Cannock Chase Clinical Commissioning Group
South East Staffordshire and Seisdon Peninsula Clinical Commissioning Group
Stafford and Surrounds Clinical Commissioning Group
East Staffordshire Clinical Commissioning Group

Diabetes Prescribing Guidelines for the Glycaemia management of Adults with Type 2 Diabetes

South Staffordshire Formulary Working Group approved this document on:
South Staffordshire Area Prescribing Group approved this document on:

Electronic copies can be obtained from the net. Formulary website: http://www.southstaffordshirejointformulary.nhs.uk/

Acknowledgments:

This document is adapted from Dudley Diabetes Management Guidelines for adults with Type 2 Diabetes and West Suffolk Type 2 diabetes adult treatment pathway. Acknowledgement to: Dudley Diabetes Clinical Advisory Team.
1. INTRODUCTION

1.1 General notes

The following information is to support prescribers regarding the management of glycaemic control in Type 2 Diabetes, refer to BNF or summary of Product Characteristics for further information on contraindications, precautions, adverse effects and interactions. The drug prices are correct at the time of publishing but please consult the current drug tariff, MIMs or Chemist and druggist for up to date information.

Patients exempt from this guideline:

- Hypoglycaemia requiring medical attention (some information in drug safety card Appendix 8)
- Hospital attendance for uncontrolled diabetes
- New onset of diabetes-related complication (some information on page 8)
- CKD stages 4-5

The patients above may need specialist input either by referral to secondary care consultant, primary or secondary care diabetes specialist nurse, GP with special interest in diabetes or use of another guideline to manage their condition.

If after following the algorithm the agreed individualised target is not achieved (or where HbA1c remains >75mmol/mol, >9%):

- Refer for specialist input by referral to secondary care consultant, primary or secondary care diabetes specialist nurse or GP with special interest in diabetes as per local CCG pathway.

Rescue therapy at any phase of treatment

If an adult with type 2 diabetes is symptomatically hyperglycaemic, consider insulin or a sulfonylurea, and review treatment when blood glucose control has been achieved.  

1.2 Glycaemic control

Glycaemic Range – A personal target HbA1c should be agreed with each patient and it is important that this is realistic. For patients managed with a single drug not associated with hypoglycaemia (and not having frequent hypoglycaemia) aim for HbA1c 48 mmol/mol (6.5%). If on a drug associated with hypoglycaemia aim for 53mmol/mol (7%), e.g. sulphonylurea (NICE NG28 1.6.7). Ideal Fasting glucose range is 4-7mmol/l.

In adults with type 2 diabetes, measure HbA1c levels at:

- 3–6-monthly intervals (tailored to individual needs), until the HbA1c is stable on unchanging therapy
- 6-monthly intervals once the HbA1c level and blood glucose lowering therapy are stable.

Involves adults with type 2 diabetes in decisions about their individual HbA1c target. Encourage them to achieve the target and maintain it unless any resulting adverse effects (including hypoglycaemia), or their efforts to achieve their target, impair their quality of life. For further information see (appendix 1)

Take particular care with those:

- Who are unlikely to achieve longer-term risk-reduction benefits, for example, people with a reduced life expectancy.
- For whom tight blood glucose control poses a high risk of the consequences of hypoglycaemia, for example, people who are at risk of falling, people who have impaired awareness of
hypoglycaemia, and people who drive or operate machinery as part of their job.

- For whom intensive management would not be appropriate, for example, people with significant comorbidities.

<table>
<thead>
<tr>
<th>Health status</th>
<th>Hba1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>&lt;7.5</td>
</tr>
<tr>
<td>Rationale: reasonable life expectancy</td>
<td></td>
</tr>
<tr>
<td>Intermediate health</td>
<td>&lt;8</td>
</tr>
<tr>
<td>- Several co-morbidities</td>
<td></td>
</tr>
<tr>
<td>- Limited functional ability</td>
<td></td>
</tr>
<tr>
<td>- Mild to moderate cognitive impairment</td>
<td>high treatment burden (polypharmacy), vulnerable to hypoglycaemia and falls</td>
</tr>
<tr>
<td>Poor health</td>
<td>&lt;9</td>
</tr>
<tr>
<td>- End stage chronic disease</td>
<td></td>
</tr>
<tr>
<td>- In long-term care/limited functional ability</td>
<td></td>
</tr>
<tr>
<td>- Moderate to severe cognitive impairment</td>
<td>Rationale: limited life expectancy. benefits of treatment uncertain</td>
</tr>
</tbody>
</table>


Once glycaemic control is achieved, a 6-month review is appropriate. If patient achieves lower than target Hba1c with no hypoglycaemia this should be maintained but be aware there are other possible causes of this such as decline in renal function and rapid weight loss.

Choice of drug agent
The choice of drug agents should be assessed both by following the guidelines and basing choices on the individual requirements of the patient. The patient needs to be involved in this discussion and the patient decision aid (NICE, 2015) is a useful tool to mutually agree the best therapy between the clinician and the patient (See Appendix 2).

1.3 Lifestyle measures, blood pressure, antiplatelet therapy and lipid management

Hypertension treatment, cardiovascular prevention and lifestyle measures are recognized to be important in diabetes care. As such we have briefly summarized some of the main points related to these areas. For more information on lifestyle advice, see the relevant NICE guidelines on: preventing excess weight gain, weight management, obesity, physical activity, smoking: brief interventions and referrals, stop smoking services, smoking: harm reduction.

Lifestyle measures from NICE NG28 guidelines (2016)

Diet: Provide individualised and ongoing nutritional advice from a healthcare professional with specific expertise and competencies in nutrition

- Emphasise advice on healthy balanced eating that is applicable to the general population
- Integrate dietary advice with a personalised diabetes management plan
- Discourage the use of foods marketed specifically for people with 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.

For adults with type 2 diabetes that are overweight, set an initial body weight loss target of 5–10%. Remember 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.
**Blood pressure management**

Measure blood pressure at least annually in an adult with type 2 diabetes without previously diagnosed hypertension or renal disease. Offer and reinforce preventive lifestyle advice.

- Repeat blood pressure measurements within:
  - 1 month if blood pressure is higher than 150/90 mmHg
  - 2 months if blood pressure is higher than 140/80 mmHg
  - 2 months if blood pressure is higher than 130/80 mmHg and there is kidney, eye or cerebrovascular damage
  - More than 180/100 seek specialist diabetic team advice urgently

Add medication if lifestyle advice fails to reduce blood pressure to target of 140/80 mmHg for patients with an absence of complications, or 130/80 mmHg for those with kidney, eye or cerebrovascular disease. Continue to monitor every 1-2 months until blood pressure consistently below target.

For those already on hypertensive treatment when diabetes is diagnosed make changes to treatment only if uncontrolled or if there are microvascular or metabolic complications.

**Antihypertensive drug treatment- First line options**

- First-line antihypertensive drug treatment should be a once daily, generic angiotensin converting enzyme (ACE) inhibitor. Exceptions to this are people of African or Caribbean family origin, or women for whom there is a possibility of becoming pregnant.
- The first-line antihypertensive drug treatment for a person of African or Caribbean family origin should be an ACE inhibitor plus either a diuretic or a generic calcium channel blocker.
- A calcium-channel blocker should be the first line antihypertensive drug treatment for a woman for whom, after an informed discussion, it is agreed there is a possibility of her becoming pregnant.
- 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.
- Do not combine an ACE inhibitor with an angiotensin II receptor antagonist to treat hypertension.

**Antihypertensive drug treatment- second line options if blood pressure not reduced to individualised treatment**

- Add a calcium channel blocker or a diuretic (usually a thiazide or thiazide related diuretic). Add the other drug (that is, the calcium channel blocker or diuretic) if the target is not reached with dual therapy.
- If the person’s blood pressure is not reduced to the individually agreed target with triple therapy, add an alpha blocker, a beta blocker or a potassium sparing diuretic (the last with caution if the person is already taking an ACE inhibitor or an angiotensin II receptor antagonist). [2009]
- Monitor the blood pressure of a person who has attained and consistently remained at his or her blood pressure target every 4–6 months. Check for possible adverse effects of antihypertensive drug treatment – including the risks from unnecessarily low blood pressure.

**Antiplatelet therapy**

- Do not offer antiplatelet therapy (aspirin or clopidogrel) for adults with T2DM without cardiovascular disease
- For guidance on the primary and secondary prevention of cardiovascular disease in adults with
Consider statin treatment for the primary prevention of CVD in all adults with type 1 diabetes. Offer statin treatment for the primary prevention of CVD to adults with type 1 diabetes who:

- are older than 40 years or
- have had diabetes for more than 10 years or
- have established nephropathy or
- have other CVD risk factors.

Primary prevention for people with type 2 diabetes only offer after estimating the level of risk using the QRISK2 assessment tool.

Offer atorvastatin 20 mg for the primary prevention of CVD to people with type 2 diabetes who have a 10% or greater 10-year risk of developing CVD.

1.4 Complications of diabetes

- **Gastroparesis**
  Think about a diagnosis of gastroparesis in adults with T2DM with erratic blood glucose control or unexplained gastric bloating or vomiting, taking into account possible alternative diagnoses.

  There is not strong evidence for antiemetic use but domperidone has the most evidence if a drug is considered necessarily, though a risk benefit assessment will be needed with the cardiac risks, metoclopramide may be also be considered. Both should be short term use only. If it is suspected but the diagnosis is in doubt or there is persistent or severe vomiting refer to specialist services.

- **Diabetic foot infections**

  See the NICE guideline on diabetic foot problems, NG19. Available at: https://www.nice.org.uk/guidance/ng19/chapter/1-Recommendations

- **Painful diabetic neuropathy**

  See the NICE guideline on neuropathic pain in adults, CG173 Available at: https://www.nice.org.uk/guidance/cg173/chapter/1-Recommendations

- **Diabetic kidney disease**

  See the NICE guideline on chronic kidney disease in adults, CG182 https://www.nice.org.uk/guidance/cg182/chapter/1-Recommendations

- **Erectile dysfunction**

  Consider a phosphodiesterase-5 inhibitor to treat problematic erectile dysfunction in men with T2DM, initially choosing the drug with the lowest acquisition cost and taking into account any contraindications

1.5 Pregnancy-preconception care for diabetic patients and gestational diabetes
Monitoring blood glucose and ketones in the preconception period for diabetic patients
- Offer monthly HbA1c levels, a blood glucose meter and if intensification of blood glucose lowering treatment is needed advise to increase frequency of monitoring to include fasting levels and a mix of pre and post meal levels.
- Also provide a ketone meter and strips to patients with Type 1 diabetes. Advise to test if feeling unwell.

Gestational diabetes
- Gestational Diabetes is induced by changes in carbohydrate metabolism and insulin sensitivity during pregnancy and it is usually asymptomatic and develops in 2nd trimester. The incidence of gestational diabetes varies from 2 – 5%
  This is associated with an increased risk of perinatal mortality and an increased risk of obesity and diabetes in the child.

  Use the 2-hour 75 g oral glucose tolerance test (OGTT) to test for gestational diabetes in women with risk factors 24–28 weeks.

Diagnose gestational diabetes if the woman has either:

- a fasting plasma glucose level of 5.6 mmol/litre or above or
- a 2-hour plasma glucose level of 7.8 mmol/litre or above

Offer women with a diagnosis of gestational diabetes a review with the joint diabetes and antenatal clinic within 1 week.
## 2. Drug treatments
### 2.1 Comparison of drug agents - Detailed

<table>
<thead>
<tr>
<th>Formulary agents</th>
<th>Metformin</th>
<th>Sulphonylurea (SU)</th>
<th>DPP4 inhibitors</th>
<th>Glitazones</th>
<th>SGLT2 (ending flozin)</th>
<th>GLP-1 Mimetic</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metformin</strong></td>
<td>Metformin</td>
<td>Gliclazide (not the MR)</td>
<td>Alogliptan lowest cost, others are sitagliptin and linagliptin</td>
<td>pioglitazone</td>
<td>dapagliflozin and canagliflozin, empagliflozin</td>
<td>Byetta twice daily or Bydureon weekly</td>
<td>See individual preparations on formulary</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td>High</td>
<td>High</td>
<td>Intermediate</td>
<td>High</td>
<td>Intermediate</td>
<td>High</td>
<td>Highest</td>
</tr>
<tr>
<td><strong>Hypo risk</strong></td>
<td>Low</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Highest</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>Neutral/loss</td>
<td>Gain (1.5-2kg approx.)</td>
<td>neutral</td>
<td>Gain (4-5kg approx.)</td>
<td>Loss (approx. 2kg)</td>
<td>Loss (1-3kg approx.)</td>
<td>Gain (4-5kg)</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>Nausea/ diarrhoea</td>
<td>Hypoglycaemia)</td>
<td>GI, pancreatitis (rare)</td>
<td>Oedema, CV, bone fracture, bladder cancer</td>
<td>GU infections, dehydration, canagliflozin only: increased lower limb amputation (mainly of toe) (MHRA 2016)</td>
<td>Pancreatitis GI</td>
<td>hypoglycaemia</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>15% of patients intolerant</td>
<td>Hypo risk: Evidence suggests accounts for 33% of admissions to A&amp;E. Also 1 year all-cause mortality risk in frail elderly (28%)</td>
<td>Sustained Hba1c levels only up to 2 years (from current trial data). Note recent MHRA guidance with relation to heart failure</td>
<td>Long list of cautions and contraindications see section summary</td>
<td>Avoid if crcl&lt;60ml/min/1.73m² in volume depleted; avoid in combination with loop diuretics; avoid in patients over 75 years old. Not got all the CV or long term safety data for all agents yet.</td>
<td>Only for those that meet the NICE criteria (see algorithm)</td>
<td>Discontinue if does not meet targets set in NICE criteria (see algorithm)</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>Low</td>
<td>Low</td>
<td>Medium</td>
<td>Low</td>
<td>Medium</td>
<td>High</td>
<td>Variable-High</td>
</tr>
</tbody>
</table>

1. MHRA drug safety update DKA risk – Test for ketones in symptomatic even if glucose levels near normal(April 2016)
2. Avoid if crcl<60ml/min/1.73m² in volume depleted
3. Long list of cautions and contraindications see section summary
4. Pancreatitis GI
5. hypoglycaemia

Type 2 diabetes prescribing guideline - Version 1.0
February 2017 Review date: February 2019
Adapted from West Suffolk Type 2 diabetes adult treatment pathway.

2.1.1 Classication of efficacy is an estimated improvement in Hb1ac; Highest >2% drop, High efficacy 1-2% drop, Intermediate up to 1% drop

2.1.2 Cost criteria per month at the usual dose: Low <£10, Medium approx. £40, High >£50

2.1.3 Pharmacological treatment of raised blood glucose in Type 2 Diabetes summary

<table>
<thead>
<tr>
<th>Healthy eating, weight control, increased physical activity + diabetes education</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agree individualised HbA1c targets based on patient, complications and co-morbidities</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Monotherapy</th>
<th><strong>Combinations depending on priorities</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>High</td>
</tr>
<tr>
<td>Hypo risk</td>
<td>Low</td>
</tr>
<tr>
<td>Weight</td>
<td>Neutral/Loss</td>
</tr>
<tr>
<td>Side effects</td>
<td>GI/lact acidosis</td>
</tr>
<tr>
<td>Cost</td>
<td>Low</td>
</tr>
</tbody>
</table>

Target failure or HbA1c ≥9% after maximum tolerated Metformin

<table>
<thead>
<tr>
<th>Dual Therapy</th>
<th>SU</th>
<th>TZD</th>
<th>DPP-4i</th>
<th>SGLT-2i</th>
<th>GLP-1 RA</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>High</td>
<td>High</td>
<td>Moderate</td>
<td>Moderate</td>
<td>High</td>
<td>Highest</td>
</tr>
<tr>
<td>Hypo risk</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Weight</td>
<td>Gain</td>
<td>Gain</td>
<td>Neutral</td>
<td>Loss</td>
<td>Loss</td>
<td>Gain</td>
</tr>
<tr>
<td>Side effects</td>
<td>Hypoglycaemia</td>
<td>Oedema, CCF, ↑BP</td>
<td>Rare</td>
<td>GU, D'hydration</td>
<td>GI</td>
<td>Hypoglycaemia</td>
</tr>
<tr>
<td>Cost</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>High</td>
<td>Variable</td>
</tr>
</tbody>
</table>

Target failure or HbA1c ≥9% after dual therapy

<table>
<thead>
<tr>
<th>Triple Therapy</th>
<th>Metformin+SU+</th>
<th>Metformin+TZD+</th>
<th>Metformin+DPP-4i+</th>
<th>Metformin+SGLT-2i+</th>
<th>Metformin+GLP 1-RA+</th>
<th>Metformin+Insulin+</th>
</tr>
</thead>
<tbody>
<tr>
<td>TZD or SU or</td>
<td>DPP-4i or</td>
<td>SGLT-2i or</td>
<td>GLP-1 RA or</td>
<td>Insulin</td>
<td>Insulin</td>
<td>Insulin</td>
</tr>
<tr>
<td>DPP-4i or</td>
<td>SGLT-2i or</td>
<td>Insulin</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>SGLT-2i or</td>
<td>Insulin</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>GLP-1 RA or</td>
<td>Insulin</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
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</tbody>
</table>

Uncontrolled hyperglycaemia ≥ 20 mmol/l or HbA1c ≥ 10%

| Combination Therapy | Basal insulin + mealtime insulin or GLP-1 RA or | Twice daily premixed insulin | Maintain Metformin |

Key: TZD = Pioglitazone, DPP4 =gliptins (Formulary=aloglipin,sitaglitpin, linagliptin), GLP1 = (exenatide, liraglutide, dulaglutide), SGLT2 flozins (dapagliflozin, empagliflozin and canagliflozin)
2.2 Individual drug summaries

For all drugs please refer to most up-to-date BNF and guidance from the MHRA for prescribing guidance.

2.2.1 Metformin

DAILY COST £0.21 (standard release tablet), £0.38 (MR tablet), £9.31 (liquid)

Place in therapy: First line for all patients where tolerated.

Indications/Benefits
- First-line choice of treatment for the vast majority of patients
- Consider in all patients with diabetes with residual functioning islet cells
- May reduce cardiovascular events in patients
- Can aid weight loss

Cautions and Contraindications
- Stop Metformin if the eGFR <30m/minute/1.73m² (NICE NG28 1.6.22)
- Review Metformin dose and prescribe with caution in those at risk of a sudden deterioration in kidney function, i.e. 2eGFR falling to <45ml/minute/1.73m² (NICE NG28 1.6.22)
- If the person has mild to moderate liver dysfunction or cardiac impairment, discuss benefits of Metformin so due consideration can be given to its cardiovascular-protective effects before any decision is made to reduce the dose.

Side Effects
- Diarrhoea occurs in up to 20%, is dose dependent and may resolve with dose reduction
- If after appropriate dose titration of Metformin, the patient experiences gastrointestinal side effects, Metformin MR should be considered as a suitable alternative prior to switching to another Oral Hypoglycaemic Agent (NICE NG28 1.6.21)

Metformin intolerance
- Ensure that patient is truly intolerant of metformin as metformin is the most established agent with proven efficacy in reducing CV events. Consider Metformin MR prep if GI tolerability issue with standard tablets, prescribe as current CCG preferred brand
- In patients where the tablet formulation cannot be administered, a licensed oral solution is available prescribed as Metformin 500mg/5ml sugar free oral solution (category A in Drug Tariff) but is expensive (currently £250 price difference for 1 month supply compared to standard release tablets).
- Start Metformin at 500mg once daily and build up dose gradually (by 500mg each week) to minimise GI side effects.

Dose
- Take tablets with or immediately after a meal to increase insulin sensitivity
- Start on a low dose and increase dose weekly to achieve glycaemic target up to a maximum of 1 gram three times daily (although most patients tolerate 1.5-2 gram total daily dose, BNF suggests maximum 2g daily dose)
- Metformin standard release tablets come as 500mg and 850mg strengths
- Metformin SR is available in a range of strengths, including 500mg, 750mg & 1g tablets
Stop Metformin 48 hours before:
- Radiological procedure needing intravenous contrast
- Re-start if renal function stable after the intervention completed
  With surgery requiring general anaesthesia patients will be advised in pre-operative assessment with regards to whether or not to stop there metformin treatment prior.

### 2.2.2 Sulphonylureas

**DAILY COST** Gliclazide £0.12 (standard release tablet)

Place in therapy: Consider mainly for non-obese younger patients as monotherapy where metformin not tolerated or as an addition to metformin in dual/triple therapy

**Note:** Longer acting sulphonylureas such as chlorpropamide and glibenclamide are not recommended and should be avoided due to the high incidence of side effects including prolonged hypoglycaemia.

Gliclazide has a short half-life and is a low cost SU, start on 40-80mg daily. Adjust the dose every 2-4 weeks to optimise glycaemic control or until maximum tolerated dose is reached (If this is 160mg daily, then can be taken as a single dose with breakfast. If maximum licensed daily dose of 320mg is reached, this should be given in divided doses).

South Staffordshire Joint Formulary has gliclazide MR as “non-formulary”, due to increased risk of hypoglycaemia and this should not be prescribed locally.

**Indications/Benefits**
- Indicated first line if Metformin is either contraindicated or not tolerated
- Additional therapy where additional agents needed – see algorithm page 3

**Cautions and Contraindications**
- Caution in mild to moderate hepatic and renal impairment due to increased risk of hypoglycaemia
- Educate patients in recognising and treating hypoglycaemia particularly if he or she has renal impairment
- Elderly

**Side Effects**
- Average weight gain is 2-4kg and in some patients this may exceed 10kg;
- Glimepiride and gliclazide have a lower risk of hypoglycaemia and weight gain than glibenclamide

**Dose**
- Tablets should be taken approximately ten minutes before meals
- Increase dose every 2-4 weeks to achieve glycaemic target or maximal dose is reached
- 40mg standard release tablets are five times the cost compared to halving 80mg tablets
- Gliclazide 80mg is equivalent to gliclazide MR 30mg if converting back to standard release.
2.2.3 Rapid-acting insulin secretagogues

**DAILY COST £0.52 (repaglinide), £1.06 (nateglinide)**

- Nateglinide and repaglinide are alternatives to sulphonylureas in patients where a rapid onset of action is necessary.
- Not recommended in over 75 year olds
- There is no licence for combination with other antidiabetic drugs, except Metformin

2.2.4 Thiazolidinediones ("Glitazones"), Pioglitazone

**DAILY COST £0.06 (standard release tablet)**

**Place in therapy:** in reality use is decreasing due to safety concerns, however may be an option where a patient does not want an injection or their job requires driving so an SU is not as appropriate

**Indications/Benefits**

- For monotherapy it is the suggested fourth line choice i.e. to be used where metformin is not appropriate (or not tolerated) if the person has marked insulin sensitivity, an SU is not appropriate or contraindicated, a DPP-4 inhibitor is contraindicated, or the person has previously had a poor response to, or did not tolerate a DPP-4 inhibitor.
- Licensed as “add on” therapy when:
  - Patient already taking one oral hypoglycaemic agent AND
  - Glycaemic targets are not achieved AND
  - Metformin/sulphonylurea not tolerated as 2nd agent
  - Any use with insulin is cautioned due to increased risk of cardiac failure (NICE NG28)³
- Reduces insulin resistance and increases glucose uptake into muscle
- If initiated, MHRA (2011) advises that ‘prescribers should review the safety and efficacy of pioglitazone in individuals after 3-6 months of treatment to ensure that only patients who are deriving the benefit continue to be treated.’⁸

**Cautions and Contraindications**

- Patients with active bladder cancer or with a history of bladder cancer, and those with un-investigated haematuria, should not receive pioglitazone.⁸
- Do not commence or continue in those with cardiac failure or in those with a history of cardiac failure, hepatic impairment and diabetic ketoacidosis. Additionally contraindicated in those with un-investigated macroscopic haematuria. (NICE NG28 1.6.24)⁹
- Little evidence to support routine use as second agent in overweight patients and as monotherapy.
- Monitor Liver Function Tests before initiating treatment and then annually. Do not use in acute liver disease or if ALT (liver enzyme) is 2.5 x upper limit of normal.⁷
- Do not commence or continue in patients at higher risk of fracture (more common in women)

**Side Effects**

- Average weight gain may be higher than with sulphonylureas (see BNF ⁶ or SPC ⁷ for more information)
Dose
- Starting dose of Pioglitazone is 15mg or 30mg once daily. The dose may be increased in increments up to 45mg once daily.
- Pioglitazone is licensed for combination with insulin and can be considered for those who have previously had a marked glucose lowering effect to “glitazone” therapy. However, patients should be observed for signs/symptoms of heart failure, weight gain and oedema.²

Stop Criteria
- Maximal effect is seen in 3-6 months; if no response to therapy in 6 months in terms of reduction to patients target review as per algorithm (NICE NG28)³

Note: it is important to take into account the advice from the EMA and the MHRA (http://www.gov.uk/drug-safety-update/pioglitazone-risk-of-bladder-cancer) before prescribing pioglitazone.

2.2.5 DPP-4 inhibitors

| DAILY COST | £0.95 (alogliptin), £1.19 (sitagliptin), £1.19 (linagliptin) |

Place in therapy: Of all second line agents most likely to be suitable for elderly patients after taking potential heart failure risk into consideration as discussed below.

- If a gliptin is to be used, it is advised that the gliptin is selected based on the appropriate licensed indications with the lowest acquisition cost (refer to South Staffordshire Joint Formulary).
- Alogliptin is currently the lowest cost acquisition, but is not licensed for monotherapy. In EXAMINE (alogliptin) results included a small and statistically non-significant increase in hospital admissions for heart failure but this was a secondary outcome and as such must be treated with caution.¹⁰ Neither the MHRA or the EMA are concerned about this at present.¹¹
- Sitagliptin has a higher cost acquisition and the patent does not expire for at least 5 years (patent expiry 2022).¹² However, it is also the only gliptin at present to have a complete 3 year study which shows it to not be associated with any increased risk of cardiovascular outcomes, which includes no increased risk of hospitalisations as a result of heart failure.¹³
- Reserve linagliptin for rapidly declining renal function or an eGFR less than 30ml/min/1.72m². We are awaiting FDA trials on cardiovascular outcomes for this agent.
- DPP-4 inhibitors increase circulatory levels of incretin – gut hormones that can boost insulin levels.

Indications/Benefits
- Increase insulin secretion and lower glucagon secretion.
- Consider using as second line therapy if either sulphonylurea or metformin are contraindicated or not tolerated.
- Discuss the benefits and risks of a DPP-4 inhibitor with the person, bearing in mind that a DPP-4 inhibitor might be preferable to a thiazolidinedione (glitazone) if:
  o Further weight gain would cause significant problems, or
  o A thiazolidinedione (glitazone) is contraindicated, or the person had a poor response to or did not tolerate a thiazolidinedione (glitazone) in the past.

Cautions and Contraindications
- Hypersensitivity is a contraindication
- Caution in renal and severe hepatic impairment, cardiac failure,14 history of pancreatitis.
- Daily dose may need reducing if used in combination with an SU, glitazone or insulin (increased risk of hypoglycaemia).
- A recent FDA warning was issued where an additional warning with regards to risk of heart failure was added to alogliptan and saxagliptin. This is related to two of the three large controlled clinical trials conducted where a slight increase in heart failure was found to be a secondary outcome and as such it is not yet clear how robust this is as it was not a primary outcome of the trials and the number of patients affected where fairly small. At present the MHRA and EMA have not added any additional warnings either alogliptin or saxagliptin and the advice to healthcare professionals is to prescribe observing the warnings and precautions within the relevant SPCS and use within the licensed indications.11,14

Side Effects
- Hypoglycaemia, gastro-intestinal disturbances, headache, rash

Criteria for Use and Dosing
- Alogliptin is licensed for use as add-on therapy to metformin, a thiazolidinedione (glitazone), a sulphonylurea, or insulin. Also as triple therapy with metformin and a thiazolidinedione (glitazone) or insulin. Please note that alogliptin is not licensed for monotherapy.
- Sitagliptin is licensed for use as monotherapy, dual and triple therapy with Metformin, sulphonylurea or thiazolidinediones (glitazones). Sitagliptin is also indicated as add on to insulin (with or without Metformin)
  - Most established gliptin but currently higher cost
- Linagliptin (for use in patients with either rapidly declining renal function or an eGFR less than 30ml/min/1.72m2 (CKD Stage 4 or 5)
  - 85% of dose is hepatically cleared, renal clearance is minor7
  - The dose of linagliptin is 5 mg once daily as monotherapy and combination therapy (in combination with metformin; in combination with sulphonylurea and metformin but not in combination with sulphonylurea alone; in combination with insulin with or without metformin)
- Both saxagliptin and Vildagliptin are non-formulary. The SAVOR-TIMI 53 study of saxagliptin is the only one with a statistically significant increase in heart failure admissions, however the increase was fairly modest (hazard ratio 1.27; 95% CI, 1.07 to 1.51; P=0.007) and the absolute increase was small at 0.7%.15

This table below is not a dose equivalence table, merely a dose comparison. Any decision to switch a patient from one type of DPP4 inhibitor to another would be at the discretion of the treating healthcare professional

<table>
<thead>
<tr>
<th></th>
<th>Alogliptin</th>
<th>Linagliptin</th>
<th>Saxagliptin</th>
<th>Sitagliptin</th>
<th>Vildagliptin</th>
</tr>
</thead>
</table>

Type 2 diabetes prescribing guideline - Version 1.0
February 2017 Review date: February 2019
OD: One daily  BD: twice  Daily ESRD: End Stage Renal Disease

For all products assessment of renal function is recommended prior to initiation and periodically thereafter.

Stop Criteria

- Maximal effect is seen in 3-6 months; if no response to therapy in 6 months in terms of achieving patients target review as per algorithm page 3. (NICE NG28)³

2.2.6 SGLT-2 inhibitors

**DAILY COST all the same £1.31 (dapagliflozin), £1.31 (empagliflozin), £1.31 (canagliflozin)**

Place in therapy: More likely to be used in younger patients due to restrictions with regards to renal function and efficacy is higher than some comparable agents in terms of Hb1ac reduction so may be preferred where more intense Hb1ac reduction needed and/or patient is obese so SU not appropriate.

Cardiovascular outcomes data suggests may be beneficial in middle aged patients at risk of cardiovascular events.
## Indications

<table>
<thead>
<tr>
<th>Monotherapy (TA 390)(^{16})</th>
<th><strong>Dapagliflozin</strong></th>
<th><strong>Canagliflozin</strong></th>
<th><strong>Empagliflozin</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes, in metformin intolerant, where SU or pioglitazone is not appropriate and a DPP4 inhibitor would otherwise be prescribed.</td>
<td>Yes, in metformin intolerant, where SU or pioglitazone is not appropriate and a DPP4 inhibitor would otherwise be prescribed.</td>
<td>Yes, in metformin intolerant, where SU or pioglitazone is not appropriate and a DPP4 inhibitor would otherwise be prescribed.</td>
</tr>
</tbody>
</table>

### Trial data

| **Comparison to other SGLT2 and DPP4 inhibitors:** Trials were vs. placebo so no direct comparison to DPP4. | **Comparison to other SGLT2 and DPP4 inhibitors:** Trials were vs. placebo so no direct comparison to DPP4. | **Comparison to other SGLT2 and DPP4 inhibitors:** Exploratory comparisons within trial showed an increase in efficacy in terms of HbA1c reduction for the higher strength (25mg) compared to sitagliptin100mg, comparable efficacy shown for the 10mg strength. |

### Company meta-analysis

| This showed greater weight and systolic BP reduction compared to DPP4 inhibitors but no difference in HbA1c reduction. | This showed for 100mg strength greater weight reduction than other SGLT-2 inhibitors. It showed greater HbA1c reduction, systolic BP and weight reduction with DPP4 inhibitors (except sitagliptin which was equivalent). |  |

### Network meta-analysis

**DPP4 inhibitor comparison**

| However this showed it to be more effective than sitagliptin in terms of HbA1c reduction. | However this showed it to be more effective than sitagliptin in terms of HB1ac reduction for both strengths. | However this showed it to be equal in efficacy to sitagliptin for both strengths. |

### Other SGLT2 comparison

| Network meta-analysis also showed this lowered HbA1c more than the other two SGLT2 inhibitors. |  |  |

### Combination with metformin

| Yes, only if SU contraindicated or not tolerated or person is at significant hypo risk | Yes, only if SU contraindicated or not tolerated or person is at significant hypo risk | Yes, only if SU contraindicated or not tolerated or person is at significant hypo risk |
Combination with insulin +/- other antidiabetic drugs

<table>
<thead>
<tr>
<th>Combination with insulin +/- other antidiabetic drugs</th>
<th>Yes</th>
<th>Yes, shown to be slightly more effective than DPP4 inhibitors and dapagliflozin in terms of weight reduction and body weight.</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination with metformin/SU or metformin/ glitazone</td>
<td>YES</td>
<td>In combination with metformin and SU showed comparable efficacy in HbA1c reduction to DPP4 inhibitors (gliptins) but with more weight and blood pressure reduction.</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In combination with metformin and SU showed comparable efficacy in HbA1c reduction to DPP4 inhibitors (gliptins) but with more weight and blood pressure reduction. In combination with metformin and glitazone- comparable to DPP4 inhibitors.</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Both triple therapy combinations as per canagliflozin have been shown to be cost effective.</td>
<td></td>
</tr>
</tbody>
</table>

Cardiovascular outcome data:

- Cardiovascular outcome data is currently available for empagliflozin and canagliflozin. We are awaiting publication of the results of DECLARE TIMI58 (dapagliflozin).
- For empagliflozin Empa-Reg) has demonstrated an overall benefit on survival rates.
- There was a 38% RRR in CV mortality and 32% RRR in all-cause mortality.
- No effects where shown on the rate of non-fatal MI and stroke, but fewer deaths after MI, fewer sudden deaths and of unknown causes were seen. Also a 33% relative reduction in hospitalisation for heart failure.
- The CANVAS trials (2017) involved patients with type 2 diabetes and an elevated risk of cardiovascular disease, patients treated with canagliflozin had a lower risk of cardiovascular events than those who received placebo but a greater risk of amputation, primarily at the level of the toe or metatarsal. It is worth noting that these patients where ones who had previously had amputations and where at high risk.

The following restrictions apply:

1. Restrict to patients less than 75 years of age who are less prone to complicated UTI.
2. Use in caution for those over 65 years of age who are at risk of volume depletion, for example patients treated with diuretics.
3. Exclude patients with Type 1 diabetes.
4. Dapagliflozin is not recommended for use in patients with eGFR below 60 ml/min/1.73m².
5. Canagliflozin and empagliflozin are not recommended for use in patients with eGFR persistently below 45 ml/min/1.73m².
6. Hepatic impairment: No dose adjustments needed in mild or moderate impairment. Empagliflozin and canagliflozin should not be used in severe impairment. Dapagliflozin in severe hepatic impairment can be dose reduced to 5mg once daily and if well tolerated increased to 10mg once daily.
7. Dapagliflozin is not recommended in combination with pioglitazone.
8. Dapagliflozin, canagliflozin and empagliflozin are not recommended in patients with cardiac failure or with elevated haematocrit.
9. Test for raised ketones in patients with symptoms of diabetic ketoacidosis (DKA) even if blood glucose levels are normal; omitting this test could delay diagnosis of DKA. Patients should be explained risks of DKA and the signs and symptoms on commencing. Patients with risk factors such as dehydration, restricted food intake, sudden reduction in insulin, increased insulin requirements due to illness, surgery, alcohol abuse should even not start taking this medication or have it held until they are better.\(^5\)

10. Canagliflozin has been associated with an increase in lower limb amputation (mainly of the toe). People with risk factors such as previous amputations, peripheral vascular disease, or neuropathy need careful monitoring if on this agent. Consideration should be given to stopping it if a lower limb complication occurs in the patient such as skin ulcer or osteomyelitis.\(^4,21\)

**Dose:**
- Dapagliflozin 10mg once daily
- Empagliflozin 10 mg once daily, if necessary and if tolerated, increase to max. 25 mg once daily
- Canagliflozin 100mg once daily. In patients tolerating canagliflozin 100 mg who have an eGFR ≥ 60 mL/min/1.73 m\(^2\) and need tighter glycaemic control, the dose can be increased to 300 mg once daily (data shows an increase in weight reduction only at this dose).\(^21\)

**Monitoring**
- Renal function (EFGR, creatinine, urea and electrolytes) should be measured prior to initiation and yearly thereafter. It should also be measured if any other medication that may reduce renal function is commenced. If patient is approaching moderate renal function it should be monitored 2-4 times a year.
- It is important to note that due to the mechanism of action the patient will have glucose present in their urine.

**Side effects:**
- Very common: hypoglycaemia (when used with a sulfonylurea or insulin)
- Common: vulvovaginitis, balantis and related genital infections, UTI’s, dizziness, back pain, dysuria, polyuria
- Uncommon: fungal infection, volume depletion, thirst, constipation, dry mouth, nocturia, renal impairment, vulvovaginal pruritus, pruritus genital, dehydration.

**Stop Criteria:**
- Maximal effect is seen in 3-6 months; if no response to therapy in 6 months in terms achieving patients target review as per algorithm. If renal function deteriorates below contraindicated levels as discussed above treatment should be stopped. (NICE NG28)\(^3\)
- If a patient develops diabetic ketoacidosis on therapy SGLT2 therapy should be stopped and they should not be put back onto this drug class

### 2.2.7 GLP-1 mimetics

**Indications/Benefits**
- Increases insulin secretion, suppresses glucagon secretion and slows gastric emptying

**Cardiovascular outcome data:**
- Exenatide (Byetta ®) & (Bydureon ®) – EXSCEL trial (2017).\(^{22}\) The incidence of major adverse cardiovascular events did not differ significantly between patients who received exenatide and
those who received placebo.

- Liraglutide – LEADER trial (June 2016). The trial compares the addition of either Victoza® or placebo to standard care and a statistically significant reduction in cardiovascular risk has been reported.

- Lixisenatide – ELIXA trial has shown it to not be associated with significant difference in rates of cardiovascular events as compared with conventional therapy plus placebo, including a neutral effect on the incidence of hospitalization for heart failure. Lixisenatide did not get a NICE TA because it did not achieve in trials a reduction of at least 1% HbA1c and as such we do not recommend prescribing in primary care and the formulary status is Red.

Cautions and Contraindications

- Caution in the elderly
- Caution in pancreatitis

Renal cautions

- Exenatide daily (Byetta®): not recommended for use in patients with end-stage renal disease or severe renal impairment.
- Liraglutide: not recommended for use in patients with moderate and severe renal impairment including patients with end-stage renal disease.
- Exenatide weekly (Bydureon®): not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance < 30 ml/min).
- Dulaglutide: not recommended for use in patients with end-stage renal disease or severe renal impairment.

Side Effects

- Pancreatitis, GI disturbances

Criteria for Use and Dosing

- GLP-1 mimetics should only be considered for triple therapy in addition to metformin and a sulphonylurea, in people where triple therapy is not effective, not tolerated or contraindicated and:
  o BMI <35kg/m² and for whom insulin therapy would have significant occupational implications, or weight loss would benefit other significant obesity related comorbidities. (NICE NG28)
  o where BMI>35kg/m², GLP1 mimetics are an option but a referral for bariatric surgery should be considered.
  o Prescriber to decide most appropriate GLP-1 agonist after discussion with patient.

- If all other patient factors are equal prescribe the GLP-1 agonist with the lowest acquisition cost should be used.
Daily treatments:
Exenatide twice daily (Byetta ®) (NICE NG28)³:

<table>
<thead>
<tr>
<th><strong>DAILY COST £2.39 (incl. cost of needles)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide is injected twice daily; the starting dose is 5 micrograms twice daily increased if necessary after at least 1 month to maximum 10 micrograms twice daily. **Liraglutide (Victoza ®) (NICE TA 203)**²⁵</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>DAILY COST £2.75 (incl. cost of needles; £4.05 if patient titrates up to 1.8mg)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Liraglutide is injected once daily, the starting dose is 0.6mg daily increased after at least 1 week to a maintenance dose of 1.2mg daily</td>
</tr>
<tr>
<td>• Liraglutide 1.2mg daily in triple therapy regimens is recommended as an option only if used as described above (NICE NG28)³</td>
</tr>
<tr>
<td>• Liraglutide 1.2mg daily in dual therapy regimens (in combination with metformin or a sulphonylurea) is recommended as an option only if (NICE NG28)³:</td>
</tr>
<tr>
<td>o triple therapy with metformin and 2 other oral drugs (as per algorithm Page 3) is not effective, not tolerated or contraindicated, consider combination therapy with metformin, a sulphonylurea and a glucagon-like peptide-1 (GLP-1) mimetic for adults with type 2 diabetics and the criteria for GLP-1 mimetic is met as above.</td>
</tr>
</tbody>
</table>

**Liraglutide 1.8mg daily is not recommended (NICE TA 203 1.5)**²⁶
- 1.2mg and 1.8mg dose are in the same pen device and it is easy for patients to up titrate dose themselves which pushes the acquisition cost greatly.

Weekly treatments
Dulaglutide (Trulicity®) (NICE ESNM59)²⁷

<table>
<thead>
<tr>
<th><strong>DAILY COST £2.62 (incl. cost of needles)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>This is the preferred weekly GLP1 mimetic therapy as the device is simpler to use and it is licensed in combination with insulin. Dulaglutide is licensed in combination with insulin and moderate renal impairment unlike Bydureon® (weekly exenatide).</td>
</tr>
</tbody>
</table>

Dulaglutide is given once weekly by subcutaneous injection as per the dosing information below in an auto inject device: **Monotherapy**
- The recommended dose is 0.75 mg once weekly.

**Add-on therapy**
- The recommended dose is 1.5 mg once weekly. For frail patients e.g. over 75 can be started at the lower dose.

- The SPC states that if adding to existing metformin and/or pioglitazone therapy, the current dose of metformin and/or pioglitazone can be continued. When it is added to existing therapy of a sulphonylurea or prandial insulin, a reduction in the dose of sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia

**Evidence**
- The EPAR states that the overall effect of dulaglutide on weight was modest across the AWARD trials (mean changes -0.87 kg to -3.03 kg), and that the clinical relevance of the observed effect size with the 1.5 mg dose is uncertain.²⁵
• There are no trials to compare it with other weekly GLP1 mimetics. Therefore dulaglutide and exenatide modified-release (Bydureon®) cannot be compared in relation to their corresponding incidences of hypoglycaemia because there are no head to head studies of the two.  

Exenatide weekly (Bydureon®) (NICE TA248)

**DAILY COST £2.81 (already includes needles)**

• For patients who experience side effects with Exenatide twice daily or those who would benefit from weekly injections from a compliance/concordance perspective
• To be prescribed by diabetes specialists only
• Exenatide weekly in dual therapy regimens (in combination with Metformin or a Sulphonylurea) is recommended as an option only if (NICE NG28)³:
  o Triple therapy with metformin and 2 other oral drugs (as per algorithm page 2) is not effective, not tolerated or contraindicated, consider combination therapy with metformin, a sulfonylurea and a glucagon-like peptide-1 (GLP-1) mimetic for adults with type 2 diabetes and the criteria for GLP1 mimetics is met as above.

**Stop criteria for GLP 1 mimetics**

• Only continue GLP-1 mimetic therapy if the person with type 2 diabetes has had a beneficial metabolic response (a reduction of at least 11 mmol/mol (1.0%) in HbA1c and a weight loss of at least 3% of initial body weight in 6 months (NICE NG28 1.6.29)³
2.2.8 Insulin

Treatment Decision Flow Chart for Insulin Initiation in Adult Type 2 Diabetes

**STEP 1**
- Check baseline investigations (venous blood glucose, FBC, U+E, LFTs, lipid profile, TFT’s, urine for protein and ketones)
- Lifestyle guidelines for patients with diabetes and poor glycaemic control (see page 18) for up to 12 weeks
- Initiate or reinforce self-blood glucose testing using a 4 point profile approach
- Agree clear targets
- Remember that poor concordance is unlikely to be affected by escalating treatment

**STEP 2**
- Repeat HbA1c after 12 weeks
- If HbA1c still>58 mmol/mol (7.5%) or agreed patient individualised target or 58 mmol/l and there is no considerable trend towards improvement of if there are other indications for immediate tight control, i.e. complications

**STEP 3**
- HbA1c>58 mmol/l (7.5%) or agreed patient individualised target – commence on individualised insulin regimen in partnership with the patient. This may be once daily, twice daily biphasic or basal bolus plus or minus oral agents.
- Metformin can usually be continued; access other oral agents (NICENG28, 1.6, 33, 1.6, 34)
- HbA1c>75 mmol/mol (9%), appropriate insulin as dictated by blood glucose profile.
- Commence insulin in GP practice or refer to specialist diabetes team (primary or secondary depending on locality)

Consider referral to Specialist Diabetes Team/Hospital for special groups:
- Pregnancy
- Pre-conception
- Renal Disease
- MI
- Very Obese
- Vulnerable people, including the elderly
- Vocational Licences

**Who to access?**
- HbA1c>58 mmol/mol (7.5%) or agreed patient individualised target
- Absence of severe osmotic symptoms
- Maximum tolerated oral agents

**Does the person need immediate insulin treatment?**

- If Yes – go directly to step 4 for guidance
- If No:
  - Review date: February 2019
  - Page 23

**GO DIRECTLY TO STEP 1**
STEP 4
Symptoms of hyperglycaemia and diagnostic blood glucose; according to WHO guidelines

YES

Exclude DKA (Diabetes Ketoacidosis, for type 1 diabetes) and HHS (Hyperosmolar Hyperglycaemic State, for type 2 diabetes). Are any of these present?
• Acutely unwell
• Vomiting
• Reduced consciousness
• Dehydrated
• Ketonuria >2+ and/or blood ketones >1.5 mmol/l
• Hyperglycaemia with any of the above

NO

Does the patient have severe osmotic symptoms, hyperglycaemia and mild to moderate ketonuria or blood ketones of between 0.6 and 1.5 mmol/l?

YES

Arrange immediate/urgent assessment in hospital to exclude DKA/HHS

NO

Are there one or more of the following present?
• Short history of any of the above symptoms
• Marked weight loss (irrespective of absolute weight)
• Marked hyperglycaemia

YES

Likely to need insulin. Discuss with the Diabetes Specialist Teams (Community or Hospital) within 24-48 hours

NO

There is no immediate need for insulin. Consider oral agents. Give dietary and lifestyle advice. If in any doubt, contact the Diabetes Specialist Terms (Community or Hospital).

GO TO STEP 1
Insulin therapy

- If other measures do not keep HbA1c to < 53 mmol/mol (7.0%) (or agreed patient individualised target), discuss benefits and risks of insulin treatment.
- Initiate with a structured one to one session (frequency of 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) [NICE NG28 1.6.33].

Insulin Regimens and Titration

Once started on insulin, it is considered appropriate to continue metformin but to usually stop sulphonylurea agents (if using more than a once daily insulin regimen) and other drugs which are not licensed to be used with insulin. Pioglitazone should be continued with caution or stopped when starting insulin -if used, regularly observe patient for signs of heart failure, oedema and weight gain, if cardiac status deteriorates discontinue. The SGLT2 inhibitors (dapagliflozin, canagliflozin and empagliflozin) and the DPP4 inhibitors (alogliptin, sitagliptin and linagliptin) may be continued with insulin therapy if needed.

- Always ensure correct insulin is prescribed and be aware of potential insulin errors – (see insulin card in appendix 7) [http://www.nrls.npsa.nhs.uk/alerts/?entryid45=74287]
- Ensure patients receive insulin safety passports – [http://www.nrls.npsa.nhs.uk/resources/?EntryId45=130397]
- For detailed information on timings different types of insulins should be given refer to appendix 11.

Insulin should only be initiated by a Health Care Professional with recognised competency. If this expertise is not available, refer to Community or Secondary Care Specialist Diabetes Teams.

Aims of insulin initiation:

- Aid smooth transition and titration of insulin unit doses
- Ensure patients develop an awareness of self-care
- Help clinicians in primary care feel confident and secure to safely advise or alter insulin unit dosages as early as possible

Insulin Prescribed Quantities

As a rule of thumb to calculate the quantity of insulin to prescribe the following formula can be used:

\[
\text{Total daily units administered} + 1 \\
10
\]

This applies to 3ml cartridge or 10ml vials and gives the number needed to be prescribed per month. The +1 device gives an additional one in case of loss/accident or malfunction. A summary chart can be found in Appendix 6.
**Adding Once Daily Insulin to Current Oral Agents**

Begin with Human (sequence) NPH insulin taken at the time most appropriate for the patients dependant on when they have elevated blood glucose levels, or twice daily according to need (NICE NG28 1.6.34)³:

Isophane insulin (Humulin l ®)

- 10-mL vial £15.68
- 5 x 3-mL cartridge (for Autopen® Classic or HumaPen®) £19.08
- 5 x 3-mL Humulin l KwikPen® prefilled disposable injection devices £21.70

Isophane insulin (Insulatard ®)

- 10-mL vial £7.48
- 5 x 3-mL cartridge (for Novopen® devices) £22.90
- 5 x 3-mL Insulatard InnoLet® prefilled disposable injection devices £19.80

Isophane insulin (Insuman ®)

- 5-mL vial £5.61
- 5 x 3-mL cartridge (for ClikSTAR® and Autopen® 24) 5 x 3-mL Insuman® £17.50
- Basal Solostar® prefilled disposable injection devices £19.80

**Suggested starting dose:**

6-10 units once daily, depending on fasting blood glucose levels.

<table>
<thead>
<tr>
<th>Self-Titration – Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fasting blood glucose &gt;6.7mmol/l</td>
</tr>
<tr>
<td>2. Increase insulin by 2 insulin units every 2-4 days depending on individual circumstance.</td>
</tr>
<tr>
<td>3. Continue with this process until:</td>
</tr>
<tr>
<td>- A fasting blood glucose target of 5.5 mmol/l on average over 2 consecutive days is reached</td>
</tr>
</tbody>
</table>

Targets may vary according to individual needs. If compliance is a problem in individuals then aim for between 3-9 mmol/l.

**NO NOT increase dose if blood glucose is less than 4mmol/l or if symptoms of hypoglycaemia are present.**

If unsure, contact your named healthcare professional.

Alternatively only consider a once daily insulin analogue (Insulin Detemir, Insulin Glargine) (NICE NG28 1.6.34 and 1.6.35)³ if:

- The person needs help with injecting insulin and the long acting insulin analogue would reduce 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 basal insulin injections plus oral glucose lowering drugs; or
- The person cannot use the device to inject NPH insulin.

**Reasons for switching patients who have already tried NPH insulin in each category to insulin analogues e.g. for the premixed (Humalog mix ®and Novomix ®) or for the long acting Levemir ® or Lantus ® (NICE NG28 1.6.35)³**

- Patients who do not reach target Hb1Ac because of hypoglycaemia
- Patients where hypoglycaemia occurs regardless of what the HBA1c reading is.
Note: If patients are not controlled on large doses of once daily insulin (i.e. greater than 0.5 units of insulin per kg of body weight or >50 units of once daily insulin) consider the benefits of changing to twice daily pre-mixed insulin, or if not suitable consider the high strength insulin glargine Toujeo Solostar®.

**Insulin glargine biosimilar (Igb) - Abasaglar**

Launched in Aug 2015, Abasaglar® and Lantus® have the same summary of product characteristics and identical indications. It is 15% less expensive than Lantus® (glargine). Abasaglar can be administered using the prefilled KwikPen or the reusable Savvio pen.

It must be prescribed by brand, as Abasaglar® and Lantus® are not interchangeable; prescriptions should no longer be issued for generic ‘insulin glargine’. Any long-standing prescriptions for generic ‘insulin glargine’ should be changed to Lantus® and any new initiations prescribed by the formulary brand at time of prescribing. Refer also to Health professional information from MHRA Drug Safety Update (April 2015).

**High strength insulin glargine (Toujeo®)**

Insulin glargine U300 (Toujeo Solostar®) dose conversion from glargine 100U/ml is quite complex. The South Staffordshire Area Prescribing Group has allowed this to be prescribed following initiation by a diabetes specialist A Ricad is no longer needed. This allows patients a patient is having an injection site reaction or hypoglycaemia or a fear of hypoglycaemia which is disrupting patients treatment, to be referred to secondary care or community team for initiation of this high strength preparation. Prescribing will be started by the specialist team then may be transferred to the GP surgery for stepping up as per the targets set within the clinical letter upon transfer.

**Insulin degludec (100 units/ml and 200 units/ml) (Tresiba®)**

This is a third line insulin after insulin glargine and insulin determir have been tried and the patient is not acceptably controlled or experiencing unacceptable side effects such as hypoglycaemia or diabetic kertoacidosis (despite good compliance with therapy).

Please note the 200 units is a high strength insulin. The 200U (Tresiba Flextouch®) will primarily be used in patients already on ≥ 80 units/dose of basal analogue insulin (e.g Absalagar®, lantus® or levemir®) to reduce injection volume whilst allowing upward titration of doses.

**Key points**

- High glucose levels – a higher dose is needed
- Low glucose levels – a lower dose is needed

Individual blood glucose targets should be agreed with the person with diabetes, sometimes short, medium and long term goals are more appropriate. It is generally regarded that there is no ‘correct dose’ and neither is there a ‘top dose’. The aim is to start low and work up slowly building the individual’s confidence at the same time. It is important that they are aware of this and that it may take several weeks or months to obtain their target blood glucose results.
Titration/Dose Adjustment

Should be individualised according to patient.

Starting dose:

Should be individualised according to patient.

Titration/Dose Adjustment – for patients and healthcare professionals

- A IM – Pre-meal morning blood sugars to range between 4-9mmol/l. Targets may vary according to individual needs.
- In practice further blood sugars other than the morning monitoring is not needed as this is a fixed dose regimen so would not adjust doses based on levels but would monitor whether it is working for the patient based on their HbA1c.

<table>
<thead>
<tr>
<th>Blood Glucose</th>
<th>Titration advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10mmol/l</td>
<td>Increase by 2 insulin units every 2 days – use with caution in patients on small doses of insulin to a maximum of 10% of original dose</td>
</tr>
<tr>
<td>&gt;7.5-10mmol/l</td>
<td>Increase by 2 insulin units every 2-4 days</td>
</tr>
<tr>
<td>4-7.5mmol/l</td>
<td>No change</td>
</tr>
<tr>
<td>Less than 4mmol/l</td>
<td>Reduce dose</td>
</tr>
</tbody>
</table>

Twice Daily Insulin Regimen (BD)

Suggested Regimen HbA1c >75 mmol/mol (9%)
(See Step 3 Treatment Decision Flow Chart for Insulin Initiation in Adult Diabetes, page 12

Biphasic isophane insulin (Humulin M3 *)

- 10-mL vial £15.68
- 5 x 3-mL cartridge (for most Autopen® Classic or HumaPen®) £19.08
- 5 x 3-mL Humulin M3 KwikPen® prefilled disposable injection devices £21.70

Biphasic isophane insulin (Insuman® Comb 25

- 5-mL vial £5.61
- 5 x 3-mL cartridge (for ClikSTAR® and Autopen® 24) £17.50
- 5 x 3-mL Insuman® Comb 25 SoloStar® prefilled disposable injection devices £19.80

Alternatively only consider pre-mixed preparations that include short-acting insulin analogues (Humalog Mix and Novomix), rather than pre-mixed preparations that include short-acting human insulin preparations, if (NICE NG28 1.6.34)³:

- a person prefers injecting insulin immediately before a meal, or
- hypoglycaemia is a problem, or
- blood glucose levels rise markedly after meals.

Professor David Cousins, NPSA’s Head of Patient Safety for Medication and Medical Devices, said “Insulin is a widely used medicine used to treat diabetes. It is given to thousands of patients each day and in the majority of cases, this procedure is safe. However, there is a real potential for serious harm if it is not administered and handled properly.”
DO NOT increase doses if blood glucose <4mmol/l or symptoms of hypoglycaemia are present. If unsure, contact named healthcare professional.

New to a Multiple Dose Injection Regimen

For type 2 diabetes patients, continue Metformin, unless contraindicated.

Indications for a multiple daily injection regimen:
- HbA1c not to target
- Unstable blood glucose profile
- Lifestyle

REGIMENS

Choice of background insulin
- Humulin I
- Insulatard
- Insuman Basal

Choice of mealtime insulins
- Novorapid
- Humalog 100 units/ml
- Apridra

Alternatively only consider a once daily insulin analogue (Insulin Detemir, Insulin Glargine, Toujeo*, Tresiba*(in line with RICaD) (NICE NG28 1.6.34) if:
- The person needs help with injecting insulin and the long acting insulin analogue would reduce 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 basal insulin injections plus oral glucose lowering drugs; or
- The person cannot use the device to inject NPH insulin.

Starting dose
Start 8-10 units of background insulin. Introduce short/rapid acting insulin at mealtimes. Start with 4 insulin units.

Titration:
Basal insulin unit dose (get this correct first and then move onto bolus adjustment)
Increase insulin by 2 insulin units every 2-4 days until target fasting blood glucose is achieved. Depending on the blood glucose readings it may only be necessary to increase one of the mealtime insulin unit doses, or you may need to increase all the mealtime doses. Tackle breakfast dose first for 7 days, then lunchtime dose for 7 days, finally teatime dose for 7 days.

Bolus insulin dose adjustment
Increase short/rapid acting mealtime insulin by 2 insulin units every 2-4 days depending upon/until
desired pre-mealtime target is achieved.

To reach blood glucose target at:
- LUNCHTIME adjust BREAKFAST insulin unit dose
- EVENING MEAL adjust LUNCHTIME insulin unit dose
- BEDTIME adjust EVENING MEAL insulin unit dose
- BEFORE BREAKFAST adjust background insulin unit dose

3. Blood Glucose Monitoring

Summary
- Patients should clearly understand why they are testing and should ask themselves: How will this test alter what I will do?
- For self-monitoring to be most useful, it should form part of the management plan. Patients should be given adequate training. Patients and health care professionals should be clear what they hope to achieve.
- Regular measurement of HbA1c can contribute to improved long-term blood glucose control and reduce morbidity. Frequency of monitoring should be agreed with the patient from the outset (see appendix 3).
- Self-monitoring is appropriate for patients with type 1 or type 2 diabetes who use insulin and adjust their dose as a result of blood glucose testing and for any person with diabetes when they have inter-current illness, are pregnant/considering pregnancy or are at particular risk of hypoglycaemia or hyperglycaemia as a result of inter-current illness.
- Some people will require increased blood glucose testing, e.g. lack of hypoglycaemia awareness, pregnancy, intercurrent illness, safety for driving and complications of diabetes.
- Clinicians and patients should be aware of current DVLA recommendations regarding driving (see appendix 2).
- As a general rule stable patients on diet alone, metformin, glitazone or a gliptin do not need to test regularly
- Housebound patients with DN teams visiting to administer insulin often have complex co-morbidities and so may have more frequent blood glucose testing.

Currently the recommended blood glucose testing strip agreed across South Staffordshire CCGs is GlucoRx Nexus for most patients.
4. REFERENCES

11. Glare, J (2016). Alogliptin etc. [jim.glare@heartofengland.nhs.uk]


Appendix 1: American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) – Approach to the management of hyperglycaemia.

Most patients should be targeted to <7%, but as previously discussed, tighter targets may benefit younger patients whereas in older individuals, a more conservative approach is necessary.
Appendix 2: NICE 2015. Patient decision aid for a second medication for Type 2 diabetic patients

NICE National Institute for Health and Care Excellence

Patient decision aid

Type 2 diabetes in adults: controlling your blood glucose by taking a second medicine – what are your options?

nice.org.uk/guidance/ng28

Published: December 2015

About this decision aid

This decision aid can help you think about your options for controlling your blood glucose to try to reduce the long-term risks of diabetes. It can help you if you are an adult with type 2 diabetes and:

- you have been taking a single medicine to control your blood glucose (sugar) level as measured by your haemoglobin A1c (HbA1c) level and
- your HbA1c level is higher than the target level you had agreed with your healthcare professional.

(We use ‘healthcare professional’ in this decision aid to mean the doctor, nurse, pharmacist or other professional who is helping you. Different healthcare professionals might help you with different parts of your care.)

This decision aid can help you make up your mind about 2 things:

- firstly, what new blood glucose (HbA1c) target level is best for you and
- secondly, which medicines you might try to achieve this target.
For the first of these, the decision aid explains the advantages and disadvantages of controlling your blood glucose. It then asks you to think about the things that are important to people who are agreeing a new HbA1c target. For the second, the decision aid covers many of the questions people with type 2 diabetes have about medicines. It can help you to make a decision that is right for you, with help from the healthcare professional who is advising you. Your decision depends on several things. Different people will feel that some of these things are more important to them than others, so it is important that you make a decision that is right for you. You might also find it helpful to talk things over with your family or friends.

This decision aid is based on the recommendations in NICE’s type 2 diabetes in adults guideline. It does not cover other parts of your care, or medicines that you might need to take later on in your condition, such as insulin. We have also produced a user guide for healthcare professionals to explain how this decision aid was put together.

NICE guidelines give advice to healthcare professionals on the care and support that should be offered to people who use health and care services. You have the right to be involved in discussions and make informed decisions about your treatment and care with your healthcare professional. You should be given information that explains the options in a way you can understand. For more information see your care.

**Your target blood glucose (HbA1c) level**

The HbA1c blood test reflects your average blood glucose level over the past 2–3 months. NICE recommends that when you are first diagnosed with type 2 diabetes, you should agree a target HbA1c level with your healthcare professional and they should support you in trying to reach it. This target level is usually 48 mmol/mol (6.5%), but may be 53 mmol/mol (7.0%) for some people.

As type 2 diabetes progresses over time, a person’s blood glucose levels naturally tend to get higher, even though they take a medicine to try to control their blood glucose. If you are taking a single medicine and your HbA1c level increases to 58 mmol/mol (7.5%) or higher, NICE recommends that your healthcare professional should:

- offer you diet and lifestyle advice and
- agree a new target HbA1c level with you and support you to aim for it, and
- talk with you about taking an additional medicine to help you reach this new target.
There is more information about what target HbA1c levels NICE recommends in ‘Agreeing a new target blood glucose (HbA1c) level’ later in this decision aid.

Tell your healthcare professional if you have any concerns or problems with any of the medicines you are currently prescribed. For example, some people find it hard to remember to take their medicines as recommended or find that the medicines don’t suit them very well. It may be that you can get better control of your blood glucose by:

- making better use of your current medicine (for example, by having something to help you remember to take it regularly) or
- changing to a different medicine.

**What are the advantages and disadvantages of controlling your blood glucose?**

*Advantages*

**Controlling the symptoms of diabetes**

High blood glucose levels can cause symptoms such as feeling very thirsty, needing to pass urine a lot and feeling more tired than usual. Controlling blood glucose can stop these symptoms.

**Preventing some long-term health problems**

In the long term, having high blood glucose levels increases the chances of other health problems. Controlling your blood glucose to an HbA1c level that is lower than is needed to stop diabetes symptoms will reduce your chance of getting some of these problems, but not others.

Controlling your blood glucose more than you need to stop diabetes symptoms:

- reduces your risk of having a heart attack, having such bad foot problems that you need an amputation, or developing kidney, eye or nerve problems.
- does not seem to change your risk of dying early, dying from heart disease (including dying from a heart attack), having a stroke, or needing surgery to repair damaged blood vessels in your heart or legs.
How will controlling your blood glucose affect you?

Few medicines work in everyone who takes them and we cannot say for sure whether you will or will not benefit:

- some people who control their blood glucose like this will still have a heart attack, or need an amputation, or develop kidney, eye or nerve problems.
- some people will not have a heart attack, or need an amputation, or develop kidney, eye or nerve problems anyway – whether or not they control their blood glucose like this.

The likelihood that you will benefit from controlling your blood glucose like this depends on how likely you are to get these problems anyway. If the chance of you getting them is already small, reducing it further might not make much real difference. If the chance of you getting them is higher, reducing it by the same proportion will make a bigger difference.

Disadvantages

Taking more medicines

The lower you want to keep your blood glucose (HbA1c level), the more medicines you are likely to need to take. (However, losing weight and keeping active can delay the time when more medicines are needed.) Taking more medicines may be inconvenient.

Side effects from medicines

Taking more medicines to keep your HbA1c level low also increases the chance that you will get side effects. Not everyone will get side effects, but we cannot tell in advance whether you will or will not get them. There is more information about possible side effects in ‘Information about medicines to help control your blood glucose (HbA1c) level’ later in this decision aid.

Hypoglycaemia (‘hypos’)

One possible side effect of taking medicines to control your HbA1c is having low blood glucose (hypoglycaemia) – often called a ‘hypo’. Most hypos are mild, but some can be severe, which means that you need help from someone else to treat the hypo. There are special rules relating to hypos for drivers who have diabetes. By law you must tell the DVLA if you have more than 1 severe hypo in 12 months or if you have a severe hypo while driving. You must
also tell the DVLA if you or your healthcare professional feel you are at high risk of developing severe hypos, or if you develop difficulty in recognising the warning symptoms of a hypo. Your healthcare professional may also advise you to check your blood glucose level at times relevant to driving, especially if you take medicines that are particularly linked with an increased chance of hypos. Ask your healthcare professional for more information. Note: there are additional rules for people who hold bus or lorry driving licences.

**What else can you do to help your diabetes?**

Controlling your blood glucose is just one of several aspects of your care. It is also important to have a healthy diet, keep active, control your weight, blood pressure and cholesterol, and stop smoking if you smoke. These will help to improve your overall health and reduce your chances of heart disease and stroke (including your chance of dying from them). Ask your healthcare professional if you would like help or support.

You can find more information about type 2 diabetes from [NHS Choices](https://www.nhs.uk) or [Diabetes UK](https://www.diabetes.org.uk). The NICE guideline on [type 2 diabetes in adults](https://guidance.nice.org.uk/TA316) has more information about what NICE recommends for your care.

**Agreeing a new target blood glucose (HbA1c) level**

There is no HbA1c target level that is right for everyone. NICE recommends that:

- for many people, a new target level of 53 mmol/mol (7.0%) will be a good choice.
- you should choose a higher target HbA1c level if that would be better suited to your individual circumstances and what is important to you.

Several things will affect the target HbA1c level you agree with your healthcare professional; these are described on the next page.

**Your target blood glucose (HbA1c) level: weighing it up**

Make a mark on the lines to show how you feel about these statements. The more you agree with the statement on the left, the further to the left you should put the mark. The more you agree with the statement on the right, the further to the right you should put the mark. You and your healthcare professional can use this to help decide the best target HbA1c level for you.
Thinking about things like driving, having severe hypos would not be a problem for me*  
I’m not bothered about the possibility of getting other side effects  
I’m happy to take more medicines if I need to  
I don’t have any health problems apart from my diabetes  
Thinking about my age and my health overall, I’m hoping to see longer-term benefits  
Thinking about things like driving, having severe hypos would be a big problem for me*  
Getting other side effects would be a big problem for me  
I don’t want to take any more medicines  
I have lots of health problems  
Thinking about my age and my health overall, shorter-term benefits are more important to me

*Hypos might also be a problem for you for other reasons, such as if you operate machinery, if you are at risk of falling, or if you find it difficult to recognise the warning symptoms of a hypo.
Information about medicines to help control your blood glucose (HbA1c) level

This section is about the different medicines you might take as well as your current medicine to try to control your blood glucose. Some medicines may not be suitable for you if you have certain other medical conditions, such as problems with your heart, kidneys or liver. Your healthcare professional will give you advice about this.

The following tables and diagrams cover many of the questions people with type 2 diabetes have about medicines. They can help you to think about what is important for you, and to discuss this information with your healthcare professional. The medicines have been put into groups or ‘families’ of medicines that work in similar ways. It is important to note that:

- the table lists medicines in alphabetical order, not in any order of preference.
- not all medicines work for everyone. Some medicines may work better at lowering blood glucose than others for an individual person, but it is not possible to tell in advance which will work best for you.
- the table provides information about side effects that are thought to concern people with type 2 diabetes most. Some people may have other less common side effects.
- not everyone taking a particular medicine will get side effects.
- you can find more information in the information leaflets that come with the medicine.
## Medicines to help control your blood glucose

<table>
<thead>
<tr>
<th>Medicine name</th>
<th>What does taking it involve?</th>
<th>Can it cause hypoglycaemia (hypos)?</th>
<th>What is its effect on weight?</th>
<th>Other issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPP-4 inhibitors</td>
<td>1 tablet usually taken once a day</td>
<td>DPP-4 inhibitors do not usually make you more or less likely to get hypos. But anyone with type 2 diabetes can get hypos.</td>
<td>Usually no effect on weight</td>
<td><strong>Digestive problems</strong> such as diarrhoea, abdominal pain and heartburn, and also <strong>rashes/itching</strong> and <strong>urine infections</strong>, have been seen in 10 to 100 people in every 1000 who take DPP-4 inhibitors. But 900 to 990 people in every 1000 do not get these problems. <strong>Inflammation of the pancreas</strong> has been seen in 1 to 10 people in every 1000 who take DPP-4 inhibitors. But 990 to 999 people in every 1000 do not get this problem.</td>
</tr>
<tr>
<td>Metformin</td>
<td>1 tablet usually taken 2 or 3 times a day</td>
<td>Metformin does not usually make you more or less likely to get hypos. But anyone with type 2 diabetes can get hypos.</td>
<td>Usually no effect or small weight loss</td>
<td><strong>Digestive problems</strong> such as nausea, vomiting, diarrhoea, abdominal pain and loss of appetite have been seen in more than 100 people in every 1000 who take metformin. Not everyone gets these problems. They most often happen at the beginning of the treatment and then usually go away. <strong>Changes in the sense of taste</strong> have been seen in 10 to 100 people in every 1000 who take it. But 900 to 990 people in every 1000 do not get this problem. <strong>Very rarely, metformin can cause a blood problem</strong> called lactic acidosis. This may affect fewer than 1 in 10,000 people who take it. Most people do not get this but it is very serious if it occurs. The risk is higher for people with liver or kidney problems, uncontrolled diabetes, prolonged fasting, or dehydration due to diarrhoea or vomiting.</td>
</tr>
<tr>
<td>Medicine name</td>
<td>What does taking it involve?</td>
<td>Can it cause hypoglycaemia (hypos)?</td>
<td>What is its effect on weight?</td>
<td>Other issues</td>
</tr>
<tr>
<td>---------------</td>
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</tr>
<tr>
<td>Pioglitazone</td>
<td>1 tablet taken once a day</td>
<td>Pioglitazone does not usually make you more or less likely to get hypos. But anyone with type 2 diabetes can get hypos.</td>
<td>Average 2–3 kg increase over 12 months</td>
<td><em>Bone fractures</em> have been seen in 10 to 100 women in every 1000 who take pioglitazone. But 900 to 990 women in every 1000 do not get this problem.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>Bladder cancer</em> has been seen in 1 to 10 people in every 1000 who take pioglitazone. But 990 to 999 people in every 1000 do not get this problem.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><em>Fluid retention</em> can occur in some people who take pioglitazone, and this could worsen heart failure in people who already have it or might get it. It is not certain how many people in 1000 would get fluid retention.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>People taking pioglitazone need a <strong>blood test</strong> from time to time to check how well their liver is working.</td>
</tr>
<tr>
<td><strong>SGLT-2 inhibitors</strong></td>
<td>1 tablet taken once a day</td>
<td>SGLT-2 inhibitors do not usually make you more or less likely to get hypos. But anyone with type 2 diabetes can get hypos.</td>
<td>Average 2–3 kg decrease over 6–12 months</td>
<td><strong>Digestive problems</strong> such as nausea and constipation, and also <strong>thirst, increased passing of urine, urine infections</strong> and <strong>thrush</strong> (in men and women) have been seen in 10 to 100 people in every 1000 who take SGLT-2 inhibitors. But 900 to 990 people in every 1000 do not get these problems.</td>
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<tr>
<td></td>
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<td></td>
<td><strong>Low blood pressure</strong> (which might lead to fainting or other problems) has been seen in 1 to 10 people in every 1000 who take SGLT-2 inhibitors. But 990 to 999 people in every 1000 do not get this problem. The risk is higher in older people and in people with heart or circulation problems, or dehydration due to diarrhoea or vomiting.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>People taking SGLT-2 inhibitors need a <strong>blood test</strong> from time to time to check how well their kidneys are working.</td>
</tr>
<tr>
<td>Medicine name</td>
<td>What does taking it involve?</td>
<td>Can it cause hypoglycaemia (hypos)?</td>
<td>What is its effect on weight?</td>
<td>Other issues</td>
</tr>
<tr>
<td>---------------</td>
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</tr>
<tr>
<td>Sulfonylureas</td>
<td>1 to 3 tablets, usually taken once a day</td>
<td>Sulfonylureas make you more likely to get hypos. The number of people affected is not certain, and anyone with type 2 diabetes could get hypos.</td>
<td>Possible increase but amount not certain</td>
<td>Digestive problems such as nausea, diarrhoea and abdominal pain have been seen in 10 to 100 people in every 1000 who take sulfonylureas. But 900 to 990 people in every 1000 do not get these problems.</td>
</tr>
<tr>
<td>● glibenclamide</td>
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<tr>
<td>● gliclazide</td>
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<tr>
<td>● glimepiride</td>
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<td>● glipizide</td>
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<tr>
<td>● tolbutamide</td>
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</tbody>
</table>
How you feel about choosing a medicine to try

You can use this table to help you think about how important the issues are to you.

<table>
<thead>
<tr>
<th>Issue</th>
<th>How important is this to me?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Very important</td>
</tr>
<tr>
<td>Getting to a lower target blood glucose (HbA1c) level</td>
<td></td>
</tr>
<tr>
<td>How many tablets I would have to take and how often</td>
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</tr>
<tr>
<td>The possibility of getting hypos</td>
<td></td>
</tr>
<tr>
<td>The possibility of gaining weight</td>
<td></td>
</tr>
<tr>
<td>The possibility of other side effects</td>
<td></td>
</tr>
<tr>
<td>Other concerns or questions I want to discuss with my healthcare professional</td>
<td></td>
</tr>
</tbody>
</table>
Diagrams to explain numbers relating to side effects

1 in 1000

[Diagram showing 1 in 1000 with smiley faces]
10 in 1000
### Appendix 3: HbA1c Conversion Chart

<table>
<thead>
<tr>
<th>DCCT (%)</th>
<th>IFCC (mmol/mol)</th>
<th>DCCT (%)</th>
<th>IFCC (mmol/mol)</th>
<th>DCCT (%)</th>
<th>IFCC (mmol/mol)</th>
<th>DCCT (%)</th>
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<th>DCCT (%)</th>
<th>IFCC (mmol/mol)</th>
<th>DCCT (%)</th>
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<td>9.7</td>
<td>83</td>
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<td>104</td>
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<td>5.8</td>
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<td>5.9</td>
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<td>42</td>
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<td>6.1</td>
<td>43</td>
<td>8.1</td>
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<td>87</td>
<td>12.1</td>
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<td>131</td>
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<td>6.2</td>
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<td>6.3</td>
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<td>89</td>
<td>12.3</td>
<td>111</td>
<td>14.3</td>
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<td>6.4</td>
<td>46</td>
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<td>6.5</td>
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<td>10.5</td>
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<td>14.5</td>
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<td>6.6</td>
<td>49</td>
<td>8.6</td>
<td>70</td>
<td>10.6</td>
<td>92</td>
<td>12.6</td>
<td>114</td>
<td>14.6</td>
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<td>6.7</td>
<td>50</td>
<td>8.7</td>
<td>72</td>
<td>10.7</td>
<td>93</td>
<td>12.7</td>
<td>115</td>
<td>14.7</td>
<td>137</td>
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<tr>
<td>6.8</td>
<td>51</td>
<td>8.8</td>
<td>73</td>
<td>10.8</td>
<td>95</td>
<td>12.8</td>
<td>116</td>
<td>14.8</td>
<td>138</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.9</td>
<td>52</td>
<td>8.9</td>
<td>74</td>
<td>10.9</td>
<td>96</td>
<td>12.9</td>
<td>117</td>
<td>14.9</td>
<td>139</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 4: Safe driving and the DVLA

DVLA GUIDANCE

- Must not drive
- Might be allowed to drive subject to medical advice and/or notifying the DVLA
- May drive and need not notify the DVLA

Diabetes mellitus

Information sent to drivers

Insulin-treated drivers are sent a detailed letter from the DVLA explaining the licensing requirements and driving responsibilities.

All drivers with diabetes must follow the information provided in ‘Information for drivers with diabetes’, which includes a notice of when they must contact the DVLA (see Appendix D, page 122).

Insulin-treated diabetes

Impaired awareness of hypoglycaemia

The Secretary of State’s Honorary Medical Advisory Panel on Driving and Diabetes has defined impaired awareness of hypoglycaemia for Group 1 drivers as ‘an inability to detect the onset of hypoglycaemia because of total absence of warning symptoms’. Group 2 drivers must have full awareness of hypoglycaemia.

Severe hypoglycaemia

‘Severe’ is defined as hypoglycaemia requiring another person’s assistance
Group 1

- Must meet the criteria to drive and must notify the DVLA. All the following criteria must be met for the DVLA to license the person with insulin-treated diabetes for 1, 2 or 3 years:
  - adequate awareness of hypoglycaemia
  - no more than 1 episode of severe hypoglycaemia in the preceding 12 months
  - practises appropriate blood glucose monitoring as defined in the box below
  - not regarded as a likely risk to the public while driving
  - meets the visual standards for acuity and visual field (see Chapter 6, visual disorders, page 93).

Group 2

- Must meet the criteria to drive and must notify the DVLA. All the following criteria must be met for the DVLA to license the person with insulin-treated diabetes for 1 year (with annual review as indicated last below):
  - full awareness of hypoglycaemia
  - no episode of severe hypoglycaemia in the preceding 12 months
  - practises blood glucose monitoring with the regularity defined in the box below
  - must use a glucose meter with sufficient memory to store 3 months of readings as detailed below
  - demonstrates an understanding of the risks of hypoglycaemia
  - no disqualifying complications of diabetes (see page 74) that would mean a licence being refused or revoked, such as visual field defect (see Chapter 5, visual disorders, page 93).

Group 1 recommendations and Group 2 requirements for insulin-treated drivers licensed on review

The Secretary of State’s Honorary Medical Advisory Panel on Driving and Diabetes has defined the self-monitoring requirements for licensing as follows.

**Group 1 car and motorcycle**
- blood glucose testing no more than 2 hours before the start of the first journey and
- every 2 hours while driving
- applicants will be asked to sign an undertaking to comply with the directions of the healthcare professionals treating their diabetes and to report any significant change in their condition to the DVLA immediately.

More frequent self-monitoring may be required with any greater risk of hypoglycaemia (physical activity, altered meal routine).

**Group 2 bus and lorry**
- regular blood glucose testing – at least twice daily including on days when not driving and
- no more than 2 hours before the start of the first journey and
- every 2 hours while driving.

More frequent self-monitoring may be required with any greater risk of hypoglycaemia (physical activity, altered meal routine), in which case a bus or lorry driver may be licensed if they:
- use one or more glucose meters with memory functions to ensure 3 months of readings that will be available for assessment.
How the DVLA checks diabetes management requirements for insulin-treated Group 2 bus and lorry licensing

The DVLA takes the following measures to ensure the requirements are met for licensing of insulin-treated Group 2 bus and lorry drivers:

- requires the applicant’s usual doctor who provides diabetes care to undertake an annual examination including review of the previous 3 months of glucose meter readings
- arranges an examination to be undertaken every 12 months by an independent consultant specialist in diabetes if the examination by their usual doctor is satisfactory
- at the examination, the consultant will require sight of blood glucose self-monitoring records for the previous 3 months stored on the memory of a blood glucose meter
- the license application process cannot start until an applicant’s condition has been stable for at least 1 month
- applicants will be asked to sign an undertaking to comply with the directions of the healthcare professionals treating their diabetes and to report any significant change in their condition to the DVLA immediately.

Continuous glucose monitoring systems (CGMS)

Because these systems measure interstitial glucose, drivers must also monitor blood glucose levels as outlined immediately above.
Impaired awareness of hypoglycaemia

– ‘hypoglycaemia unawareness’

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>car and motorcycle</td>
<td>bus and lorry</td>
</tr>
<tr>
<td>🔴 Must not drive and must notify the DVLA. Driving may resume after a clinical report by a GP or consultant diabetes specialist confirms that hypoglycaemia awareness has been regained.</td>
<td>🔴 Must not drive and must notify the DVLA. The licence will be refused or revoked. Refer to the requirements for insulin-treated diabetes on page 69.</td>
</tr>
</tbody>
</table>

**Diabetes complications**

**Visual complications**

– affecting visual acuity or visual field

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>car and motorcycle</td>
<td>bus and lorry</td>
</tr>
<tr>
<td>🔴 May need to stop driving and notify the DVLA. Refer to Chapter 6, visual disorders (page 93).</td>
<td>🔴 Must not drive and must notify the DVLA. The licence will be refused or revoked. Refer to insulin-treated diabetes (page 69) and Chapter 6, visual disorders (page 93).</td>
</tr>
</tbody>
</table>

**Renal complications**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>car and motorcycle</td>
<td>bus and lorry</td>
</tr>
<tr>
<td>🔴 May need to stop driving and notify the DVLA. Refer to Chapter 7, renal and respiratory disorders (page 101).</td>
<td>🔴 May need to stop driving and notify the DVLA. Refer to Chapter 7, renal and respiratory disorders (page 101).</td>
</tr>
</tbody>
</table>
Limb complications
– including peripheral neuropathy

<table>
<thead>
<tr>
<th>Group 1 car and motorcycle</th>
<th>Group 2 bus and lorry</th>
</tr>
</thead>
</table>
| **Any complication such as peripheral neuropathy that means a driver must meet requirements (such as vehicle adaptations) for disabilities** | **May need to stop driving and notify the DVLA.**  
See Appendix F, disabilities and vehicle adaptations (page 128).  
Limb problems or amputations are of themselves unlikely to prevent driving since they may be assisted by suitable vehicle adaptations. The ability to safely control a vehicle at all times is the essential requirement. | **May need to stop driving and notify the DVLA.**  
See Appendix F, disabilities and vehicle adaptations (page 128).  
Limb problems or amputations are of themselves unlikely to prevent driving since they may be assisted by suitable vehicle adaptations. The ability to safely control a vehicle at all times is the essential requirement. |

Temporary insulin treatment
– including gestational diabetes or post-myocardial infarction

<table>
<thead>
<tr>
<th>Group 1 car and motorcycle</th>
<th>Group 2 bus and lorry</th>
</tr>
</thead>
</table>
| **Trial participants for oral or inhaled insulin are also examples to be included as receiving temporary insulin treatment** | **May drive and need not notify the DVLA, provided:**  
- under medical supervision  
- not advised by clinician as at risk of disabling hypoglycaemia.  
**May continue to drive but must notify the DVLA if:**  
- disabling hypoglycaemia occurs  
- treatment continues for more than 3 months – or in gestational diabetes, continues for 3 months after delivery. | **Must notify the DVLA and meet the above standards.** |
Severe hypoglycaemia
The Secretary of State’s Honorary Medical Advisory Pane on Driving and Diabetes has defined ‘severe’ as hypoglycaemia requiring another person’s assistance.

<table>
<thead>
<tr>
<th>Management of Hypoglycaemia</th>
<th>Group 1 (car and motorcycle)</th>
<th>Group 2 (bus and lorry)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Including sulphonylureas and glinides</strong></td>
<td>May drive and need not notify the DVLA, provided:</td>
<td>May drive but must notify the DVLA.</td>
</tr>
<tr>
<td></td>
<td>- no more than 1 episode of severe hypoglycaemia in the last 12 months</td>
<td>All the following criteria must be met for the DVLA to issue a licence for 1, 2 or 3 years:</td>
</tr>
<tr>
<td></td>
<td>- if needed, detection of hypoglycaemia is by appropriate blood glucose monitoring at times relevant to driving and clinical factors, including frequency of driving</td>
<td>- <strong>no episode</strong> of severe hypoglycaemia in the last 12 months</td>
</tr>
<tr>
<td></td>
<td>- under regular review. It is appropriate to offer self monitoring of blood glucose at times relevant to driving to enable the detection of hypoglycaemia.</td>
<td>- <strong>full awareness</strong> of hypoglycaemia</td>
</tr>
<tr>
<td></td>
<td>If the above requirements and those set out in Appendix D (page 122) are met, the DVLA need not be informed. The DVLA must be notified if clinical information indicates the agency may need to undertake medical enquiries.</td>
<td>- regular self-monitoring of blood glucose – at least twice daily and at times relevant to driving i.e. no more than 2 hours before the start of the first journey and every 2 hours while driving</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- demonstrates an understanding of the risks of hypoglycaemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- has no disqualifying complications of diabetes that mean a licence will be refused or revoked, such as visual field defect.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Management of Hypoglycaemia</th>
<th>Group 1 (car and motorcycle)</th>
<th>Group 2 (bus and lorry)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Excluding sulphonylureas and glinides</strong></td>
<td>May drive and need not notify the DVLA, provided the requirements set out in Appendix D (page 122) are met and the driver is under regular medical review.</td>
<td>May drive but must notify the DVLA.</td>
</tr>
<tr>
<td></td>
<td>May drive but must notify the DVLA if clinical information indicates the agency may need to undertake medical enquiries.</td>
<td>The DVLA may issue a licence if the requirements set out in Appendix D (page 122) are met and the driver is under regular medical review.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A licence is refused or revoked if relevant disqualifying complications have developed, such as diabetic retinopathy affecting visual acuity or visual fields.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A short-term licence may be issued if diabetes complications have developed but the required medical standards have been met.</td>
</tr>
</tbody>
</table>
## Diabetes managed by diet/lifestyle alone

<table>
<thead>
<tr>
<th>Group 1 car and motorcycle</th>
<th>Group 2 bus and lorry</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="https://via.placeholder.com/15" alt="Green" /> May drive and need not notify the DVLA.</td>
<td><img src="https://via.placeholder.com/15" alt="Green" /> May drive and need not notify the DVLA.</td>
</tr>
<tr>
<td><img src="https://via.placeholder.com/15" alt="Red" /> Must not drive and must notify the DVLA if, for example:</td>
<td><img src="https://via.placeholder.com/15" alt="Red" /> Must not drive and must notify the DVLA if, for example:</td>
</tr>
<tr>
<td>- relevant disqualifying complications develop such as diabetic retinopathy affecting visual acuity or visual fields</td>
<td>- relevant disqualifying complications develop such as diabetic retinopathy affecting visual acuity or visual fields</td>
</tr>
<tr>
<td>- insulin treatment is required (see the requirements for insulin-treated diabetes on page 69).</td>
<td>- insulin treatment is required (see the requirements for insulin-treated diabetes on page 69).</td>
</tr>
</tbody>
</table>

### Hypoglycaemia due to other causes

<table>
<thead>
<tr>
<th>Group 1 car and motorcycle</th>
<th>Group 2 bus and lorry</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="https://via.placeholder.com/15" alt="Red" /> If there are episodes of severe hypoglycaemia from any cause other than diabetes treatment driving must stop while the liability to episodes remains. Examples include hypoglycaemia post-bariatric surgery or in association with eating disorders, and the restriction applies for both car and motorcycle, and bus and lorry drivers.</td>
<td></td>
</tr>
</tbody>
</table>

### Pancreas transplant

<table>
<thead>
<tr>
<th>Group 1 car and motorcycle</th>
<th>Group 2 bus and lorry</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="https://via.placeholder.com/15" alt="Green" /> May drive but must notify the DVLA. Licensing is on the provision that the patient has no disqualifying condition. If the patient is on insulin, refer to page 69 for the section on insulin-treated diabetes.</td>
<td><img src="https://via.placeholder.com/15" alt="Green" /> May drive but must notify the DVLA. Licensing will require individual assessment. If the patient is on insulin, refer to page 69 for the section on insulin-treated diabetes.</td>
</tr>
</tbody>
</table>
Islet cell transplantation

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>car and motorcycle</td>
<td>bus and lorry</td>
</tr>
</tbody>
</table>

⚠️ May drive but must notify the DVLA. Licensing is on the provision that the patient has no disqualifying condition, and is issued for a term requiring medical review. If the patient is on insulin, refer to page 69 for the section on insulin-treated diabetes.

⚠️ May drive but must notify the DVLA. Licensing will require individual assessment. If the patient is on insulin, refer to page 69 for the section on insulin-treated diabetes.
INF188/2 leaflet ‘Information for drivers with diabetes’ and DIABINF leaflet ‘A guide to insulin treated diabetes and driving’

Information for drivers with diabetes treated by non insulin medication, diet, or both

Please keep this leaflet safe so you can refer to it in the future

Drivers do not need to tell us if their diabetes is treated by tablets, diet, or both and they are free of the complications listed over the page.

Some people with diabetes develop associated problems that may affect their driving.
Hypoglycaemia (low blood sugar)

Hypoglycaemia (also known as a hypo) is the medical term for a low blood glucose (sugar) level. **Severe hypoglycaemia** means the assistance of another person is required. The risk of hypoglycaemia is the main danger to safe driving and can occur with diabetes treated with insulin or tablets or both. This may endanger your own life as well as that of other road users. Many of the accidents caused by hypoglycaemia are because drivers carry on driving even though they get warning symptoms of hypoglycaemia. If you get warning symptoms of hypoglycaemia while driving you must stop as soon as safely possible — **do not ignore the warning symptoms.**

**Early symptoms of Hypoglycaemia include:**

- Sweating, shakiness or trembling, feeling hungry, fast pulse or palpitations, anxiety, tingling lips. If you don’t treat this it may result in more severe symptoms such as:
  - Slurred speech, difficulty concentrating, confusion, disorderly or irrational behaviour, which may be mistaken for drunkenness. If left untreated this may lead to unconsciousness.

**What you need to tell us about**

By law you must tell us if any of the following applies:

- You suffer more than one episode of severe hypoglycaemia within the last 12 months. You must also tell us if you or your medical team feel you are at high risk of developing severe hypoglycaemia. For Group 2 drivers (bus/lorry), one episode of severe hypoglycaemia must be reported immediately. You develop impaired awareness of hypoglycaemia. (Difficulty in recognising the warning symptoms of low blood sugar).
- You suffer severe hypoglycaemia while driving.
- You need treatment with insulin.
- You need laser treatment to both eyes or in the remaining eye if you have sight in one eye only.
- You have problems with vision in both eyes, or in the remaining eye if you have sight in one eye only. By law, you must be able to read, with glasses or contact lenses if necessary, a car number plate in good daylight at 20 metres. In addition, the visual acuity (with the aid of glasses or contact lenses if worn) must be at least 6/12 (0.5 decimal) with both eyes open, or in the only eye if monocular.
You develop any problems with the circulation, or sensation in your legs or feet which makes it necessary for you to drive certain types of vehicles only, for example automatic vehicles, or vehicles with a hand operated accelerator or brake. This must be shown on your driving licence.

An existing medical condition gets worse or you develop any other condition that may affect your driving safety. In the interests of road safety, you must be sure that you can safely control a vehicle at all times.

**How to tell us**

If your doctor, specialist or optician tells you to report your condition to us, you need to fill in a Medical Questionnaire about diabetes (DIAB1). You can download this from www.gov.uk/driving-medical-conditions

**Phone:** 0300 790 6806.

**Write to:**

Drivers Medical Group DVLA
Swansea SA99 1TU

**Useful address**

**Diabetes UK Central Office**
Macleod
House 10
Parkway
London
NW1 7AA

**Diabetes UK**
Website:
www.diabetes.org.uk

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Find out about DVLA’s online services

**Go to:** www.gov.uk/browse/driving
-The applicant or licence holder must notify DVLA unless stated otherwise in the text

DIABINF
A Guide to Insulin Treated Diabetes and Driving Drivers who have any form of diabetes treated with any insulin preparation must inform DVLA (Caveat: See Temporary Insulin Treatment)

HYPOGLYCAEMIA
Hypoglycaemia (also known as a hypo) is the medical term for a low blood glucose (sugar) level.
Severe hypoglycaemia means the assistance of another person is required.
The risk of hypoglycaemia is the main danger to safe driving and this risk increases the longer you are on insulin treatment. This may endanger your own life as well as that of other road users. Many of the accidents caused by hypoglycaemia are because drivers carry on driving even though they get warning symptoms of hypoglycaemia. If you get warning symptoms of hypoglycaemia whilst driving, you must always stop as soon as safely possible – do not ignore the warning symptoms.

EARLY SYMPTOMS OF HYPOGLYCAEMIA INCLUDE:
Sweating, shakiness or trembling, feeling hungry, fast pulse or palpitations, anxiety, tingling lips.
If you don’t treat this it may result in more severe symptoms such as:
Slurred speech, difficulty concentrating, confusion, disorderly or irrational behaviour, which may be mistaken for drunkenness.
If left untreated this may lead to unconsciousness.

DRIVERS WITH INSULIN TREATED DIABETES ARE ADVISED TO TAKE THE FOLLOWING PRECAUTIONS:

- You should always carry your glucose meter and blood glucose strips with you. You should check your blood glucose no more than 2 hours before the start of the first journey and every two hours whilst you are driving. If driving multiple short journeys, you do not necessarily need to test before each additional journey as long as you test every 2 hours while driving. More frequent testing may be required if for any reason there is a greater risk of hypoglycaemia for example after physical activity or altered meal routine. The intention is to ensure that blood glucose is always above 5.0mmol/l while driving.
- In each case if your blood glucose is 5.0mmol/l or less, take a snack. If it is less than 4.0mmol/l or you feel hypoglycaemic, do not drive.
- If hypoglycaemia develops while driving, stop the vehicle as soon as possible.
- You should switch off the engine, remove the keys from the ignition and move from the driver’s seat.
- You should not start driving until 45 minutes after blood glucose has returned to normal (confirmed by measuring blood glucose). It takes up to 45 minutes for the brain to recover fully.
- Always keep an emergency supply of fast-acting carbohydrate such as glucose tablets or sweets within easy reach in the vehicle.
- You should carry personal identification to show that you have diabetes in case of injury in a road traffic accident.
- Particular care should be taken during changes of insulin regimens, changes of lifestyle, exercise, travel and pregnancy.
- You must take regular meals, snacks and rest periods on long journeys. Always avoid alcohol.

EYESIGHT
All drivers are required by law to read, in good daylight (with glasses or corrective lenses if necessary), a car number plate from a distance of 20 metres. In addition, the visual acuity (with the aid of glasses or contact lenses if worn) must be at least 6/12 (0.5 decimal) with both eyes open, or in the only eye if monocular.

LIMB PROBLEMS
Limb problems/amputations are unlikely to prevent driving. They may be overcome by driving certain types of vehicles e.g. automatics or one with hand controls.

YOU MUST INFORM DVLA IF:

- You suffer more than one episode of severe hypoglycaemia (needing the assistance of another person) within the last 12 months. For Group 2 drivers (bus/lorry) one episode of severe hypoglycaemia must be reported immediately. You must also tell us if you or your medical team feels you are at high risk of developing hypoglycaemia.
- You develop impaired awareness of hypoglycaemia (difficulty in recognising the warning symptoms of low blood sugar)
- You suffer severe hypoglycaemia while driving.
- An existing medical condition gets worse or you develop any other condition that may affect you driving safely.

CONTACT US
Web site: www.gov.uk/browse/driving
Tel: 0300 790 6806 (8.00am to 5.30pm, Mon – Fri) & (8.00 am. to 1pm. Saturday) Write:
Drivers’ Medical Group, DVLA, Swansea SA89 1TU
For further information on diabetes visit www.diabetes.org.uk
## Appendix 5: Insulin Quantity Calculator Chart

<table>
<thead>
<tr>
<th>Daily dose</th>
<th>With air shots used when changing pen needles. Daily units</th>
<th>Number of units used per month with airshots (Pens and cartridges)</th>
<th>Number of 3ml cartridges or pens needed per monthly prescription (contain 300 units)</th>
<th>Number of units required per month with no airshot (Syringes)</th>
<th>Number of 10ml vials needed per monthly prescription (1,000 units). No airshot</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 units</td>
<td>22</td>
<td>616</td>
<td>2</td>
<td>280</td>
<td>1 will last 3</td>
</tr>
<tr>
<td>20 units</td>
<td>32</td>
<td>896</td>
<td>3</td>
<td>560</td>
<td>1</td>
</tr>
<tr>
<td>30 units</td>
<td>42</td>
<td>1176</td>
<td>4</td>
<td>840</td>
<td>1</td>
</tr>
<tr>
<td>40 units</td>
<td>52</td>
<td>1456</td>
<td>5</td>
<td>1120</td>
<td>2</td>
</tr>
<tr>
<td>50 units</td>
<td>62</td>
<td>1736</td>
<td>6</td>
<td>1400</td>
<td>2</td>
</tr>
<tr>
<td>60 units</td>
<td>72</td>
<td>2016</td>
<td>7</td>
<td>1680</td>
<td>2</td>
</tr>
<tr>
<td>70 units</td>
<td>82</td>
<td>2296</td>
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Insulin calculation will be needed for each type of insulin being used. At times of sickness, infection, pregnancy, steroid treatment more insulin will be required for that period. People with type 1 and type 2 diabetes who vary insulin dose with meals will need enough to cover the average amount taken each month. Gluco RX needles are suitable for all devices. Lengths longer than 8 mm should not be used. Skin lifts are important to inject into the subcutaneous layer of skin.
Appendix 6: Drug Safety Card INSULIN in ADULTS

<table>
<thead>
<tr>
<th>Short-acting</th>
<th>Pre-mix/biphasic</th>
<th>Intermediate</th>
<th>Long-acting</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Soluble insulins</em>&lt;br&gt;Actrapid&lt;br&gt;Humulin-S&lt;br&gt;Insuman Rapid</td>
<td><em>Biphasic</em>&lt;br&gt;NovoMix30&lt;br&gt;Humalog Mix25&lt;br&gt;Humalog Mix50&lt;br&gt;Humulin-M3&lt;br&gt;Insuman Comb15&lt;br&gt;Insuman Comb25&lt;br&gt;Insuman Comb50</td>
<td><em>Isophane insulins</em>&lt;br&gt;Insulatard&lt;br&gt;Humulin-I&lt;br&gt;Insuman Basal</td>
<td><em>Levemir (insulin detemir)</em>&lt;br&gt;<em>Lantus (insulin glargine)</em>&lt;br&gt;<em>Tresiba (insulin degludec)</em></td>
</tr>
</tbody>
</table>

*Insulin analogues*<br>Novorapid *(insulin aspart)*<br>Apidra *(insulin glulisine)*<br>Humalog *(insulin lispro)*

**STOP:** Confirm all doses greater than 25 units

**STOP:** Confirm all doses greater than 50 units

*Use 50 unit (0.5mL) insulin syringes or prefilled pens to measure doses!*
Appendix 7: Treating Hypoglycaemia

Treating hypoglycaemia = **Blood Glucose (CBG) less than 4.0 mmol/L**

**Symptoms:** sweating, tremor, tiredness, dizziness, drowsiness, confusion

**Able to swallow**
1. Give Fruit juice / oral glucose
2. Repeat CBG measurement
3. Give long-acting carbohydrate, e.g. sandwich, biscuits, fruit
4. DO NOT omit the next dose of insulin / oral anti-diabetic

**Nil by mouth**
- **CBG <3 mmol/L or symptomatic**
  - Glucagon or IV Glucose
- **CBG 3 to 3.5 mmol/L or asymptomatic**
  - Consider increasing glucose infusion rate (if applicable)
  - Recheck capillary blood glucose after 10 - 15 mins

**REVIEW insulin / oral anti-diabetic prescription**

Only if patients blood glucose is above 4 mmol/L, otherwise if able to swallow, repeat those steps, for NIL by mouth patients infusions will be adjusted accordingly.
### Appendix 8: Dual therapy

<table>
<thead>
<tr>
<th>Alphabetical</th>
<th>Acarbose</th>
<th>Alogliptin</th>
<th>Canagliflozin</th>
<th>Dapagliflozin</th>
<th>Dulaglutide</th>
<th>Exenatide</th>
<th>Exenatide MR</th>
<th>Gliclazide</th>
<th>Gliclazide MR</th>
<th>Insulin</th>
<th>Linagliptin</th>
<th>Liraglutide</th>
<th>Lixisenatide</th>
<th>Metformin</th>
<th>Metformin MR</th>
<th>Pioglitazone</th>
<th>Sitagliptin</th>
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**Key**
- X: Not licensed/not recommended
- NICE: Licensed, but not NICE approved
- LOCAL: Licensed, but not approved for use locally
- Combination licensed & can be used as per guideline
- NICE*: Combination can be used as per guideline, but outside of NICE
- Combination not appropriate
## Appendix 9: Triple therapy

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<th>Met + Pioglitazone</th>
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## Appendix 10 Optimal timings of insulins

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<th>Insulins</th>
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| Short-acting / neutral | Actrapid  
                          | Humulin S  
                          | Hypurin Bovine Neutral  
                          | Hypurin Porcine Neutral  
                          | Insuman Rapid  |
| Mixed                | Humulin M3  
                          | Hypurin Porcine 30/70 Mix  
                          | Insuman Comb 15  
                          | Insuman Comb 25  
                          | Insuman Comb 50  |
| Rapid-acting Analogue | NovoRapid  
                          | Humalog U100  
                          | Humalog U200  
                          | Apidra  |
| Medium and Long-acting | Insulatard  
                          | Humulin I  
                          | Hypurin Bovine Isophane  
                          | Hypurin Porcine Isophane  
                          | Insuman Basal  |
| Analogue Mixture     | Humalog Mix 25  
                          | Humalog Mix 50  
                          | NovoMix 30  |
| Long-acting Analogue | Lantus  
                          | Abasaglar  
                          | Leveimir  
                          | Toujeo U300  
                          | Tresiba U100  
                          | Tresiba U200 |