



## module 220

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**THIS IS** the two hundred and twentieth module in the *Pharmacy Magazine* Continuing Professional Development Programme, which looks at current thinking on the treatment of type 2 diabetes.

Continuing professional development (CPD) is a statutory requirement for pharmacists. Journal-based educational programmes are an important means of keeping up-to-date with clinical and professional developments and can form a significant element of your CPD. Completion of this module will contribute to the nine pieces of CPD that must be recorded a year, as stipulated by the GPhC.

Before reading this module, test your existing understanding of the topic by completing the pre-test at [www.pharmacymag.co.uk](http://www.pharmacymag.co.uk). Then, after studying the module in the magazine, work through the six online learning scenarios and post-test.

Record your learning and how you applied it in your practice using the CPD report form available online or on pviii of this module.

### Self-assess your learning needs:

- What are the main factors influencing insulin initiation in type 2 diabetes?
- Do I understand the place in therapy of the newer hypoglycaemic agents?

## for this module

### GOAL

To update pharmacists on the treatment of type 2 diabetes.

### OBJECTIVES:

After completing this module you should be able to:

- List the five factors that can reduce potential future complications from diabetes
- Help patients to identify any side-effects they may be experiencing from medicines for type 2 diabetes
- Discuss lifestyle interventions that patients can make to best manage their long-term health.

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This module is suitable for use by pharmacists as part of their continuing professional development. After reading this module, complete the learning scenarios and post-test at [www.pharmacymag.co.uk](http://www.pharmacymag.co.uk) and include in your CPD portfolio. Previous modules in the Pharmacy Magazine CPD Programme are available to download from the website.

## Type 2 diabetes

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### Introduction

Type 2 diabetes is a major public health issue that can result in many complications including:

- Premature death
- Cardiovascular disease – 75 per cent of people with diabetes will die of CVD<sup>1</sup>
- Renal failure – 20 per cent of people with diabetes will develop renal failure
- Blindness – diabetic retinopathy is the main cause of blindness in the UK<sup>2</sup>
- Amputation and other effects of neuropathy and autonomic dysfunction such as erectile dysfunction, diarrhoea, urinary retention and postural hypotension.

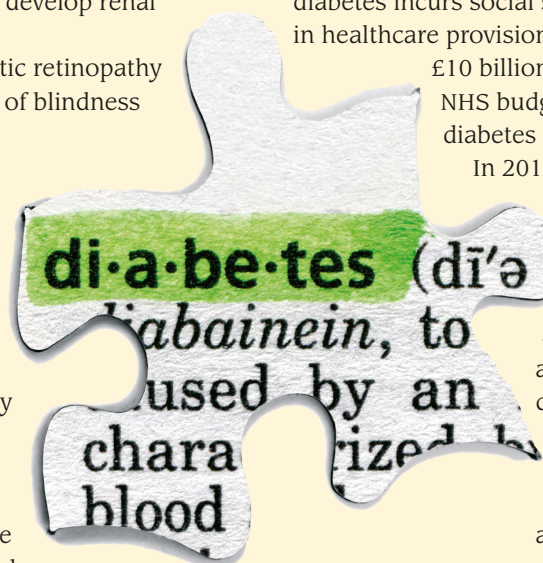
Three million people have been diagnosed with diabetes in the UK<sup>3</sup>, equating to around 6 per cent of men and 5 per cent of women in England (90 per cent with type 2 diabetes). It is estimated that a further 850,000 people in the UK have yet to be diagnosed<sup>4</sup>.

Prevalence rises sharply with age with an increase from 11.1 per cent in men aged 55–64 years to 15.9 per cent in those 75+ and in women from 8.0 per cent to 13.2 per cent for the same age groups in England<sup>5</sup>.

Diabetes is a very costly condition, both personally (one in 20 people with diabetes incurs social services costs<sup>6</sup>) and in healthcare provision. Currently around £10 billion – 10 per cent of the NHS budget – is spent on diabetes each year<sup>7</sup>.

In 2010 37.7m prescription items for treating diabetes were dispensed in primary care across England at a net ingredient cost of nearly £713m<sup>8</sup>. Type 2 diabetes usually develops slowly over years and may be picked up by accident

during a medical examination for another reason. However, with public awareness campaigns and increasing internet access, people may recognise the symptoms and present initially in the pharmacy.



Acute hyperglycaemia is not often seen in type 2 diabetes but is characterised by weight loss, polyuria, polydipsia, nocturia and acute illness or infection such urinary tract or vaginal infection. Hyperglycaemia can also be drug-induced following treatment historically with corticosteroids, thiazide diuretics and beta-blockers, and more recently reported with protease inhibitors and atypical antipsychotics.

Owing to the progressive nature of the disease, more patients with type 2 diabetes are moving onto insulin to control their condition.

## Diagnosis

When symptoms suggest diabetes, further investigations are required to confirm a firm diagnosis to World Health Organization (WHO) standards. These are:

- An HbA1c of 48mmol/mol (6.5 per cent) is recommended as the cut-off point for diagnosing diabetes. A value less than this does not exclude diabetes diagnosed using glucose tests. (HbA1c is not recommended for diagnosis in e.g. children, suspected type 1 diabetes, short-term symptoms less than two months, acutely ill, taking medicines that may increase blood glucose)
- A fasting plasma glucose in the diabetic range (7.0mmol/L or greater and repeated if the patient is asymptomatic), or
- An oral glucose tolerance test in the diabetic range (two-hour plasma glucose level equal to 11.1mmol/L or greater).

Random plasma glucose in the diabetic range or glycosuria on urine dipstick testing are only screening methods and cannot be used for diagnosis.

Evidence now suggests that complications begin much earlier than originally thought, with prolonged blood glucose levels over 7mmol/L being harmful. Diagnosis must be secure as legal consequences can result once the condition is confirmed. It may affect life insurance and also the ability to carry out certain occupations (e.g. heavy goods vehicle driver, airline pilot, armed forces).

## Implications of a diagnosis

It is estimated that a person newly diagnosed with diabetes needs to absorb between 40

and 50 pieces of information concerning monitoring and managing their condition. This information needs to be communicated clearly and should not conflict with information provided by other healthcare professionals, otherwise confusion will result. Education should also include carers and/or relatives as they may cook for the person or need to treat an episode of hypoglycaemia.

It is important to ensure that people are aware that there is no such thing as 'mild' diabetes and that type 2 diabetes is a serious, progressive disease. HbA1c will rise over time no matter how hard they try to control their blood glucose. Patients should agree with their healthcare



**Figure 1: Annual diabetes review**

### Laboratory tests and investigations

- Blood glucose control (HbA1c)
- Renal function
- Blood lipids

### Physical examinations

- Body mass index (BMI)
- Legs and feet should be examined to check skin, circulation and nerve supply. If necessary this may be carried out by a podiatrist
- Blood pressure
- Eyes should be examined at least annually using a digital camera, where the pupils are dilated and a photograph is taken to check for retinopathy. This is normally carried out by an optometrist/ophthalmologist
- If using insulin, injection sites should be examined

### Lifestyle issues

- General wellbeing; how the person is coping with diabetes at home, work, school or college
- Current treatment
- Diabetes control, including any home blood glucose monitoring results and incidence of hypoglycaemia
- Problems the person may be having
- Smoking
- Alcohol consumption
- Stress/depression
- Sexual problems (e.g. erectile dysfunction)
- Healthy eating

professional a documented, personalised HbA1c target, usually between 48mmol/mol and 58mmol/mol (6.5 per cent and 7.5 per cent), and receive an ongoing review of treatment to minimise hypoglycaemia<sup>9</sup>.

Many people will have complications at the time of presentation and it is important to prevent these progressing. However health professionals need to be aware that treatment should involve balancing alleviation of acute

symptoms, preventing long-term complications and avoiding the precipitation of hypoglycaemic attacks resulting from medication. This is why adherence with all prescribed medication (not just hypoglycaemics) is vitally important and supporting this is an important role for all pharmacy staff.

All people with diabetes should have an annual review and need to know what this will include. Figure 1 shows the Diabetes UK recommendations for an annual review.

## Managing diabetes

The cornerstones of diabetes management are education, dietary advice, alcohol reduction and smoking cessation (where necessary), exercise, weight management and promoting self-management of the disease.

## Education and lifestyle

The first priority must be encouraging people to make lifestyle changes. This includes stopping smoking (the single biggest modifiable risk factor for CVD) and losing weight by modifying their diet and increasing their physical activity. Type 2 diabetes is often thought of as being managed by diet, oral treatment then insulin in that order but, in fact, correct dietary modification underpins treatment at all times alongside medication.

Initially people should be tried on dietary changes alone for three months before medication is commenced (unless the initial blood glucose is very high). Ideally people with diabetes should see a dietician soon after diagnosis but, given the increasing numbers of people diagnosed, this may be a problem. Waiting lists can be lengthy and other healthcare professionals (including community pharmacy staff) are increasingly seen as good sources of dietary advice.

In the case of type 2 diabetes, a normal healthy diet should be followed. Diabetes UK recommends 'Ten steps to healthy eating':

1. Eat three regular meals a day
2. At each meal include starchy carbohydrate foods
3. Cut down on the fat eaten, especially saturated fats linked to CVD
4. Eat more fruit and vegetables.
5. Include more beans and lentils



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 **Figure 2: Effect of lifestyle interventions on blood pressure**

Intervention	Average reduction in systolic and diastolic blood pressure	% with 10mmHg reduction in systolic blood pressure (<1 year)	Other comments (from NICE guideline 2006)
Diet (healthy, low-calorie)	5-6mmHg	Around 40%	Average weight changes were from 2-9kg
Exercise (aerobic 30-60 minutes, 3-5 times a week)	2-3mmHg	Around 30%	
Relaxation therapy (structured)	3-4mmHg	Around 33%	Cost in primary care unknown. Availability?
Multiple interventions	4-5mmHg	Around 25%	Education alone unlikely to be effective
Alcohol reduction (structured)	3-4mmHg	Around 30%	< 21 units/week men, 14 units/week women → raised BP, poorer health
Salt reduction (< 6g/day)	2-3mmHg	Around 25%	Effects diminish over time (2-3 years)
<b>Other: caffeine (≥ 5 cups of coffee a day) increases BP by around 2/1mmHg; smoking (per se) has no effect on BP; mineral supplements – no robust evidence</b>			

6. Aim for at least two portions of oily fish a week
7. Limit sugar and sugary foods
8. Reduce salt to 6g or less a day as higher amounts can increase blood pressure
9. Drink alcohol in moderation
10. Don't be tempted by diabetic foods or drinks.

### Blood pressure

Controlling blood pressure (BP) is an important modifiable risk factor for preventing both macro- and microvascular events. Figure 2 gives an indication of the BP effects that are likely to be obtained by lifestyle interventions.

Hypertension increases the risk of nephropathy and CVD, and ambulatory blood pressure monitoring should be carried out in all patients with a BP > 140/90mmHg to confirm the diagnosis<sup>11</sup>. The first-line blood pressure lowering therapy for people under 55 years should be a once-daily generic angiotensin converting enzyme inhibitor (ACEI) or low-cost angiotensin receptor blocker (ARB).

People aged over 55 years and black people of African or Caribbean family origin of any age should be prescribed a calcium channel blocker (CCB). If this is not suitable, for example because of oedema or intolerance, or if there is evidence of heart failure or a high risk of heart failure, a thiazide-like diuretic, such as chlorthalidone or indapamide, should be used<sup>11</sup>.

ACEIs and ARBs should not be used in women of child-bearing age. For further treatment of hypertension when the first-line agent fails to control BP adequately, refer to NICE CG127 Hypertension – August 2011<sup>11</sup>.

Clinical trials such as UKPDS have shown that adherence to hypotensive medication is as important as to oral hypoglycaemics in preventing future macrovascular complications. In people with diabetes a target BP of 140/80mmHg is often applied.

### Statins

Treatment of dyslipidaemia is a priority after lifestyle advice and controlling BP as it is a risk factor for CVD and macrovascular disease and may be aggravated by insulin resistance.

A statin should automatically be prescribed for secondary prevention of CVD and, in the case of primary prevention in people with type 2 diabetes, statin therapy is recommended as part of the management strategy for the primary prevention of CVD for adults over 40 years with type 2 diabetes who have a 20 per cent or greater 10-year risk of developing CVD<sup>12</sup>.

For people under 40 years where CV risk is poor (e.g. metabolic syndrome, conventional risk factors, microalbuminuria, at-risk ethnic group, strong family history of premature CVD), a statin should be prescribed<sup>13</sup>.

The effect of treatment should be assessed no longer than three months after starting the statin and then annually thereafter (as part of the annual review). Statins should not normally be used in women of child-bearing age.

### Blood glucose control

Blood glucose lowering therapies are traditionally used in a step-wise approach based on NICE guidance. This is often dependent on HbA1c results and further treatments are added in when current treatment fails to adequately control glycosylated haemoglobin (HbA1c).

Glucagon-like peptide-1 (GLP-1) mimetics, dipeptidylpeptidase-4 (DPP-4) inhibitors and sodium-glucose co-transporter 2 (SGLT2) inhibitors now offer scope for earlier alternative management, although the ACCORD study showed that "as compared with standard therapy, the use of intensive therapy to target normal glycosylated haemoglobin levels for 3.5 years increased mortality and did not significantly reduce major cardiovascular events".<sup>14</sup>

This suggests that targeting blood glucose alone and not other CVD risk factors (such as BP and lipids) can have a detrimental effect in high-risk patients with diabetes.

The most appropriate first-line treatment in type 2 diabetes is metformin.

An individualised approach to blood glucose control is recommended because it requires a careful balance between treating symptoms (such as increased urination frequency) and preventing complications without causing hypoglycaemia or other adverse effects.

Dose escalation should be the first option if blood glucose remains uncontrolled. However, if the patient still has symptoms and his/her blood glucose remains extremely high, the most appropriate choice of second blood glucose-lowering agent would be a sulfonylurea.

This should ideally be a generic drug with a short duration of action, such as gliclazide, in order to reduce the risk of hypoglycaemia.

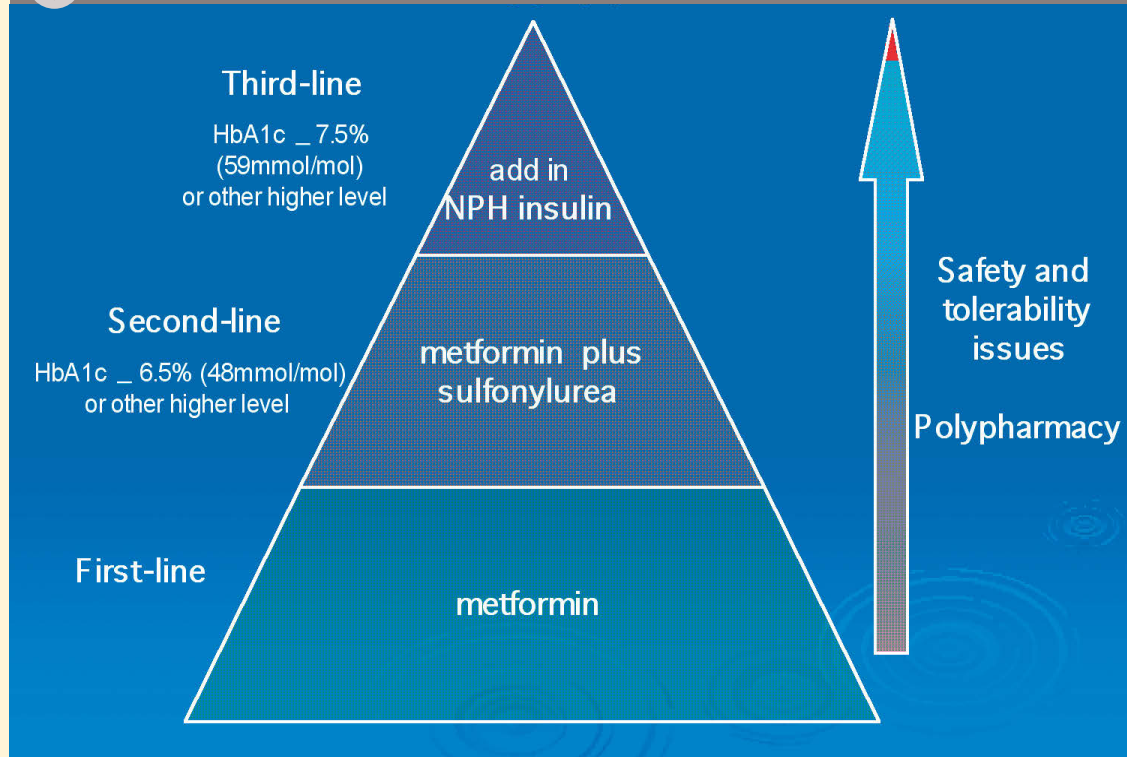
NICE guidance also simplifies the preferred drug treatment for blood glucose control with metformin first-line, metformin plus sulfonylurea second-line and adding in NPH insulin third-line<sup>13</sup> (see Figure 3). While newer



**'The most appropriate first-line treatment for patients with type 2 diabetes is metformin'**



Figure 3: Preferred drug treatment for blood glucose control



agents are indicated in specific situations related to patient characteristics, a systematic review found that newer, more expensive oral hypoglycaemic agents offer no advantages over metformin and sulfonylureas<sup>15</sup>. In addition, the evidence of benefit for newer drugs on patient-orientated, clinical outcome data, such as effects on CV endpoints, is very limited<sup>16</sup>.

HbA1c should be measured every two to six months until it is stable on unchanging therapy, and then every six months after that. If patients are unsure about what the HbA1c measurement means, the diagram in Figure 4 may help to illustrate what it means in terms of the amount of glucose in the blood.

Within the last three years UK laboratories have changed the way in which HbA1c results are reported. The International Federation of Clinical Chemistry put forward a new reference measurement method after discussion with diabetes groups worldwide. This makes comparing HbA1c results from different laboratories and from research trials throughout the world much easier. The measurement is in millimoles per mol (mmol/mol) instead of percentage (per cent). See Figure 5.

### Drug treatment

#### Biguanides

Metformin should be started at a low dose and stepped up gradually over weeks to minimise the risk of gastrointestinal (GI) side-effects to the maximum of 2g/day in divided doses.

Sustained-release metformin tablets are more expensive but may result in fewer GI adverse effects. Diarrhoea is usually transient, while other GI side-effects, such as anorexia, nausea and vomiting, are commoner at higher doses. Attempting to maximise the metformin

dose is always worth trying before adding in other agents.

Metformin is the only drug of this class available in the UK and probably acts by inhibiting gluconeogenesis (hepatic production of glucose), increasing its peripheral utilisation and reducing intestinal glucose absorption. It does not induce weight gain, so should always be used in obese or normal weight patients. It also has a mildly favourable effect on lipid profile. Lactic acidosis occurs in one in 10,000 treated cases and is extremely rare if the contraindications are observed. These include:

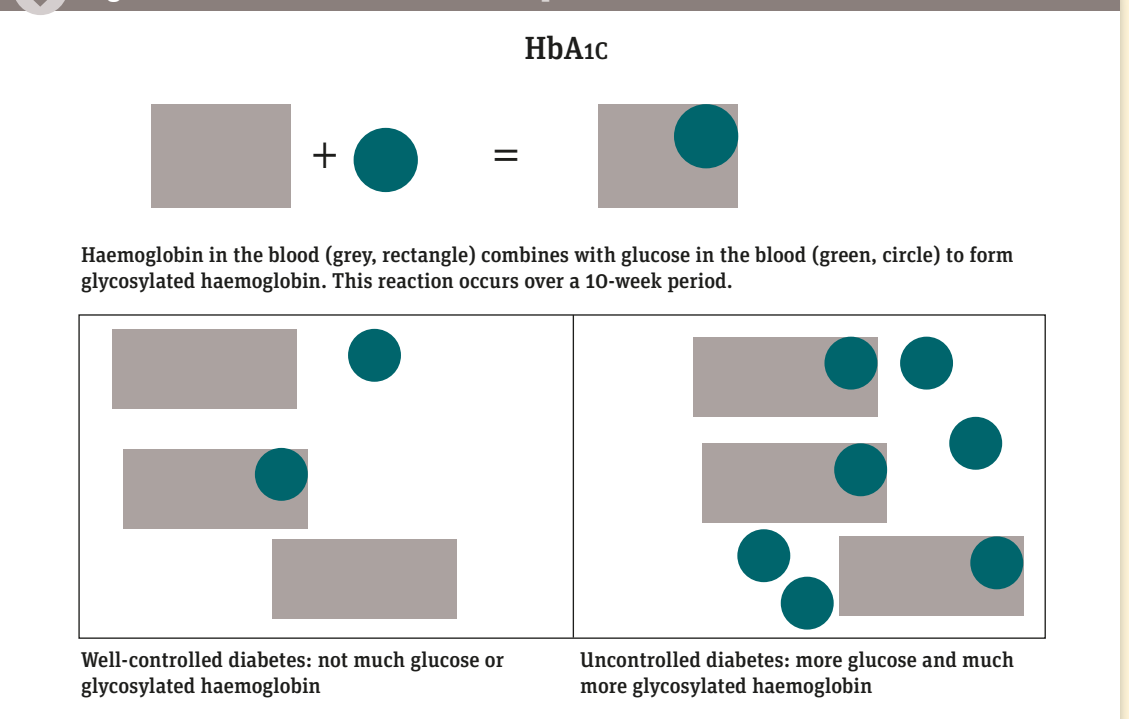
- Renal disease or renal dysfunction
- Congestive heart failure
- Age >80 years
- Hepatic disease
- Hypoxic conditions (COPD, MI).

#### Sulfonylureas

A sulfonylurea is a first-line alternative in certain circumstances (e.g. metformin contraindicated, patient not overweight or rapid control of hyperglycaemia needed).

Sulfonylureas act on the beta cells of the pancreas, stimulating insulin release, and become less effective over time as the beta cells fail. Significant weight gain is an undesirable side-effect and agents with long half-lives can lead to insidious development of hypoglycaemia, while those metabolised or excreted via the kidney have the potential to produce hypoglycaemia in patients with end-stage renal failure. People should be reminded to eat while taking sulfonylureas to reduce the likelihood of hypoglycaemia, which can also be precipitated by excess alcohol intake.

Figure 4: The HbA1c measurement explained



**Figure 5: HbA1c in per cent and mmol/mol**

HbA1c per cent	HbA1c mmol/mol
4.0	20
5.0	31
6.0	42
6.5	48
7.0	53
7.5	59
8.0	65
9.0	74
10.0	86

### Other hypoglycaemics

NICE guidance suggests that the next step in blood glucose control should be the introduction of insulin therapy. However, in practice, one or more of the newer oral hypoglycaemics is often tried first, although data on major clinical endpoints such as CV mortality is limited.

A systematic review of 216 studies<sup>17</sup> and two earlier systematic reviews of oral hypoglycaemics to January 2006 concluded that the older agents (metformin, sulfonylureas) have similar or superior effects to newer, more expensive agents (glitazones, alpha-glucosidase inhibitors, meglitinide analogues) on glycaemic control, lipids and other intermediate endpoints (body weight, BP, adverse effects). The newer hypoglycaemics currently available are described below.

### Thiazolidinediones ('glitazones')

Pioglitazone (the only glitazone available in the UK) enhances glucose uptake in liver and muscle, reducing both blood levels and insulin resistance. It has additive effects on blood glucose combined with sulfonylureas and/or metformin. The main side-effects are fluid retention (inducing oedema and CHF, which can be serious and sometimes fatal), anaemia and significant weight gain, although a favourable effect on lipids may be seen.

Other safety issues with pioglitazone are an increased risk of fractures and bladder cancer. The former has been seen in women, not men, and the risk of fracture should be considered in

patients, especially women, treated with pioglitazone, with an approximately doubled relative risk of fractures.

The Medicines and Healthcare products Regulatory Agency (MHRA) has issued advice on CV safety<sup>18</sup> and risk of bladder cancer<sup>19</sup> with pioglitazone and this has now been underpinned by a 'Pioglitazone prescriber's guide: patient selection and risk minimisation', demanded by the European Medicines Agency (EMA), which includes a prescribing algorithm for its use as a second or third-line agent in the treatment of type 2 diabetes. NICE guidance<sup>13</sup> recommends how pioglitazone should be used in combination and, importantly, that treatment should only be continued if there is a beneficial metabolic response, defined as a reduction in HbA1c of at least 0.5 percentage points at six months.

### Meglitinide analogues (prandial glucose regulators)

Repaglinide and nateglinide are short-acting drugs that stimulate insulin secretion from beta cells by a different mechanism than sulfonylureas but resulting in a quicker but shorter lasting effect. They only work in people with remaining beta cell function and can be used in combination with metformin. They have lower but not absent risks of hypoglycaemia and weight gain compared with sulfonylureas.

As they allow more flexible dosing around meals they may have a place in the treatment of people who work shifts or have erratic meal times for any reason. Unlike with sulfonylureas, doses can be omitted if meals are missed but must be taken with or not longer than 30 minutes before meals.

### Alpha-glucosidase inhibitor

Acarbose inhibits intestinal alpha-glucosidase, slowing down the absorption of starchy foods from the intestine and the rise in blood glucose after meals. It tends to be used when other oral drugs are unsuitable as, although it improves glycaemic control, it has been shown to be less effective than sulfonylureas and has no outcome data. GI adverse effects, such as flatulence and diarrhoea, can be a problem and, because of its mode of action, glucose must be used to treat hypoglycaemia in patients taking the drug.

### Glucagon-like peptide 1 (GLP-1) analogues

Glucagon-like peptide 1 (GLP-1) is secreted from the intestinal mucosa in response to food and inhibits glucagon secretion, decreases gut motility and increases satiety, so having a blood glucose lowering effect in type 2 diabetes.

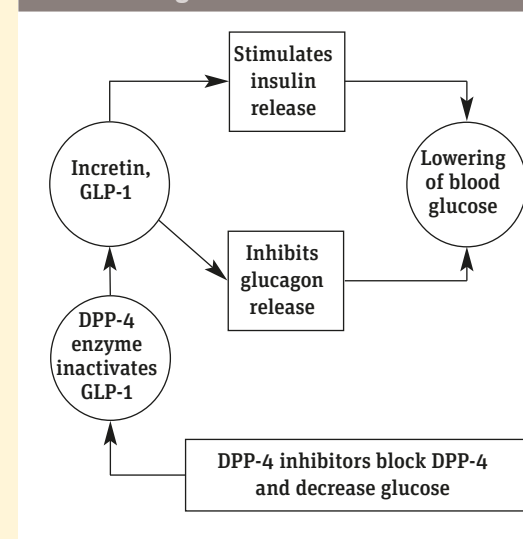
GLP-1 is rapidly metabolised, so analogues (exenatide, liraglutide and lixisenatide) are needed to replicate its effect and have to be administered by subcutaneous injection.

Exenatide is used twice daily (or once weekly as Bydureon), and liraglutide and lixisenatide are used once daily. Exenatide and lixisenatide should be given before food, not after a meal and, as they slow gastric emptying, should be used one hour before potentially interacting drugs such as antibiotics or gastro-resistant preparations.

Main adverse effects with GLP-1 analogues are gastrointestinal in nature (e.g. nausea). Patient-oriented outcome (micro- and macrovascular disease) and long-term safety data is unavailable (although observational data suggest exenatide's CV safety may be favourable) and safety concerns, such as severe pancreatitis and renal failure, have been noted.

As with glitazones, NICE recommends that exenatide or liraglutide should only be continued if there is a beneficial metabolic response – being in this case a reduction of at least one percentage point in HbA1c and

**Figure 6: Mode of action of GLP-1 analogues and DPP-4 inhibitors**



### Reflection exercise 1

Are all your pharmacy staff aware of the symptoms of hypo- and hyperglycaemia and how to treat them? As a number of new medicines to treat type 2 diabetes have been introduced recently, review your knowledge of their common adverse effects.



a weight loss of at least 3 per cent of initial body weight at six months. It is important to note that NICE does not recommend use of the liraglutide 1.8mg injection.

### Dipeptidyl peptidase-4 inhibitors ('gliptins')

Dipeptidyl peptidase-4 (DPP-4) inactivates GLP-1. Inhibiting this enzyme using one of the orally active agents (linagliptin, saxagliptin, sitagliptin and vildagliptin) can raise GLP-1 activity again, having similar beneficial effects on blood glucose but by a different route to the incretin mimetics.

The mode of action of GLP-1 analogues and DPP-4 inhibitors is shown in Figure 6 (previous page). Gliptins show similar reductions in HbA1c to the glitazones but again there is no patient-oriented outcome or long-term safety data available. Potential safety concerns include skin rashes, pancreatitis<sup>20</sup>, acute renal failure and liver dysfunction. As with GLP-1 analogues and glitazones, NICE says gliptins should only be continued if there is a beneficial metabolic response, defined as a reduction in HbA1c of at least 0.5 percentage points at six months.

### Sodium-glucose co-transporter 2 (SGLT2) inhibitor

Dapagliflozin is a reversible inhibitor of SGLT2 in the renal proximal convoluted tubule, reducing glucose reabsorption and increasing its excretion. SGLT2 proteins are responsible for 90 per cent of the glucose that is reabsorbed. This should reduce blood glucose without increasing the likelihood of weight gain as long as a balanced diet is followed and regular exercise is undertaken.

Side-effects (other than hypoglycaemia) include genital and urinary tract infection, dysuria, polyuria, thirst and constipation, which might be expected as a result of its mode of action. Again, its effectiveness would be expected to depend on the patient's renal function and the SPC recommends monitoring renal function before treatment commences and at least once a year after that (or more often in moderate renal impairment).

As with all newer hypoglycaemics patient-oriented outcome data is currently unavailable. NICE<sup>21</sup> recommends dapagliflozin as a possible

treatment for some people with type 2 diabetes with:

- Metformin, as long as dapagliflozin is used in the same manner as NICE recommends for DPP-4 inhibitors
- Insulin (with or without other antidiabetic drugs)
- Metformin and a sulfonylurea, only as part of a clinical trial.

Canagliflozin, the second drug in this class, was approved in the EC in November 2013 for treatment of type 2 diabetes in adults in order to improve glycaemic control. However at the time of writing a UK launch date is unavailable.

### Insulin

The main factors influencing insulin initiation should be compliance with NICE guidance and HbA1c results, together with a reduction of secondary risk factors, but the following would be definite indications to change a patient with type 2 diabetes to insulin therapy:

- Chronic kidney disease
- Pre-conceptual management of diabetes
- Pregnancy
- Acute symptomatic hyperglycaemia.

A National Patient Safety Agency (NPSA) alert<sup>22</sup> highlighted several issues that can lead to errors in insulin prescribing, dispensing and administration, such as inappropriate abbreviations (ml instead of units), wrong injection device, wrong insulin and wrong dose. This has led to the development of an 'insulin passport'. All patients prescribed insulin should

be supplied with a passport to carry at all times and show to any healthcare professionals treating them. One effect of this alert that pharmacy staff should see is that insulin must always be prescribed by brand.

### Types of insulin

- Short-acting – soluble and analogue
- Intermediate-acting
- Long-acting
- Biphasic.

A quick reference to the species, administration format and action profile of insulins available in the UK is the MIMS Insulin Preparations table.

Basic information about the types of insulins is as follows:

#### Short-acting human insulin – soluble

Examples: Actrapid, Humulin S.

These insulins are often used pre-meals (20-30 minutes before) combined with intermediate or long-acting background insulin.

#### Rapid-acting analogue

Examples: Apidra, Humalog, NovoRapid.

Due to their rapid onset of action these insulins can be injected immediately before meals or up to 15 minutes after. They may cause less hypoglycaemia due to a shorter duration of action and may be more effective in reducing post-prandial hyperglycaemia than human insulin. Like soluble insulin they are used before meals with intermediate or long-acting background insulin.

#### Medium intermediate-acting

Examples: Insulatard, Humulin I.

Can be used daily/twice daily on their own or in combination with analogue or short-acting insulin

#### Long-acting analogue

Examples: Lantus, Levemir, Tresiba.

Duration of action requires a once (or in some cases twice) daily dose. These insulins exert less variation in absorption than intermediate-acting insulins and exhibit a 'peak-less' profile, possibly producing less nocturnal hypoglycaemia.

### Pre-mixed insulin

#### Pre-mixed short-acting and intermediate insulin

Examples: Humulin M3, Insuman comb 15/25/50. Needs to be administered 30 minutes before meals (usually twice a day).

### Managing insulin risks

- Beware of confusion between similar product names, devices and presentations
- Long-acting analogue insulins (e.g. Lantus) are clear in appearance unlike older intermediate and long-acting insulins (e.g. Insulatard), which are cloudy. This may be a problem for patients who identify their insulins visually
- The use of abbreviations such as 'U' or 'IU' for units when prescribing a dose. When abbreviations are added to the intended dose, the dose may be misread (e.g. 10U is read as 100). The dose must always be written in 'units'
- Percentage dosage errors are more dangerous than the total dose administered. For example giving four extra units to a patient prescribed four units (100 per cent increase) is more dangerous than giving four extra units to a patient prescribed 50 units (8 per cent increase)
- Absorption of insulin is affected by temperature; therefore insulin in use must remain out of the fridge
- In the case of mixes these must be re-suspended by gentle mixing before administration, as not re-suspending alters the mix
- Patients should be advised against injecting into the same area all the time or using the arms. Repeated injection without rotation of the site can lead to lipodystrophy leading to poor control (hypo- and hyperglycaemia), trauma to injection site, infection and varying degrees of insulin absorption due to the different sites, with an increased risk of IM injection if using the arms (which should be avoided).

### Reflection exercise 2

Make a list of all the information that will need to be provided to a person prescribed insulin with respect to ensuring:

- The correct dose is administered
- They know how to monitor their blood glucose
- They know how to dispose of used sharps
- The steps to take when suffering from intercurrent illness (e.g. flu, nausea and vomiting)



All patients prescribed insulin should carry an 'insulin passport'

### Pre-mixed analogue rapid insulin combined with intermediate insulin

Examples: Novomix 30, Humalog Mix 25/50. Administered immediately prior to a meal or shortly after a meal (usually twice or possibly three times a day). Pre-mixed insulins can suit people who have a regular lifestyle pattern.

### Human insulins vs analogue insulins

Insulin analogues are artificial derivatives of the natural hormone and are claimed to offer a more predictable profile than genetically modified human insulins. They may have advantages concerning dose flexibility and less risk of hypo- and hyperglycaemia, but this isn't matched by superior outcome data compared with standard human insulin and they are more costly.

### Insulin regimens

Regimens should be individualised depending on various factors (e.g. patient choice and

cognitive abilities, age, meal times, diet, exercise, shift work, target HbA1c, risk or experience of hypoglycaemia and previous control if already on insulin). In practice, the regimens normally employed in patients are either:

- Once-daily intermediate/long-acting insulin, which may be combined with an oral hypoglycaemic. Metformin may help minimise weight gain commonly associated with insulin therapy and may necessitate less insulin to be used. The gliptins, pioglitazone and sulfonylureas such as glimepiride and gliclazide MR are also licensed for use in combination with insulin
- Twice-daily biphasic insulin (injected before breakfast and before evening meal).

### Insulin strengths

For many years insulin has only been available as a 100 unit strength (100 unit/ml) in the UK but the recently introduced insulin degludec (Tresiba) is also available in a 200 unit strength.

Care is therefore needed to minimise the risk of prescribing and dispensing errors and also in providing appropriate training for patients.

In the case of insulin mixes the numerical figure represents the percentage of short-acting insulin in the mix (e.g. Humulin M3 contains 30 per cent short-acting insulin and Humalog Mix 25 contains 25 per cent short-acting insulin).

### Insulin administration devices

Insulins are supplied in vials, pre-filled pens and cartridges for refilling pens – the latter two forms are now the mostly widely prescribed.

All pen devices now have a 3ml capacity and cartridges will only fit the same manufacturer's pens, with the exception of Wockhardt insulins, which are compatible with the Autopen Classic.

Although specific needles are designed for specific pen devices, they are in practice interchangeable. The recommended needle length is now 4mm to prevent inadvertent intramuscular injection and hence unpredictable insulin effects. A new needle is required for each injection, not when the cartridge or pen is empty.

Some pens may be easier to use if patients have dexterity or sight problems. As pens come in different colours it is useful to have two different coloured pens if the patient is using two different types of insulin. A spare pen is needed in case the one in use breaks.

The total dose to be administered needs to be borne in mind as the maximum single dose that can be dialled using any pen is 80 units. So if the dose to be administered is greater than this maximum, the ease of redialling a further dose with the pen *in situ* in the skin is an important factor.

Lancets and needles must be disposed of safely by using a sharps disposal bin or a B-D Safe Clip (for used needles only).

- *References are available from the editor on request*



Pharmacy Magazine's CPD modules are available on Cegedim Rx's PMR systems, Pharmacy Manager and Nexphase. Just click on the 'Professional Information & Articles' button within Pharmacy KnowledgeBase and search by therapy area. Please call the Cegedim Rx helpdesk on 0844 630 2002 for further information.



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Use this form to record your learning and action points from this module on type 2 diabetes and include it in your CPD portfolio and record online at [www.uptodate.org.uk](http://www.uptodate.org.uk)

TYPE 2 DIABETES

# assessment questions

**1. What type of insulin is Levemir?**

- a. Short-acting
- b. Intermediate-acting
- c. Long-acting
- d. Biphasic mixture

- b. Intensive management of HbA1c to reach a normal target level decreases cardiovascular mortality

**2. Onset 5 minutes, peak 1 hour, duration 3-5 hours is the time profile of which type of insulin?**

- a. Humalog Mix 25
- b. Lantus
- c. Humulin S
- d. NovoRapid

- c. Metformin is the first-line hypoglycaemic in obese people only
- d. Newer oral hypoglycaemics offer advantages over metformin and sulfonylureas in terms of cardiovascular endpoints

**3. Which statement is TRUE concerning Humulin M3 insulin?**

- a. It is usually administered once daily
- b. It contains 30 per cent intermediate-acting insulin
- c. It has a duration of action of approximately 22 hours
- d. It contains a short-acting analogue insulin

**6. An HbA1c measurement of 66mmol/mol is approximately equal in percentage terms to:**

- a. 6 per cent
- b. 7 per cent
- c. 8 per cent
- d. 9 per cent

**4. Which statement is TRUE concerning the GLP-1 (or incretin) analogues?**

- a. They inhibit the enzyme that inactivates GLP-1
- b. Their action results in an increase in glucagon secretion
- c. They have an effect on glucose reabsorption in the collecting duct of the kidney
- d. They may result in weight loss

**7. Which is NOT a major safety factor relating to the use of pioglitazone?**

- a. Bladder cancer
- b. Pancreatitis
- c. Heart failure
- d. Fractures in post-menopausal women

**5. In relation to preventing future complications, which statement is TRUE?**

- a. Adherence with oral hypoglycaemics and

**8. Which statement about insulin is FALSE?**

- a. Long-acting analogue insulins are clear in appearance
- b. Biphasic mix insulins should be gently resuspended before administration
- c. Glimepiride is licensed to be used with insulin
- d. Insulin should be administered into the arms, buttocks, stomach or thighs

Activity completed. (Describe what you did to increase your learning. Be specific) *(ACT)*

Date:

Time taken to complete activity:

What did I learn that was new in terms of developing my skills, knowledge and behaviours? Have my learning objectives been met? *(EVALUATE)*

How have I put this into practice? (Give an example of how you applied your learning) Why did it benefit my practice? (How did your learning affect outcomes?) *(EVALUATE)*

Do I need to learn anything else in this area? (List your learning action points. How do you intend to meet these action points?) *(REFLECT & PLAN)*

\* If as a result of completing your evaluation you have identified another new learning objective, start a new cycle. This will enable you to start at Reflect and then go on to Plan, Act and Evaluate. This form can be photocopied to avoid having to cut this page out of the module. Complete the learning scenarios at [www.pharmacymag.co.uk](http://www.pharmacymag.co.uk)

**ENTER YOUR ANSWERS HERE** Please mark your answers on the sheet below by placing a cross in the box next to the correct answer. Only mark one box for each question. Once you have completed the answer sheet in ink, return it to the address below together with your payment of £3.75. Clear photocopies are acceptable. **You may need to consult other information sources to answer the questions.**

- |    |    |                          |    |    |                          |    |    |                          |    |    |                          |    |    |                          |    |    |                          |    |    |                          |    |    |                          |
|----|----|--------------------------|----|----|--------------------------|----|----|--------------------------|----|----|--------------------------|----|----|--------------------------|----|----|--------------------------|----|----|--------------------------|----|----|--------------------------|
| 1. | a. | <input type="checkbox"/> | 2. | a. | <input type="checkbox"/> | 3. | a. | <input type="checkbox"/> | 4. | a. | <input type="checkbox"/> | 5. | a. | <input type="checkbox"/> | 6. | a. | <input type="checkbox"/> | 7. | a. | <input type="checkbox"/> | 8. | a. | <input type="checkbox"/> |
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Name (Mr, Mrs, Ms) \_\_\_\_\_

Business/home address \_\_\_\_\_

Town \_\_\_\_\_ Postcode \_\_\_\_\_ Tel \_\_\_\_\_ GPhC/PSNI Reg no.

I confirm the form submitted is my own work (signature) \_\_\_\_\_

Please charge my card the sum of £3.75 Name on card \_\_\_\_\_  Visa  Mastercard  Switch/Maestro

Card No. \_\_\_\_\_ Start date \_\_\_\_\_ Expiry date \_\_\_\_\_

Date \_\_\_\_\_ Switch/Maestro Issue Number \_\_\_\_\_

**Processing of answers**  
Completed answer sheets should be sent to Precision Marketing Group, Precision House, Bury Road, Beyton, Bury St Edmunds IP30 9PP (tel: 01284 718918; fax: 01284 718920; email: [cpd@precisionmarketinggroup.co.uk](mailto:cpd@precisionmarketinggroup.co.uk)), together with credit/debit card/cheque details to cover administration costs. This assessment will be marked and you will be notified of your result and sent a copy of the correct answers. The assessors' decision is final and **no correspondence** will be entered into.