publication: March 2008)
   c. Hypertension: management of hypertension in adults in primary care (partial update of NICE (partial update of CG18) NICE clinical guideline no. 34 (2006)
   d. Obesity: the prevention, identification, assessment and management of overweight and obesity in adults and children (date of publication: December 2006)
   e. Type 1 diabetes: diagnosis and management of Type 1 diabetes in children, young people and adults NICE clinical guideline no. 15 (2004, expected review date: July 2008)
   f. Type 2 diabetes: prevention and management of foot problems. NICE clinical guideline no. 10 (2004).

4.12 Development of recommendations

The development of the guideline recommendations began in June 2006.

5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesprocess). Information on the progress of the guideline will also be available from the website.