Key messages:

- Education and lifestyle advice are fundamental to patient management, as is overall consideration to the patient's risk of macrovascular complications and microvascular complications (e.g. glycaemic control, blood pressure management, smoking status, and cholesterol).

- A structured education programme for adults with type 2 diabetes is an integral part of diabetes care and should be offered to patients and family members/carers. (For further details of local programmes see appendix 9).

- An individualised approach to diabetes care should be tailored to the needs and circumstances of the adult with type 2 diabetes in association with patient (considerations include life expectancy, risks from polypharmacy, comorbidities etc). An adult with type 2 diabetes should be involved in the discussion about target setting.

- NICE recommends that if 2 drugs in the same class are appropriate, to choose the option with the lowest acquisition cost.

- Metformin is the most cost effective of the initial therapy treatments, and is suitable for most adults with type 2 diabetes.

- Metformin is contraindicated or not tolerated in approximately 15% of individuals but there is little evidence, for some adults, to guide management strategies on treatment combinations that do not include metformin (NICE NG28).

- Evidence for combination treatments beyond second intensification is limited (when 2 or more non-insulin based treatment combinations fail to adequately control blood glucose levels).

- There is limited emerging evidence in relation to the long-term effects of blood glucose lowering therapies, particularly newer agents in terms of efficacy and adverse events (for example, cardiovascular outcomes).

- Evidence from a meta-analysis looking at the association between the newer blood glucose lowering therapies (SGLT2 inhibitors, GLP1 agonists and DPP4i (gliptins)) with all-cause mortality, suggests SGLT-2 inhibitors or GLP-1 agonists were associated with better all-cause mortality outcomes than DPP-4 inhibitors. When moving patients to the newer agents, prescribers should consider this evidence, but individual treatment circumstances should be taken into account.

- A HBA1c reduction of 5mmol/mol (0.5%) is considered clinically important. At each review re-assess the person’s needs and circumstances and think about stopping any medicines that are not effective at 6 months. NICE recommend for continued therapy with DPP4i (gliptins) /pioglitazone / SGLT2i must show HbA1c reduction ≥5.5 mmol/mol (0.5%) in 6 months

- Routine self-monitoring of blood glucose is not recommended except for particular circumstances. E.g. insulin use, oral medication that may increase their risk of hypoglycaemia while driving or operating machinery or the person is pregnant, or is planning to become pregnant.

- Do not offer antiplatelet therapy for adults with type 2 diabetes mellitus without cardiovascular disease.

- Driving advice: this should be an individualised decision by the clinician, using the DVLA guidance (https://www.gov.uk/government/publications/at-a-glance) and advice from diabetes.org.uk.

- Patient decision aids can help patients think about their options for controlling their blood glucose to try to reduce the long-term risks of diabetes. NICE patient decision aids can be found here.
**Document updates**

<table>
<thead>
<tr>
<th>Description</th>
<th>Date updated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendices for GLP1 have been merged Pg. 26-28; Dulaglutide added to list p.28</td>
<td>July 2018</td>
</tr>
<tr>
<td>P14. dapagliflozin – renal impairment recommendations updated to reflect current SPC</td>
<td>Dec 2018</td>
</tr>
<tr>
<td>Semaglutide added p.18, 20,34</td>
<td>February 2019</td>
</tr>
<tr>
<td>Appendix 3 updated in line with current GLP1 traffic light classification</td>
<td>March 2019</td>
</tr>
<tr>
<td>Insulin glargine biosimilar (Semglee) inserted into table 1 p.23</td>
<td>May 2019</td>
</tr>
<tr>
<td>Formulary choice inserted- GlucoRx Carepoint needles/ Tee2 &amp; WaveSense Jazz BGT</td>
<td>May 2019</td>
</tr>
<tr>
<td>Insert erufiluzin prescribing information p.15; insert MHRA warning on GLP-1 receptor agonist risk of diabetic ketoacidosis when concomitant insulin was rapidly reduced or discontinued. P.17</td>
<td>June 2019</td>
</tr>
</tbody>
</table>

**NICE define**

Interventions that should be used - strong recommendation
- 'Offer' as an intervention which will do more good than harm and be cost effective, for the vast majority of patients.

Interventions that could be used:
- 'Consider' as an intervention which will do more good than harm for most patients and be cost effective, but other options may be similarly cost effective

**Key**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI</td>
<td>Angiotensin converting enzyme inhibitor</td>
</tr>
<tr>
<td>ARB</td>
<td>Angiotensin receptor blockers</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CCB</td>
<td>Calcium channel blocker</td>
</tr>
<tr>
<td>DPP4i</td>
<td>Dipeptidyl peptidase-4 inhibitor ('gliptin')</td>
</tr>
<tr>
<td>DVLA</td>
<td>Driver and vehicle licensing agency</td>
</tr>
<tr>
<td>eGFR</td>
<td>Estimated glomerular filtration rate</td>
</tr>
<tr>
<td>GI</td>
<td>Gastro-intestinal</td>
</tr>
<tr>
<td>GLP1</td>
<td>Glucagon-like peptide-1 mimetic</td>
</tr>
<tr>
<td>HbA1c</td>
<td>Glycated haemoglobin</td>
</tr>
<tr>
<td>HF</td>
<td>Heart failure</td>
</tr>
<tr>
<td>Met</td>
<td>Metformin</td>
</tr>
<tr>
<td>NG</td>
<td>National guidance</td>
</tr>
<tr>
<td>PDE5i</td>
<td>Phosphodiesterase type 5 inhibitor</td>
</tr>
<tr>
<td>Pio</td>
<td>Pioglitazone</td>
</tr>
<tr>
<td>SGLT2i</td>
<td>Sodium-glucose cotransporter 2 inhibitor</td>
</tr>
</tbody>
</table>

**Reference**

NICE NG28 Type 2 diabetes in adults: management (2015)
SIGN 154 Pharmacological management of glycaemic control in people with type 2 diabetes (2017)

**Consultee**

Dr Frances Game Consultant Diabetes & Endocrinology RDH
Dr Robinson Consultant Endocrinologist CRH
Derbyshire Medicines Management Guideline Group
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Antihypertensive drug treatment – Type 2 Diabetes

**BP targets for diabetics with hypertension**
- People with diabetes: < 140/80 mmHg
- People with retinopathy or cerebral vascular disease or with microalbuminuria: < 130/80 mmHg

**BP monitoring for diabetics**
- Annually BP measurement for adults with T2DM without previously diagnosed hypertension or renal disease.
- Repeat BP measurements (adding or intensifying treatment as appropriate):
  - Within 1 month if BP > 150/90
  - Within 2 months if BP > 140/80
  - Within 2 months if BP > 130/80 and there is kidney/eye or cerebrovascular damage.
- Reinforce preventative lifestyle advice, at every given opportunity.

**Measure BP annually if not hypertensive or renal disease**
- If > 140/80 mmHg confirm consistently raised
- Above target
  - Trial lifestyle measures alone unless > 140/90 mmHg
  - Above target
    - ACEi
      - If African-Caribbean: ACEi + diuretic or CCB
      - If women with possibility of pregnancy: CCB
    - Above target
      - Add CCB (amlodipine) or diuretic (bendroflumethiazide*)
    - Above target
      - Add diuretic (bendroflumethiazide*) or CCB (amlodipine)
    - Above target
      - Add α-blocker, β-blocker, or potassium-sparing diuretic
    - Above target
      - Add α-blocker, β-blocker, or potassium-sparing diuretic, or refer to specialist

*thiazide-like diuretics are 2nd line options after bendroflumethiazide. Indapamide 2.5mg and modified release have been classified as brown.
**TREATMENT ALGORITHM FOR TYPE 2 DIABETES IN ADULTS**

Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preference.

**Initiation of lifestyle and diet intervention:** Refer to structured education programme. (See appendix 9 for further details)

**Aim for HbA1c – 48mmol/mol (6.5%)**

**MONOTHERAPY**

Move to this step if HbA1c rises above 48mmol/mol (6.5%) with lifestyle alone

**START METFORMIN**

Slow titration over several weeks (if intolerance develops due to side effects consider the modified release formulation)

(Preferred cost effective modified release brand – Sukkarto)

**Dual therapy options:**

- Metformin + Gliclazide
- Metformin + alogliptin**
- Metformin + empagliflozin
- Metformin + ‘pio’

**MONOTHERAPY**

- Met + Insulin
- Met + GLP1
- Met + SGLT2
- Met + Pio
- Met + Gli

**FIRST INTENSIFICATION**

(dual therapy)

Consider moving to this step if HbA1c ≥58mmol/mol (7.5%) (or individualised target not met)

- Triple therapy options:
  - Met + Glic + alogliptin**
  - Met + Glic + empagliflozin
  - Met + ’pio’ + empagliflozin
  - Insulin therapy

**SECOND INTENSIFICATION**

(triple therapy or insulin)

Consider moving to this step if HbA1c ≥58mmol/mol (7.5%) (or individualised target not met)

- Triple therapy options:
  - Met + Glic + GLP-1 (lixisenatide)** if BMI≥35kg/m² AND specific psychological or other medical problems associated with obesity or BMI<35kg/m² AND insulin therapy would have significant occupational implications OR weight loss would benefit other significant obesity-related morbidities.

- GLP-1 + insulin

Only offer GLP1 in combination with insulin with specialist care advice and on-going support from a consultant-led service.

**EVIDENCE FROM A META-ANALYSIS LOOKING AT THE ASSOCIATION BETWEEN THE NEWER BLOOD GLUCOSE LOWERING THERAPIES (SGLT2 inhibitors, GLP1 agonists and DPP4 inhibitors) WITH ALL-CAUSE MORTALITY, SUGGESTS SGLT2 inhibitors or GLP-1 agonists were associated with better all-cause mortality outcomes than DPP-4 inhibitors. When moving patients to the newer agents, prescribers should consider this evidence, but individual treatment circumstances should be taken into account.

**Comparison of efficacy, hypoglycaemia, weight, side effects and cost for metformin-based combinations.**

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Efficacy (HbA1c)</th>
<th>Hypoglycaemia</th>
<th>Weight</th>
<th>Side effects</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>High</td>
<td>Low risk</td>
<td>Neutral /loss (~ 0.5kg)</td>
<td>Gl. lactic acidosis</td>
<td>Low</td>
</tr>
<tr>
<td>Met + Gli</td>
<td>High</td>
<td>Moderate risk</td>
<td>Gain (~ 1.5 -2kg)</td>
<td>Hypoglycaemia</td>
<td>Low</td>
</tr>
<tr>
<td>Met + Pio</td>
<td>High</td>
<td>Low risk</td>
<td>Gain (~ 4 -5kg)</td>
<td>Oedema, HF, fractures</td>
<td>Low</td>
</tr>
<tr>
<td>Met + DPP4i (Gliptin)</td>
<td>Intermediate</td>
<td>Low risk</td>
<td>Neutral</td>
<td>Rare</td>
<td>High</td>
</tr>
<tr>
<td>Met + SGLT2</td>
<td>Intermediate</td>
<td>Low risk</td>
<td>Loss (~2kg)</td>
<td>GU infections, dehydration</td>
<td>High</td>
</tr>
<tr>
<td>Met + GLP1</td>
<td>High</td>
<td>Low risk</td>
<td>Loss (~1 - 3kg)</td>
<td>Gl</td>
<td>High</td>
</tr>
<tr>
<td>Met + insulin</td>
<td>Highest</td>
<td>High risk</td>
<td>Gain (~ 4 -5kg)</td>
<td>Hypoglycaemia</td>
<td>Variable</td>
</tr>
</tbody>
</table>

NICE recognise that repaglinide is both clinically effective and cost effective in adults with type 2 diabetes.

**MANAGEMENT OF TYPE 2 DIABETES**

First produced: June 2009 Updated: July 2018
Review date: June 2020
Page 5 of 37
Treatment algorithm for type 2 diabetes if metformin is contra-indicated or not tolerated

Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preference.

Initiation of lifestyle and diet intervention: Refer to structured education programme. (See appendix 9 for further details)

Aim for HbA1c < 48mmol/mol (6.5%) if on alogliptin or
- 53mmol/mol (7%) if on Gliclazide (or individualised target not met)

FIRST INTENSIFICATION
(dual therapy without metformin)

Move to this step if HbA1c ≥ 58mmol/mol/7.5% (or individualised target not met)

SECOND INTENSIFICATION
(without metformin)

Move to this step if HbA1c ≥ 58mmol/mol/7.5% (or individualised target not met)

Consider Insulin-based treatment

Insulin-based treatment
- Review continued need for other hypoglycaemics.
- Offer NPH insulin once or twice daily according to need.
- Consider starting both NPH + short-acting insulin separately or as biphasic human insulin (particularly if HbA1c ≥ 75mmol/mol (9%); consider biphasic preparations containing a short-acting insulin analogue if persons prefer injecting immediately before a meal, hypoglycaemia is a problem or blood glucose levels rise markedly after meals).

If metformin is CI or not tolerated, repaglinide is both clinically effective and cost effective in adults with type 2 diabetes. However discuss with any person for whom repaglinide is being considered, that there is no licensed non-metformin-based combination containing repaglinide that can be offered at first intensification. (Maybe appropriate for people who have irregular meals or if mealtimes are unpredictable. Use should be limited mainly to early diabetes when the patient is still producing a reasonable amount of endogenous insulin).

Comparison of efficacy, hypoglycaemia, weight, side effects and cost for Gliclazide-based combinations.

<table>
<thead>
<tr>
<th></th>
<th>Efficacy (HbA1c)</th>
<th>Hypoglycaemia</th>
<th>Weight</th>
<th>Side effects</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gliclazide</td>
<td>High</td>
<td>Moderate risk</td>
<td>Gain (~1.5 – 2kg)</td>
<td>Hypoglycaemia</td>
<td>Low</td>
</tr>
<tr>
<td>Glic + met</td>
<td>High</td>
<td>Moderate risk</td>
<td>Gain (~1.5 -2kg)</td>
<td>Hypoglycaemia</td>
<td>Low</td>
</tr>
<tr>
<td>Glic + DPP4i (gliptin)</td>
<td>Mid</td>
<td>Moderate risk</td>
<td>Neutral</td>
<td>Rare</td>
<td>High</td>
</tr>
<tr>
<td>Glic + pio</td>
<td>High</td>
<td>Moderate risk</td>
<td>Gain (~ 4- 5kg)</td>
<td>Oedema, HF, fractures</td>
<td>Low</td>
</tr>
<tr>
<td>Glic + GLP1</td>
<td>High</td>
<td>Moderate risk</td>
<td>Loss (~1 -3 kg)</td>
<td>GL</td>
<td>High</td>
</tr>
<tr>
<td>Glic + insulin</td>
<td>Highest</td>
<td>High risk</td>
<td>Gain (~ 4 - 5kg)</td>
<td>Hypoglycaemia</td>
<td>Variable</td>
</tr>
</tbody>
</table>

Alternative to NPH insulin:
- Insulin detemir or glargine if person needs assistance to inject insulin, lifestyle restricted by recurrent symptomatic hypoglycaemia or would otherwise need twice daily NPH insulin + oral hypoglycaemics.
- Offer insulin + GLP1 agonist only with specialist advice and consultant-led multidisciplinary support.
- An SGLT2 inhibitor + insulin +/- other antidiabetic drugs is an option after consultant/specialist initiation and assessment.
Scope of guideline
This guideline primarily considers drug treatments used in type 2 diabetes. It does not address the management of impaired glucose tolerance, impaired fasting glucose, type 1 diabetes or diabetes in pregnancy.

Management of diabetes requires a multifactorial approach in its management
Diabetes is a complex condition which requires regular monitoring. NICE recommend that patients with diabetes should receive the following nine key tests/processes done at least once a year:

- Weight (aim: health weight between a BMI of 18.5 – 24.9kg/m²). Overweight patients should aim for a 5-10% target loss.
- Blood pressure (aim: <140/80mmHg or <130/80mmHg with evidence of kidney, eye or CV damage)
- Smoking status
- HbA1c (tailored to individual needs)
- Urinary albumin (Aim: <2.5mg/mol for men, <3.5mg/mmol for women)
- Serum Creatinine (>150 micromol/L – discontinue metformin)
- Cholesterol (See section 6)
- Eye examination
- Foot examination (Risk scored as low, moderate and high)

The relative benefit of different treatments.
People with diabetes have a greater chance of developing a variety of complications and health problems, especially if their blood glucose is not well managed. Good glycaemic control will reduce the incidence of micro and macrovascular complications such as blindness, kidney failure and lower limb amputation.

However lifestyle advice, blood pressure monitoring and control of cholesterol level are essential components in the management of type 2 diabetes; blood glucose control is less effective in reducing cardiovascular disease when compared to blood pressure or cholesterol lowering, as demonstrated in the chart below.

The table/chart below shows for every 1000 people (similar to those recruited to major trials) treated with more intensive blood glucose control (HbA1c reduction of 0.9 percentage points) only about eight would avoid a cardiovascular event, compared with 23 in every 1000 whose cholesterol is reduced by 1mmol/L and about 29 in every 1000 whose blood pressure is reduced by 10/5mmHg.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Number of cardiovascular events prevented for every 1000 people treated over 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowering blood sugar by 0.9%</td>
<td>8</td>
</tr>
<tr>
<td>Lowering cholesterol by 1mmol/L</td>
<td>23</td>
</tr>
<tr>
<td>Reducing BP by 10/5</td>
<td>29</td>
</tr>
</tbody>
</table>

Relationship of reductions in cholesterol, blood pressure and HbA1c with improvements in CHD and CV outcomes
Young adults

It should be noted that young adults who develop type 2 diabetes have significantly elevated mortality, up to six times higher than age matched controls and double that of age matched peers with type 1 diabetes. Anyone with diabetes, whether type 1 or type 2, under the age of 25 years should be referred into the young adult diabetes clinic.

Factors to consider when setting a HbA1c target between the clinician and patient

The diagram below is a depiction of the elements of decision making used to determine appropriate efforts to achieve glycaemic targets. Greater concerns about a particular domain are represented by increasing height of the ramp. Thus characteristics /predicaments towards the left justify more stringent efforts to lower HbA1c, whereas those towards the right are compatible with less stringent efforts. Where possible such decisions should be made in conjunction with the patient, reflecting his or her preferences, needs and values.

![Diagram](image)

This "scale" is not designed to be applied rigidly but to be used as a broad construct to help guide clinical decisions. (Adapted from Silvio E. Inzucchi et al. Dia Care 2015; 38:140-149).

Targets

When setting a target HbA1c level, NICE recommends to:

- Involve patients with type 2 diabetes in the decision regarding individual HbA1c targets. Encourage them to achieve and maintain their targets unless any resulting adverse effects or their efforts to achieve their target impair their quality of life. (See diabetes algorithm on p5 for recommended target levels)
- Consider relaxing target HbA1c level on a case-by-case basis, with particular consideration for patients who are older or frail.
- Inform a person with a higher HbA1c that any reduction in HbA1c towards the agreed target is advantageous to future health.
- If adults achieve a HbA1c level below target and if you are certain that the patient is not experiencing hypoglycaemia, encourage them to maintain it.
- Avoid pursuing highly intensive management to levels below 42mmol/mol (6.0%).

Patient decision aids can help adults with type 2 diabetes think about their options for controlling their blood glucose to try to reduce the long-term risks of diabetes. NICE patient decision aids can be found here.
Management strategies

Individualised care
Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preferences. An example of individualised treatment options is to consider the ABCD approach -

- **Age** - less stringent HbA1c targets with decreasing life expectancy;
- **Body weight**. Be aware of which drugs affect body weight – weight neutral – metformin and DPP4i (gliptins), weight gain – insulins, pioglitazone, sulphonylueas, weight loss – SGLT I and GLP1.
- **Complications** – co-incident complications will impact drug selection e.g. patient with eGFR< 30ml/min/1.73m² should avoid metformin.
- **Duration** – disease duration is a consideration when setting HbA1c levels. The shorter the disease duration the greater the cardiovascular protection offered by strict glycaemic control. Once disease duration is 10-12 years the beneficial effects of strict glycaemic control may be lost or reversed.

- Reassess the person’s needs and circumstances at each review and consider discontinuing any medicines that are not effective.
- Be aware of AKI, diabetes and sick day rules. See also think kidney.

Patient education
- Offer therapy (lifestyle and medication) to help achieve and maintain the HbA1c target level.
- Offer structured education to adults with type 2 diabetes and/or their family members/carers (as appropriate) at diagnosis, with annual reinforcement and review. Explain that structured education is an integral part of diabetes care.

Dietary advice
- Provide individualised and on-going nutritional advice from a healthcare professional with specific expertise and competencies in nutrition.
- Integrate dietary advice with a personalised diabetes management plan, including other aspects of lifestyle modification, such as increasing physical activity and losing weight.
- For recommendations on lifestyle advice see NICE guidelines on: preventing excess weight gain, weight management, obesity, physical activity, smoking: brief interventions and referrals, stop smoking services, smoking: harm reduction and smoking: acute, maternity and mental health services.

Physical Activity
- Exercise is associated with improved glucose control and lower cardiovascular mortality. Individuals should be encouraged to perform at least 150 minutes (2.5 hours) of moderate intensity physical activity in bouts of 10 minutes or more over a week.
- Individuals should be encouraged to minimise the amount of time spent being sedentary (sitting) for extended periods. (NICE PH44).

Bariatric surgery
Consider bariatric surgery as an option for people with a BMI ≥35 and significant co-morbidities as long as they are also receiving assessment through a tier 3 service (or equivalent).

Blood Pressure (BP) management (See p4 for treatment algorithm of BP)
- Measure blood pressure at least annually in adults with T2DM without previously diagnosed hypertension or renal disease. Consider measuring BP using ambulatory BP monitoring.
- Repeat BP measurements (adding or intensifying treatment as appropriate):
  - Within 1 month if BP> 150/90
  - Within 2 months if BP>140/80
  - Within 2 months if BP>130/80 and there is kidney/eye or cerebrovascular damage.
  - Reinforce preventative lifestyle advice, at every given opportunity.
- Reinforce lifestyle/dietary advice for the management of blood pressure.
- Add medications if lifestyle advice does not reduce blood pressure to<140/80mmHg (<130/80mmHg if there is kidney, eye or cerebrovascular damage)
- 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.
Lipid management
Patients with Type 2 diabetes are considered to be at high risk of cardiovascular disease, requiring prevention therapies. Risk assess the patient for eligibility for statin therapy using QRISK 2. See Lipid modification guidance for further details.

Anti-platelet therapy
Do not offer antiplatelet therapy (aspirin or clopidogrel) for adults with type 2 diabetes without cardiovascular disease.

HbA1c measurement
NICE recommends the following frequencies for the measurement of HbA1c; however local advice is to tailor measurements according to the individual’s needs.

<table>
<thead>
<tr>
<th>In adults with type 2 diabetes measure HbA1c levels at:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 3-6 monthly intervals until the HbA1c is stable on unchanging therapy</td>
</tr>
<tr>
<td>• 6 monthly interval once the HbA1c level and blood glucose lowering therapy are stable</td>
</tr>
</tbody>
</table>

If HbA1c remains above target levels, but pre-meal self-monitored glucose levels are well controlled, consider self-monitoring to detect postprandial hyperglycaemia and manage this if detected.

If HbA1c monitoring is suspected to be inaccurate (because of disturbed erythrocyte turnover or abnormal haemoglobin type), seek advice from a diabetologist, clinical biochemistry or appropriate specialist if required.

Self-monitoring of blood glucose (SMBG)

NICE recommendations
Do not routinely offer SMBG for adults with type 2 diabetes unless:
- the person is on insulin or
- there is evidence of hypoglycaemic episodes or
- the person is on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery or
- the person is pregnant, or is planning to become pregnant.

Consider short-term SMBG levels (and review treatment as necessary):
- When starting treatment with oral or intravenous corticosteroids or
- To confirm suspected hypoglycaemia

Be aware that adults with type 2 diabetes who have acute intercurrent illness are at risk of worsening hyperglycaemia and review their treatment as necessary.

Preferred formulary choices
See Blood glucose monitoring meter formulary
- Tee 2+
- WaveSense JAZZ

If none of the above is suitable for clinical reasons, then any meter with blood glucose test strips costing less than £9 for 50 are recommended for patients with type 2 diabetes or gestational diabetes.

Blood glucose testing for people with diabetes who drive
See chapter 3 “Assessing fitness to drive - guide for medical professionals” for further guidance.

Preconception advice
NICE recommend all women of child bearing age should regularly be informed that establishing good glycaemic control before conception and continuing this throughout pregnancy will reduce the risk of miscarriage, congenital malformation, stillbirth and neonatal death. It is important to explain that risks can be reduced but not eliminated. www.nice.org.uk/diabetes and pregnancy

For HBA1c targets for women with T2DM who are pregnant or planning to be pregnant see NICE guideline on diabetes in pregnancy.
### Oral hypoglycaemic agents

Please check full specific product characteristics for more detailed and current information. [http://www.medicines.org.uk/emc/](http://www.medicines.org.uk/emc/)

#### BIGUANIDES – METFORMIN

*Decreases gluconeogenesis and increases peripheral utilisation of glucose*

<table>
<thead>
<tr>
<th>Traffic light status</th>
<th>Standard release</th>
<th>Modified release GREEN 2nd line</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GREEN 1st line</strong></td>
<td></td>
<td>If standard-release metformin is not tolerated due to GI side effects consider a trial of modified-release metformin tablets <em>(Sukkarto SR is the preferred, cost-effective choice)</em></td>
</tr>
</tbody>
</table>

**Regimen**

- Take with meals and **start low and go slow**.
- 500mg OD for at least 1 week, then increase in 500mg steps at weekly intervals to highest tolerated dose or maximum dose.
- Maximum dose in BNF is 2g/day, but doses up to 3g/day are commonly used in clinical practice. There is additional glucose lowering benefit by increasing doses from 2 to 3g/day, although the UKPDS used a dose of metformin of 1700mg in the morning and 850mg in the evening.
- Titrate dose over several weeks to minimise risk of gastro-intestinal side effects. N.B. often side effects settle after approximately one week.

**Place in therapy**

- First line choice for all patients

**Advantages**

- Long-term safety data - strong evidence for the beneficial cardiovascular effect of metformin; Low risk of hypoglycaemia; weight loss
- Review metformin dose if the eGFR is below 45 ml/min/1.73-m²
- Stop the metformin if the eGFR is below 30 ml/minute/1.73-m².
- Prescribe metformin with caution for those at risk of a sudden deterioration in kidney function and those at risk of eGFR falling below 45ml/min/1.73-m².

**Renal impairment**

- (NICE CG87) The benefits of metformin therapy should be discussed with a person with mild to moderate liver dysfunction or cardiac impairment so that:
  - due consideration can be given to the cardiovascular-protective effects of the drug
  - an informed decision can be made on whether to continue or stop the metformin

**Hepatic impairment**

- Lactic acidosis is a rare, but serious (high mortality in the absence of prompt treatment) metabolic complication that can occur due to metformin accumulation. Reported cases of lactic acidosis in patients on metformin have occurred primarily in diabetic patients with significant renal failure.

#### SULFONYLUREAS- GLICLAZIDE

*Augments insulin secretion and consequently is only effective when some residual pancreatic beta-cell activity is present*

<table>
<thead>
<tr>
<th>Traffic light status</th>
<th>GREEN 1st line</th>
<th>(Gliclazide MR is classified as BROWN. This preparation is more costly than the immediate release preparation. The MR preparation may be beneficial for patients with compliance problems requiring once daily dosing.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GREEN 2nd line</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Regimen**

- Initially, 40-80mg daily, adjusted according to response; up to 160mg as a single dose with breakfast. Maximum dose 320mg daily.
- Increase the dose every 4-6 weeks to achieve glycaemic target or maximal dose is reached.

**Place in therapy**

- Consider a sulfonylurea as an option for first-line glucose lowering therapy if:
  - the person is underweight
  - the person does not tolerate metformin (or it is contraindicated) or
  - a rapid response to therapy is required because of hyperglycaemic symptoms.

- Consider adding a sulfonylurea at the first intensification when blood glucose control remains or becomes inadequate with metformin.
- Continue with a sulfonylurea if blood glucose control remains or becomes inadequate and another oral glucose-lowering medication is added.

**Advantages**

- Long-term safety data - no significant concerns identified

**Renal impairment**

- Used with care in those with mild to moderate renal impairment due to hazard of hypoglycaemia. Avoid in severe renal impairment and hepatic insufficiency.

**Adverse effects**

- Risk of hypoglycaemia: Weight gain (a few kilograms)

**Warning**

- Drivers need to be particularly careful to avoid hypoglycaemia and should be warned of the problems. See [Fitness to drive document](http://www.medicines.org.uk/emc/) and [http://www.diabetes.org.uk/](http://www.diabetes.org.uk/) website for the latest recommendations.
- Group 1 drivers (car/motorcycle) - it may be appropriate to monitor blood glucose at times relevant to driving to enable the detection of hypoglycaemia.
- Group 2 drivers (bus/lorry) are required to monitor glucose level at least twice daily and at times relevant to driving.
**THIAZOLIDINEDIONE- PIOGLITAZONE**  
Reduces peripheral insulin resistance, leading to a reduction of blood glucose concentration

<table>
<thead>
<tr>
<th>Traffic light status</th>
<th>BROWN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Regimen</strong></td>
<td>Initially 15-30mg once daily, adjusted according to response to 45mg once daily. In elderly patients, initiate with lowest possible dose and increase gradually; review treatment after 3-6 months and regularly thereafter.</td>
</tr>
</tbody>
</table>

| Place in therapy | NICE NG28 Recommends use of pioglitazone in patients as an option:  
- initial drug treatment (if metformin is contraindicated or not tolerated)  
- at first intensification in combination with metformin or  
- at first intensification with a DPP4i (gliptin) or SU (if metformin is CI or not tolerated)  
- at second intensification if dual therapy has achieved desired HbA1c, in combination with metformin and SU  
Continue pioglitazone therapy only if there is a reduction of $\geq 5.5$mmol/mol (0.5% points) in HbA1c in 6 months |

| C/I | Do NOT start or continue pioglitazone in people who:  
- have heart failure (NYHA class I-IV) or a history of heart failure  
- diabetic ketoacidosis  
- are at a higher risk of fracture  
- macula oedema  
- hepatic impairment  
- current bladder cancer or a history of bladder cancer. See [MHRA safety update](#)  
- patients with uninvestigated macroscopic or microscopic haematuria |

| Renal impairment | No dosage adjustment is necessary in patients with impaired renal function (CrCL $>$4ml/mim) |

| Adverse effects | Risk of hypoglycaemia – rare **Weight change - gain** |

| Monitoring | Baseline - weight and LFTs. |

**Long-term safety data** - concerns about bladder cancer, heart failure and fractures (use with caution in elderly where these issues are all more common)  

**Lack of outcome data**  
Discuss the potential benefits and risks of treatment with pioglitazone with the person to enable them to make an informed decision.  
Warn a person prescribed pioglitazone about the possibility of significant oedema and advise on what action to take if it develops.  
Pioglitazone should be used in patients at significant risk of hypoglycaemia or who are intolerant or contra-indicated to metformin or a sulfonylurea when used in combination.  
Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for the development of cardiac failure. If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain, and oedema.  
See [MHRA risk of cardiac failure when combined with insulin](#).
DPP-4 INHIBITORS (GLIPTINS)
Inhibit dipeptidylpeptidase-4 to increase insulin secretion and lower glucagon secretion

<table>
<thead>
<tr>
<th>Traffic light status</th>
<th>Alogliptin</th>
<th>Linagliptin</th>
<th>Sitagliptin</th>
<th>Saxagliptin</th>
<th>Vildagliptin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GREEN</strong> Preferred 1st line DPP4i</td>
<td>Inhibit dipeptidylpeptidase-4 to increase insulin secretion and lower glucagon secretion.</td>
<td>Inhibits dipeptidylpeptidase-4 to increase insulin secretion and lower glucagon secretion.</td>
<td>Alternative 1st line choice in renal and hepatic impairment.</td>
<td>By exceptionality defined as intolerance to the preferred first line choices or restricted by their licensing.</td>
<td><strong>BROWN</strong></td>
</tr>
<tr>
<td>Regimen</td>
<td>25mg od</td>
<td>5mg od</td>
<td>100mg od</td>
<td>5mg od</td>
<td>50mg bd</td>
</tr>
</tbody>
</table>

**Place in therapy**
NICE NG28 recommends DPP4i as monotherapy, dual therapy (DPP4i + met or SU or Pio) and triple therapy (DPP4i + Met + SU).

**HOWEVER JAPC ADVICE:**
There is a lack of outcome data for these drugs; circumstances for use of DPP4i should follow as per diabetes management flowchart on page 5 and 6. Potential exceptions include:
- When the aim of treatment is to control symptoms of hyperglycaemia in the short term and in whom prevention of long term diabetes complications is not an issue (e.g. a symptomatic elderly patient, for whom hypoglycaemia is a problem and where insulin is impracticable)
- Treatment with a thiazolidinedione is not ideal due to: risk of further weight gain; thiazolidinedione contraindicated or not tolerated.

**DPP4i should only be continued if there is a reduction of ≥5.5mmol/mol (0.5% points) in HbA1c in 6 months.**

**Advantages**
Low risk of hypoglycaemia, (however hypoglycaemia may occur when used in combination with sulphonylurea therapy), generally DPP4i are weight neutral and similar HbA1c reduction to pioglitazone.

**Contraindications**
- Ketoacidosis
- Congestive HF of NYHA, class III-IV, due to limited experience in this population

**Renal function**
Reduce dose - 12.5mg od if eGFR 30-50ml/min/1.73m²
Reduce dose to 6.25mg od if eGFR <30ml/min/1.73m².
Reduce dose - 50mg od if eGFR <30ml/min/1.73m²
Reduce dose 25mg od if eGFR <30ml/min/1.73m²

**Hepatic function**
Avoid in severe hepatic impairment (Child-Pugh score >9)
No dose adjustment is required for patients with hepatic impairment
Not studied in severe hepatic impairment therefore care should be exercised
Use with caution in moderate impairment
Avoid in severe impairment
Avoid in hepatic impairment

**Adverse effects**
Abdominal pain, gastro-oesophageal reflux and upper respiratory tract infection.
Nasopharyngitis and cough
GI disturbances, pain, peripheral oedema and upper respiratory tract infection
Dizziness, dyspepsia, gastroenteritis, upper respiratory tract infection and UTI
Rare reports of liver dysfunction discontinue if jaundice or other signs of liver dysfunction occur.

**Monitoring**
Baseline renal function before commencing treatment and periodically thereafter is recommended.
Baseline renal function before commencing treatment and periodically thereafter is recommended.
Baseline renal function before commencing treatment and periodically thereafter is recommended.
Baseline renal function before commencing treatment and periodically thereafter is recommended.

**Warning**
The FDA, August 2015 have issued a warning that DPP-4 inhibitors may cause joint pain that can be severe and disabling. Health care professionals should consider discontinuation of therapy with this class of drugs if severe and persistent joint pain occurs.
The MHRA, (Sept 2012) have issued a warning that DPP-4 inhibitors and risk of acute pancreatitis. Discontinue treatment if symptoms of acute pancreatitis occur (persistent, severe abdominal pain)
The FDA, April 2016 has added warnings about heart failure risk to labels of medicines containing saxagliptin and alogliptin as a safety review they conducted found that they may increase the risk in patients with heart/kidney disease.

Management of Type 2 Diabetes
First produced: June 2009 Updated: July 2018
Review date: June 2020
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**SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITOR**

Reversibly inhibits sodium-glucose co-transporter-2 (SGLT2) in the renal proximal convoluted tubule to reduce glucose reabsorption and increase urinary glucose excretion.

**Dapagliflozin, canagliflozin and empagliflozin are licensed for monotherapy and in combination with other glucose-lowering agent.**

<table>
<thead>
<tr>
<th>Traffic light status</th>
<th>Empagliflozin</th>
<th>Canagliflozin</th>
<th>Dapagliflozin</th>
<th>Ertugliflozin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Regimen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Starting dose: 10mg od</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can be increased to: 25mg od*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NICE guidance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NICE TA336 - Empagliflozin in combination therapy for treating type 2 diabetes. (March 2015)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can be increased to: 15mg od if additional glycaemic control is needed.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Place in therapy as per NICE**

| Monotherapy | Y | Y | Y | Y |
| Dual therapy (+Met) | | | | |
| Triple therapy (+met &SU or + met &glitazone) | Y | Y | Y (+ met & SU only) | Y |
| With insulin (± other antidiabetics) | Y | Y | Y | Y |
| Advantages | Y | Y | Y | Y |
| Contraindications | Y | Y | Y | Y |
| Renal function | Y | Y | Y | Y |

| **Monotherapy** | NICE TA390-Canagliflozin, dapagliflozin and empagliflozin as monotherapies are recommended as options for treating type 2 diabetes in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if: |
|                | • a DPP4i (gliptin) would otherwise be prescribed and |
|                | • a sulfonylurea or pioglitazone is not appropriate. |
| Dual therapy (+Met) | | | | |
| Triple therapy (+met &SU or + met &glitazone) | | | | |
| With insulin (± other antidiabetics) | | | | |
| Advantages | No hypoglycaemia, weight loss (~2kg stabilising over 6-12 months) and lowering of systolic and diastolic blood pressure in the order of ~ 2-4 / ~ 1-2mmHg. (Silvio E. Inzucchi et al. Dia Care 2015; 38:140-149) |
| Contraindications | Diabetic ketoacidosis |
| Renal function | No dose adjustment is required for patients with an eGFR ≥60ml/min/1.73m² or CrCl ≥60ml/min. In patients tolerating empagliflozin whose eGFR falls persistently below 60 Canagliflozin should not be initiated in patients with an eGFR < 60mL/min/1.73 m² or CrCl < 60 mL/min. In patients tolerating canagliflozin Dapagliflozin should not be initiated in patients with GFR < 60 mL/min and should be discontinued at GFR persistently below 45 mL/min (SPC) Ertugliflozin should not be initiated in patients with eGFR<60ml/min/1.73m² or CrCL <60ml/min. Discontinued when eGFR is | Ketoacidosis |
| NICE guidance | Same as other SGLT2i |

---

*Table continued...*
<table>
<thead>
<tr>
<th>Hepatic function</th>
<th>Avoid use in severe hepatic impairment</th>
<th>Avoid use in severe hepatic impairment</th>
<th>Initial dose 5mg daily in severe impairment, increased according to response.</th>
<th>No dosage adjustment is necessary in patients with mild or moderate hepatic impairment. Avoid use in severe hepatic impairment.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse effects</td>
<td>Hypoglycaemia in combination with insulin or a sulfonylurea, vulvovaginal candidiasis, urinary tract infection and polyuria or pollakiuria, genital infection</td>
<td>Hypoglycaemia in combination with insulin or a sulfonylurea, vulvovaginal candidiasis, UTI, polyuria, genital infections and nausea.</td>
<td>Hypoglycaemia (when used with a sulfonylurea or insulin), urinary tract and genital infection, back pain, dysuria, polyuria, dyslipidaemia and elevated haematocrit.</td>
<td>Hypoglycaemia, vulvovaginal mycotic infection and other female and male genital mycotic infections. Volume depletion, increased urination, vulvovaginal pruritus, thirst, serum lipid changes, haemoglobin increased.</td>
</tr>
<tr>
<td>Long-term data</td>
<td>Long-term safety data – concerns about diabetic ketoacidosis at only moderately elevated blood sugars, limited long-term data.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring (SPC advice on renal function)</td>
<td>Prior to empagliflozin initiation and periodically during treatment, i.e. at least yearly. Prior to initiation of any concomitant medicinal product that may have a negative impact on renal function.</td>
<td>Prior to initiation of canagliflozin and at least annually, thereafter. Prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter. For renal function approaching moderate renal impairment, at least 2 times to 4 times per year.</td>
<td>Prior to initiation of dapagliflozin and at least yearly, thereafter. Prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter. For renal function approaching moderate renal impairment, at least 2 to 4 times per year.</td>
<td>Prior to initiation and periodically thereafter. More frequently in patients with an eGFR &lt;60ml/min/1.73m² or a CrCl &lt;60ml/min.</td>
</tr>
</tbody>
</table>
**Warning**

**MHRA, April 2016** - SGLT2 inhibitors (canagliflozin, dapagliflozin and empagliflozin) used in type 2 diabetes, may lead to **ketoacidosis**, a serious condition where the body produces high levels of blood acids – ketones that may require hospitalisation.

When treating patients who are taking an SGLT2 inhibitors:
- Test for raised blood ketones in patients with symptoms of diabetic ketoacidosis (DKA); omitting this test could delay diagnosis of DKA.
- If you suspect DKA, stop SGLT2 inhibitor treatment.
- Do not restart treatment with any SGLT2 inhibitor in patients who experienced DKA during use, unless another cause for DKA was identified and resolved.
- If DKA is confirmed, take appropriate measures to correct the DKA and to monitor glucose levels.
- Inform patients of the symptoms and signs of DKA (e.g. nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness); advise them to get immediate medical help if these occur.
- Interrupt treatment with the SGLT2 inhibitor in patients who are hospitalised for major surgery or acute serious illnesses; treatment may be restarted once the patient’s condition has stabilised.

**MHRA, June 2016** - increased **lower limb amputation** (primarily of the toe) in people taking canagliflozin compared with placebo.

**Advice for healthcare professionals**
- As a precaution, consider stopping canagliflozin if a patient develops a significant lower limb complication (e.g., skin ulcer, osteomyelitis, or gangrene), at least until the condition has resolved, and continue to monitor the patient closely.
- Carefully monitor patients receiving canagliflozin who have risk factors for amputation (e.g., previous amputations, existing peripheral vascular disease, or neuropathy).
- Monitor all patients for signs and symptoms of water or salt loss; ensure patients stay sufficiently hydrated to prevent volume depletion in line with recommendations in the product information; note that diuretics can exacerbate dehydration.
- Advise patients to: stay well hydrated, carry out routine preventive foot care; seek medical advice promptly if they develop skin ulceration, discolouration, or new pain or tenderness.

Start treatment for foot problems (e.g. ulceration, infection, or new pain or tenderness) as early as possible.
GLP-1 (Glucagon-like peptide-1) AGONISTS
Increase insulin secretion, suppress glucagon secretion, slow gastric emptying and reducing appetite and food intake
See appendices 1-5 for further information regarding GLP-1 agonist

<table>
<thead>
<tr>
<th>Lixisenatide</th>
<th>Liraglutide</th>
<th>Exenatide</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE guidance</td>
<td>NICE NG28 recommends GLP-1’s as an option with metformin and gliclazide when triple therapy is not effective/not tolerated/contra-indicated for adults who: • Have a BMI of ≥35kg/m² or higher in those of European decent with appropriate adjustment in tailoring this advice for other ethnic groups and specific psychological or other medical problems associated with obesity or • Have a BMI &lt;35kg/m² and o For whom insulin therapy would have significant occupational implications or o Weight loss would benefit other significant obesity-related co-morbidities.</td>
<td></td>
</tr>
<tr>
<td>Therapy must be reviewed at 6 and 12 months. Criteria for continuing therapy: • a weight reduction of ≥3% (of initial body weight) in those with a BMI≥ 35kg/m² and • a reduction of ≥11mmol/mol (1%) by 6 months, with stable renal function.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NICE NG28 also recommends GLP-1 in combination with insulin with specialist care advice and on-going support from a consultant-led multidisciplinary team.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NICE NG28 recommends GLP-1’s as an option with metformin and gliclazide when triple therapy is not effective/not tolerated/contra-indicated for adults who: • Have a BMI of ≥35kg/m² or higher in those of European decent with appropriate adjustment in tailoring this advice for other ethnic groups and specific psychological or other medical problems associated with obesity or • Have a BMI &lt;35kg/m² and o For whom insulin therapy would have significant occupational implications or o Weight loss would benefit other significant obesity-related co-morbidities.</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Traffic light status</td>
<td>GREEN 1st line</td>
<td>BROWN</td>
</tr>
<tr>
<td>Traffic light status</td>
<td>GREEN 1st line</td>
<td>BROWN</td>
</tr>
<tr>
<td>Regimen</td>
<td>10microg od for 14 days and increased to 20microg od thereafter, administered by subcut injection, within 1 hour before a meal.</td>
<td>Initially 0.6mg od for at least 7 days, then increased to 1.2mg od for at least 7 days, administered by subcut injection. Patients who fail trial with lixisenatide can be considered for liraglutide.</td>
</tr>
<tr>
<td>Advantages</td>
<td>Weight loss - which can be modest in most patients, but significant in some, no hypoglycaemia and decrease in some cardiovascular risk factors.</td>
<td>Pregnancy and lactation.</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Diabetic ketoacidosis has been reported in patients with type 2 diabetes on a combination of a GLP-1 receptor agonist and insulin who had doses of concomitant insulin rapidly reduced or discontinued. GLP-1 receptor agonists are not substitutes for insulin, and any reduction of insulin should be done in a stepwise manner with careful glucose self-monitoring. See MHRA June 2019</td>
<td></td>
</tr>
<tr>
<td>Renal function</td>
<td>Not recommended for use in patients with a CrCl&lt;30ml/min and end stage renal disease.</td>
<td>Not recommended for use in patients with a CrCl&lt;15ml/min</td>
</tr>
<tr>
<td>Hepatic function</td>
<td>No dose adjustment is necessary for patients with hepatic impairment</td>
<td></td>
</tr>
<tr>
<td>Adverse effects</td>
<td>Nausea, vomiting, diarrhoea and headache are common adverse effects</td>
<td>Nausea and diarrhoea, vomiting, constipation, abdominal pain, and dyspepsia</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Criteria for continuing therapy: • a weight reduction of ≥3% (of initial body weight) in those with a BMI≥ 35kg/m2 and • a reduction of ≥11mmol/mol (1%) by 6 months, with stable renal function.</td>
<td></td>
</tr>
<tr>
<td>Warnings</td>
<td>MHRA March 2009-There have been reports of necrotising and haemorrhagic pancreatitis with GLP-1 agonists, some of which were fatal. If pancreatitis is suspected, treatment with the GLP-1 agonist should be suspended immediately; if pancreatitis is diagnosed, the GLP-1 agonist should be permanently discontinued. Routine monitoring of blood glucose levels is only required if the GLP-1 agonist is given in combination with another agent likely to cause hypoglycaemia e.g. sulfonylurea. This has implications for drivers holding Group 2 (LCV or PCV) licences and will require individual DVLA assessment.</td>
<td></td>
</tr>
</tbody>
</table>
**Weekly GLP-1 (Glucagon-like peptide-1) AGONISTS**

Increase insulin secretion, suppress glucagon secretion, slow gastric emptying and reducing appetite and food intake

See appendices 1-5 for further information regarding GLP-1 agonist

<table>
<thead>
<tr>
<th>Exenatide prolonged release</th>
<th>Dulaglutide prolonged release</th>
<th>Semaglutide</th>
<th>Albiglutide prolonged release</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NICE guidance</strong></td>
<td>As per NICE NG28 Exenatide MR can be considered if tolerability and compliance remains a major issue with conventional GLP-1 agonist therapy among patients whose HbA1c remains &gt;59 mmol/mol (7.5%) and BMI&gt;35kg/m².</td>
<td>Not included in NG28. (ESNM59: June 2015)</td>
<td>Not included in NG28</td>
</tr>
<tr>
<td><strong>Traffic light status</strong></td>
<td>BROWN (when weekly preparation is indicated)</td>
<td>BROWN (when weekly preparation is indicated)</td>
<td>BROWN (when weekly preparation is indicated)</td>
</tr>
<tr>
<td><strong>Product</strong></td>
<td>Dual chamber pre-filled pen which requires mixing before injection:</td>
<td>Pre-filled pen available as:</td>
<td>Pre-filled pen available as:</td>
</tr>
<tr>
<td></td>
<td>• 2mg pre-filled pen</td>
<td>• 750mcg/0.5ml pre-filled pen</td>
<td>• 250 micrograms pre-filled pen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 1.5mg/0.5ml pre-filled pen</td>
<td>• 500 micrograms pre-filled pen</td>
</tr>
<tr>
<td><strong>Regimen</strong></td>
<td>2mg by subcut injection once weekly.</td>
<td>750microgram by subcut injection once weekly.</td>
<td>250microgram by subcut injection once weekly, increasing to 500microgram once weekly after 4 weeks. The dose can be increased to 1 mg once weekly, if necessary, after a further 4 weeks.</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>As per GLP1s above. Advantage of a weekly preparation</td>
<td>If compliance is an issue or</td>
<td>The patient requires regular visits from a nursing team to administer the drug.</td>
</tr>
<tr>
<td></td>
<td>• if compliance is an issue or</td>
<td>• the patient requires regular visits from a nursing team to administer the drug.</td>
<td></td>
</tr>
<tr>
<td><strong>Contra-indications</strong></td>
<td>Type 1 diabetes, pregnancy and breastfeeding</td>
<td>Type 1 diabetes, pregnancy and breastfeeding</td>
<td>Type 1 diabetes, pregnancy and breastfeeding</td>
</tr>
<tr>
<td><strong>Renal function</strong></td>
<td>Not recommended for use in patients with an eGFR 30 - 50ml/min</td>
<td>Not recommended for use in patients with end-stage renal disease</td>
<td>Not recommended for use in patients with end-stage renal disease</td>
</tr>
<tr>
<td><strong>Hepatic function</strong></td>
<td>No dosage adjustment is recommended for patients with hepatic impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adverse effects</strong></td>
<td>Acute pancreatitis serious but rare Common AE include diarrhoea, nausea, and injection site rash.</td>
<td>Acute pancreatitis serious but rare Nausea, vomiting, diarrhoea.</td>
<td>Acute pancreatitis serious but rare Common AE include nausea, diarrhoea and vomiting</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>Criteria for continuing therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• a weight reduction of ≥3% (of initial body weight) in those with a BMI≥ 35kg/m² and</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• a reduction of ≥11mmol/mol (1%) by 6 months, with stable renal function.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Warning</strong></td>
<td>See warning in GLP1 section above</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Management of Type 2 Diabetes**

First produced: June 2009  Updated: July 2018

Review date: June 2020

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Drug therapy and renal and hepatic impairment

<table>
<thead>
<tr>
<th>Drug</th>
<th>CKD 1 &amp; 2 eGFR &gt;60</th>
<th>3a (59-45)</th>
<th>3b (44-30)</th>
<th>4 (29-15)</th>
<th>5 (&lt; 15)</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin / Metformin MR</td>
<td>✓</td>
<td>✓</td>
<td>✓ (review regularly)</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>X contraindicated in hepatic insufficiency</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (use lowest effective dose)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ contraindicated</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (but not with dialysis)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ contraindicated</td>
</tr>
<tr>
<td>Dapagliflozin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>✓</td>
<td>✓</td>
<td>✓ (do not initiate - GFR&lt;60ml/min )</td>
<td>✓ (discontinue if GFR falls below 45ml/min)</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>✓</td>
<td>✓</td>
<td>✓ (do not initiate - GFR&lt;60ml/min )</td>
<td>✓ (discontinue if GFR falls below 45ml/min)</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Lixisenatide</td>
<td>✓</td>
<td>✓</td>
<td>✓ (use with caution)</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>X No experience</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Exenatide</td>
<td>✓</td>
<td>✓</td>
<td>✓ (conservative dose escalation)</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Drug</td>
<td>CKD 1 &amp; 2 eGFR &gt;60</td>
<td>3a (59-45)</td>
<td>3b (44-30)</td>
<td>4 (29-15)</td>
<td>5 (&lt; 15)</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------------</td>
<td>------------</td>
<td>------------</td>
<td>-----------</td>
<td>----------</td>
<td>------</td>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>Exenatide MR</td>
<td>✓</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Dulaglutide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Semaglutide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Albiglutide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>x</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Insulin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✗ (dose adjustment required)</td>
<td>x (requirements may be altered in hepatic impairment - monitor and adjust dose accordingly.)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>100mg</td>
<td>50mg</td>
<td>50mg</td>
<td>25mg</td>
<td>25mg</td>
<td>✓</td>
<td>✓</td>
<td>✗ (no studies in severe hepatic impairment)</td>
</tr>
<tr>
<td>Linagliptin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>✓</td>
<td>2.5mg</td>
<td>2.5mg</td>
<td>(use with caution)</td>
<td>x (not recommended)</td>
<td>✓</td>
<td>use with caution</td>
<td>✗ (not recommended)</td>
</tr>
<tr>
<td>Vildagliptin</td>
<td>✓</td>
<td>50mg</td>
<td>50mg</td>
<td>50mg</td>
<td>(limited experience)</td>
<td>x (not recommended)</td>
<td>x (not recommended)</td>
<td>x (not recommended)</td>
</tr>
<tr>
<td>Alogliptin</td>
<td>✓</td>
<td>12.5mg</td>
<td>12.5mg</td>
<td>(limited experience)</td>
<td>6.25mg (limited experience)</td>
<td>✓</td>
<td>✓</td>
<td>✗ (not recommended)</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (use with caution)</td>
<td>✓ (use with caution)</td>
<td>✓</td>
<td>✓</td>
<td>✗ (contraindicated)</td>
</tr>
</tbody>
</table>

N.B. In patients at extremes of weight (BMI<18.5kg/m² or >30kg/m²) or age (>70 yrs), calculate renal function using Cockcroft and Gault equation.
Insulin Therapy in Type 2 Diabetes
Insulin treatment initiation

**Insulin indicated**
- Structured education programme
- Optimised oral medicines
- Individual target

- **Once-daily basal insulin**
  - Intermediate or long-acting, usually at bedtime, in addition to oral hypoglycaemic drugs
  - Commonly initiated after oral medication fails to control blood glucose concentrations or symptoms

  **Advantages:**
  - Relatively easy to initiate and titrate.
  - Involves only one injection a day.
  - Achieves reasonable glycaemic control with low risk of hypoglycaemia.

  **Disadvantages:**
  - May not be enough to maintain control, or good control may be achieved only at the expense of hypoglycaemia.

  **Choice of insulin**
  - Isophane (NPH) insulin (insulatard, Humulin I, Insuman Basal)

- **Twice daily bi-phasic insulin**
  - Premixed biphasic human insulin or analogues are commonly used in twice daily regimens given before or at the time of eating.

  **Advantages:**
  - Better glycaemic control than once daily basal insulin.

  **Disadvantages:**
  - Need to eat lunch and a bedtime snack to balance the insulin peaks produced.
  - Greater likelihood of weight gain and hypoglycaemia.
  - Not suitable for every patient (e.g. people who do shift work)

  **Choice of insulin**
  - Biphasic isophane insulin (Soluble insulin 30%+isophane insulin 70%, humulin M3), Insuman Comb 15, Insuman Comb 25, Insuman Comb 50

- **Basal bolus insulin**
  - Involves both basal and prandial insulins

  **Recommended regimen for intensification of treatment if glycaemic or symptoms control is not achieved or maintained on basal insulin alone**

  **Advantages:**
  - Greater flexibility of patient over when and what to eat.

  **Disadvantages:**
  - Multiple injections
  - Measurement of blood glucose concentrations to titrate insulin dose.
  - Poor adherence
  - Bedtime snack to prevent hypoglycaemia.

**Choice of Insulin**
- Bolus
  - Soluble insulin (e.g., Humulin S, Insuman rapid)
- Basal
  - Isophane (NPH) insulin (insulatard, Humulin I, Insuman Basal)

- If other measures do not keep HbA1c to individualised target (NICE CG87), discuss benefits and risk of insulin treatment.
- Use insulin ALONGSIDE metformin (if there are no contraindications or intolerance). Also review the continued need for other oral hypoglycaemic drugs.
- When starting insulin therapy, use a structured programme employing active insulin titration that encompasses:
  - Injection technique, including rotating injection sites and avoiding repeated injections at same point within sites,
  - Continuing telephone support
  - Self-monitoring
  - Dose titration to target levels
  - Dietary understanding
  - DVLA guidance
  - Management of hypoglycaemia
  - Management of acute changes in plasma glucose control,
  - Support from an appropriately trained and experienced healthcare professional.
- Insulin therapy should be initiated from a choice of a number of insulin types and regimens by a practitioner with the appropriate knowledge, competencies and experience to choose the most appropriate starting regimen tailored to each patient.
- Begin with human NPH insulin (Isophane insulin e.g. Insulatard®, Humulin I®, Insuman®) taken at bedtime or twice daily according to need. Human NPH (isophane) insulin is used routinely in preference to a long acting human insulin analogue, at bedtime or twice a day. It is the preferred first choice insulin recommended by NICE based on cost effectiveness and its safety profile. There is limited evidence of a clinical benefit of insulin analogues over human NPH insulin for type 2 diabetes and they are considerably more expensive.

- However a long acting human insulin analogue (as an alternative to NPH insulin) may be considered in patients (after education and lifestyle advice) if:
  - The person requires assistance from a carer or health care professional to administer insulin and in whom use of a long-acting insulin analogue would reduce the frequency from twice to once a day; or
  - The persons’ lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes; or
  - The person would otherwise need twice daily isophane insulin (intermediate-acting) in combination with hypoglycaemic drugs; or
  - who are unable to use the device to inject isophane insulin

- Consider twice-daily, as a pre-mixed – biphasic human insulin regimens in particular where HbA1c >75 mmol/mol (9.0%). A once-daily regimen may be an option when initiating this therapy.

- Insulin analogues rather than pre-mixed human insulin preparations should only be considered when:
  - immediate injection before a meal is needed, or
  - hypoglycaemia is a problem, or
  - there are marked postprandial blood glucose rises.

- Recurrent symptomatic hypoglycaemia should prompt a re-examination of the current insulin regimen, injection sites, a search for other comorbidities (such as liver or renal disease) and a review of the agreed HbA1c target. If tight control is still required, then consider a trial of analogue insulin.

- Monitor a person using a basal insulin regimen (NPH or a long-acting insulin analogue [insulin glargine/detemir]) for the need for mealtime insulin (or a pre-mixed insulin preparation). If blood glucose control remains inadequate (not to agreed target levels without problematic hypoglycaemia), move to a more intensive, twice/three times daily mixed insulin or mealtime plus basal insulin regimen.

- Human insulin’s (such as Humulin S®, Insuman Rapid®, Isophane insulin, biphasic isophane insulin) should be considered as first line therapy before moving to analogue or analogue mixtures. Insulin analogues should only be considered if one of the criteria described above is met.

- Monitor a person using pre-mixed insulin once or twice daily for the need for a further pre-prandial injection or for an eventual change to a mealtime plus basal insulin regimen, based on human or analogue insulin’s, if blood glucose control remains inadequate.

- New insulin analogue biosimilars have been launched, with Abasaglar being the preferred 1st line glargine choice over Lantus. In new patients needing an insulin analogue or in existing patients on Lantus who are poorly controlled, Abasaglar is an appropriate alternative. Switching stable patients is not advised.

**Keep it simple and safe whenever possible**

Health professionals should continue to follow NICE guidance and agree individual HbA1c targets with the patient, taking account of the patient’s own preferences and the balance of likely benefits and burden of treatment.

Insulin preparations may vary from the previously standardised strength of 100 iu/ml. If insulin extracted from a pen or cartridge is of higher strength and that is not considered in determining the volume required, it can lead to significant and potentially fatal overdose. Patient safety alert, Nov 2016 warns against withdrawing insulin from pen devices due to risk of severe harm or death.
Table 1 & 2 lists the various insulins available and their properties. There is a significant difference in costs between insulin analogues and NPH insulin, and between different devices such as vials, cartridges and disposable pens. For price comparisons please see Derbyshire formulary chapter 6 endocrine.

<table>
<thead>
<tr>
<th>Insulin (all preparations are 100units/ml unless stated)</th>
<th>Timing of injection</th>
<th>Onset of action</th>
<th>Peak</th>
<th>Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short active human insulins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soluble insulin (e.g. Actrapid, Humulin S, Insman rapid)</td>
<td>Within 30 mins before meal</td>
<td>Within 30 mins</td>
<td>1.5-3.5 hrs</td>
<td>7-8 hrs</td>
</tr>
<tr>
<td><strong>Rapid-acting analogues</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin aspart (Fiasp) (After specialist recommendation) -an option for type 1 diabetes (NG17) in new adult patients</td>
<td>Within 0-15 mins of meal</td>
<td>4 mins</td>
<td>1-3 hrs</td>
<td>3-5 hrs</td>
</tr>
<tr>
<td>Insulin aspart (Novo Rapid) -an option for children and type 1 diabetes in patients already on treatment (NG17)</td>
<td>Immediately before meal</td>
<td>10-20 mins</td>
<td>1-3 hrs</td>
<td>3-5 hrs</td>
</tr>
<tr>
<td>Insulin lispro (Humalog) -an option for type 1 diabetes (NG17)</td>
<td>Within 0-15 mins of meal</td>
<td>About 15 mins</td>
<td>30-70 mins</td>
<td>2-5 hrs</td>
</tr>
<tr>
<td>Insulin glulisine (Apidra)</td>
<td>Within 0-15 mins of meal</td>
<td>10-20 mins</td>
<td>About 1 hr</td>
<td>1.5-4 hrs</td>
</tr>
<tr>
<td><strong>Intermediate (NPH) human insulin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isophane (NPH) insulin (Insulatard, Humulin I, Insman Basal) - first line for most patients with type 2 diabetes</td>
<td>At bedtime/12 hrly</td>
<td>4-12 hrs</td>
<td>About 24 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Long-acting analogues</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin detemir (Levemir) - preferred choice for adult type 1 diabetes (NG17)</td>
<td>Once/twice daily</td>
<td>0.5-1 hr</td>
<td>3-14 hrs</td>
<td>Up to 24 hrs</td>
</tr>
<tr>
<td>Insulin glargine biosimilar (Semglee) - positioned ahead of insulin glargine (Lantus), when a long-acting insulin analogue is indicated in new patients or patients who are having a review of treatment due to suboptimal control</td>
<td>Once daily</td>
<td>0.5-1 hr</td>
<td>No peak</td>
<td>Up to 24 hrs</td>
</tr>
<tr>
<td>Insulin glargine biosimilar (Abasaglar) - when a long-acting insulin analogue is indicated. Patients already initiated on Abasaglar should remain on this</td>
<td>Once daily</td>
<td>0.5-1 hr</td>
<td>No peak</td>
<td>Up to 24 hrs</td>
</tr>
<tr>
<td>Insulin glargine 300 units/ml (Toujeo)- BROWN</td>
<td>Once daily</td>
<td>0.5-1 hr</td>
<td>No peak</td>
<td>24-36 hrs</td>
</tr>
<tr>
<td>Insulin degludec (Tresiba) 100units/ml BROWN</td>
<td>Once daily</td>
<td>0.5-1.5 hrs</td>
<td>No peak</td>
<td>&gt;42 hrs</td>
</tr>
<tr>
<td><strong>Pre-mixed human insulin (commonly used in twice daily regimens in type 2 diabetes)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biphasic isophane insulin (soluble insulin 30%+isophane insulin 70%; Humulin M3; Insman Comb 15 (15% soluble/85% Isophane); Insman Comb 25 (25%soluble/75% Isophane); Insman Comb 50 (50% soluble/50% Isophane))</td>
<td>Within 30 mins before meal</td>
<td>Within 30 mins</td>
<td>2 and 8hrs</td>
<td>Up to 24hrs</td>
</tr>
<tr>
<td><strong>Pre-mixed analogues (an option in type 2 diabetes if a person prefers to inject insulin immediately before a meal)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biphasic aspart (insulin aspart 30%+ insulin aspart protamine 70%; novomix 30)</td>
<td>Within 0-10 mins of meal</td>
<td>Within 10-20 mins</td>
<td>1-4 hrs</td>
<td>up to 24hrs</td>
</tr>
<tr>
<td>Biphasic insulin lispro (insulin lispro 25%+ insulin lispro protamine 75%; Humalog Mix 25)</td>
<td>Within 0-15 mins of meal</td>
<td>About 15 mins</td>
<td>About 2 hrs</td>
<td>up to 24hrs</td>
</tr>
<tr>
<td>Biphasic insulin lispro (insulin lispro 50%+insulin lispro protamine 50%; Humalog Mix 50)</td>
<td>Within 0-15 mins</td>
<td>About 15 mins</td>
<td>About 2 hrs</td>
<td>up to 24hrs</td>
</tr>
</tbody>
</table>

Timings of action of insulin's are approximate as they vary between individuals, and with injection sites, blood supply, temperature and physical activity.

Long-acting insulin analogues are designed not to have a peak action as such but to release insulin consistently over their duration of activity.
### Table 2: Traffic light classification for high strength insulins and insulin degludec

<table>
<thead>
<tr>
<th>Insulin/strength</th>
<th>Traffic light status</th>
</tr>
</thead>
</table>
| Insulin glargine **300** units/ml (Toujeo) | **BROWN** after consultant/specialist initiation:  
- for patients on insulin Degludec or  
- for patients being considered for insulin pump therapy or  
- for patients currently on high dose of insulin (>150 units/day) who would otherwise have been started with Humulin R U-500 or degludec. |
| Insulin degludec **200** units/ml (Tresiba) | **BROWN** after consultant/specialist initiation for patients currently on high dose of insulin (>150 units/day) after consideration of Toujeo. |
| Insulin degludec 100 units/ml (Tresiba) | **BROWN** after consultant/specialist initiation - restricted to those with documented nocturnal hypoglycaemia or loss of hypoglycaemia awareness despite using long acting insulin analogue, who would otherwise have been started on an insulin pump in type 1 diabetes. |
| Humulin R U500 **500** units/ml | **BROWN** after consultant/specialist initiation for patients unable to use Toujeo or Insulin Degludec. (Only KwikPens currently available) |

These insulin’s have been designated **BROWN** after consultant/specialist initiation; patients should be initiated and stabilised in secondary care before handing over to primary care.

**GlucoRx Carepoint pen needles** (4mm/31g, 5mm/31g, 6mm/31g, 8mm/31g) are the formulary choice of insulin pen needles. If this is unsuitable consider other brands costing less than £6 per 100 needles.

Safety needles should **NOT** be used by patients who self-administer insulin. **MyLife Clickfine AutoProtect** (5mm/31g, 8mm/29g) is the preferred brand for safety needles if indicated.

### Table 3: Licenced and NICE approved insulin combinations.

<table>
<thead>
<tr>
<th>Combination</th>
<th>Licenced (SPC)</th>
<th>NICE approved</th>
<th>Derbyshire comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin + Metformin</td>
<td>Yes</td>
<td>NICE NG28</td>
<td>As per diabetes guidance and algorithm</td>
</tr>
<tr>
<td>Insulin + Gliclazide</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin + Pioglitazone</td>
<td>Yes</td>
<td></td>
<td>After consultant/specialist initiation and assessment.</td>
</tr>
<tr>
<td>Insulin + Alogliptin</td>
<td>Yes</td>
<td></td>
<td>Only on advice of specialist and with ongoing support from a consultant-led service</td>
</tr>
<tr>
<td>Insulin + Linagliptin*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin + Sitagliptin*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin + Saxagliptin*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin + Vildagliptin*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin + Empagliflozin</td>
<td>Yes</td>
<td>NICE TA336 - with insulin +/- other antidiabetic drugs</td>
<td>After consultant/specialist initiation and assessment</td>
</tr>
<tr>
<td>Insulin + Dapagliflozin</td>
<td>Yes</td>
<td>NICE TA288 - with insulin +/- other antidiabetic drugs</td>
<td></td>
</tr>
<tr>
<td>Insulin + Canagliflozin</td>
<td>Yes</td>
<td>NICE TA315 - with insulin +/- other antidiabetic drugs</td>
<td></td>
</tr>
<tr>
<td>Insulin + Exenatide</td>
<td>Yes</td>
<td>NICE NG28</td>
<td></td>
</tr>
<tr>
<td>Insulin + Liraglutide</td>
<td>Yes</td>
<td>NICE NG28</td>
<td>Only on advice of specialist and with on-going support from a consultant-led service</td>
</tr>
<tr>
<td>Insulin + Lixisenatide</td>
<td></td>
<td>NICE NG28</td>
<td></td>
</tr>
<tr>
<td>Insulin + Dulaglutide¹</td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Insulin + Albiglutide¹</td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Insulin + Semaglutide¹</td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Insulin + Exenatide MR</td>
<td>No</td>
<td>NICE NG28</td>
<td></td>
</tr>
<tr>
<td>Insulin + Metformin (&amp; MR) + Gliclazide</td>
<td>Yes</td>
<td></td>
<td>As per diabetes guidance and algorithm</td>
</tr>
<tr>
<td>Insulin + Metformin + Pioglitazone</td>
<td>No</td>
<td></td>
<td>As per diabetes guidance and algorithm</td>
</tr>
</tbody>
</table>

¹ with or without metformin

¹ Albiglutide, dulaglutide and semaglutide were not included in NICE NG28 review.
|                | Metformin | Metformin MR | Gliclazide | Gliclazide MR | Pioglitazone | Alogliptin | Linagliptin | Saxagliptin | Vildagliptin | Empagliflozin | Dapagliflozin | Canagliflozin | Lixisenatide | Liraglutide | Exenatide | Exenatide MR | Dulaglutide | Albiglutide | Insulin |
|----------------|-----------|-------------|------------|--------------|--------------|------------|------------|------------|-------------|---------------|---------------|---------------|-------------|------------|-----------|----------|-----------|-----------|-----------|---------|
| Metformin      | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Metformin MR   | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Gliclazide     | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Gliclazide MR  | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Pioglitazone   | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Alogliptin     | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Linagliptin    | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Sitagliptin    | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Saxagliptin    | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Vildagliptin   | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Empagliflozin  | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Dapagliflozin  | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Canagliflozin  | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Lixisenatide   | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Liraglutide    | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Exenatide      | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Exenatide MR   | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Dulaglutide    | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Albiglutide    | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |
| Insulin        | NICE      | NICE        | NICE       | NICE         | NICE         | NICE       | NICE       | NICE       | NICE        | NICE          | NICE          | NICE          | NICE        | NICE      | NICE     | NICE     | NICE     | NICE     | NICE     |

1 combination is licenced  
2 combination is not licenced  
NICE - covered by NICE guidance  
NICE - not covered by NICE guidance
## Appendix 2: NICE approved – triple therapy combinations

|                   | Metformin | Metformin MR | Gliclazide | Gliclazide MR | Pioglitazone | Alogliptin | Linagliptin | Sitagliptin | Vildagliptin | Empagliflozin | Dapagliflozin | Canagliflozin | Lixisenatide | Liraglutide | Exenatide | Dulaglutide | Albiglutide |
|-------------------|-----------|--------------|------------|---------------|--------------|------------|-------------|-------------|--------------|---------------|---------------|---------------|--------------|-------------|------------|-----------|------------|------------|
| Met + Gliclazide  | NICE¹    | NICE¹        | NICE¹      | NICE¹         | NICE¹        | NICE¹      | NICE¹       | NICE¹       | NICE¹        | NICE¹         | NICE¹         | NICE¹         | NICE¹        | NICE¹      | NICE¹      | NICE¹      | NICE¹      |
| Met MR + gliclazide | NICE¹   | NICE¹        | NICE²      | NICE³         | NICE²        | NICE²      | NICE¹       | NICE¹       | NICE¹        | NICE¹         | NICE¹         | NICE¹         | NICE¹        | NICE¹     | NICE¹      | NICE¹      | NICE¹      |
| Met + pio         | NICE     | NICE         | NICE¹      | NICE¹         | NICE¹        | NICE¹      | NICE¹       | NICE¹       | NICE¹        | NICE¹         | NICE¹         | NICE¹         | NICE¹        | NICE¹     | NICE¹      | NICE¹      | NICE¹      |
| Alogliptin + pio  | NICE²    | NICE²        | NICE²      | NICE²         | NICE²        | NICE²      | NICE¹       | NICE¹       | NICE¹        | NICE¹         | NICE¹         | NICE¹         | NICE¹        | NICE¹     | NICE¹      | NICE¹      | NICE¹      |
| Linagliptin + pio | NICE²    | NICE²        | NICE²      | NICE²         | NICE²        | NICE²      | NICE¹       | NICE¹       | NICE¹        | NICE¹         | NICE¹         | NICE¹         | NICE¹        | NICE¹     | NICE¹      | NICE¹      | NICE¹      |
| Sitagliptin + pio | NICE²    | NICE²        | NICE²      | NICE²         | NICE²        | NICE²      | NICE¹       | NICE¹       | NICE¹        | NICE¹         | NICE¹         | NICE¹         | NICE¹        | NICE¹     | NICE¹      | NICE¹      | NICE¹      |
| Saxagliptin + pio | NICE²    | NICE²        | NICE²      | NICE²         | NICE²        | NICE²      | NICE¹       | NICE¹       | NICE¹        | NICE¹         | NICE¹         | NICE¹         | NICE¹        | NICE¹     | NICE¹      | NICE¹      | NICE¹      |
| Vildagliptin + pio| NICE²    | NICE²        | NICE²      | NICE²         | NICE²        | NICE²      | NICE¹       | NICE¹       | NICE¹        | NICE¹         | NICE¹         | NICE¹         | NICE¹        | NICE¹     | NICE¹      | NICE¹      | NICE¹      |

¹Combination is licenced
²Combination not licenced

NICE - covered by NICE guidance
NICE – not covered by NICE guidance
Appendix 3 – Further Information for GLP-1 agonists

**Benefit**
- Randomized controlled trials have showed a lowering of HbA1c by 1.0-1.5% across the class and weight loss ranging from 1-2.3kg (maintained beyond 12 months)
- The natural hormone glucagon-like peptide-1 (GLP-1) acts by stimulating insulin secretion, suppressing glucagon secretion, inhibiting gastric emptying, and reducing appetite and food intake.

**Initiation of therapy**
- Firstline GLP-1 agonist recommended locally is lixisenatide.
- Only offer GLP1 in combination with insulin with specialist care advice and on-going support from a consultant-led multidisciplinary team.
- Individual DVLA assessment is required for Group 2 license holders who use GLP-1 agonists in combination with a sulfonylurea due to the risk of hypoglycemia.

**Review**
Therapy must be reviewed at 6 and 12 months. If HbA1c decrease is <11mmol/mol (1.0%) at 6 months and weight loss is <3% at 6 months, then stop GLP1 treatment.

- If a patient fails on initial GLP-1 therapy because of side effects or inadequate response, consider an alternative GLP-1 agonist.
- Often a patient loses weight but their HbA1c rises. They should not continue with GLP-1 agonist therapy because this may indicate beta cell failure and uncontrolled diabetes. Insulin should be considered instead.

**Side effects**
- Side effects include significant nausea (20-26% of patients were affected in trials) and there are rare reports of acute pancreatitis. It should therefore be avoided in those with previous pancreatitis or considered high risk. Other gastrointestinal side effects may occur and commonly settle after a few days or weeks on therapy.
- Existing patients on exenatide or liraglutide who stop due to adverse effects/lack of efficacy can be tried on lixisenatide.

**Remember the following:**
- Be alert to the signs and symptoms of acute pancreatitis.
- Instruct patients taking GLP-1 agonists to seek prompt medical care if they experience persistent severe abdominal pain.
- Discontinue the GLP-1 agonist if pancreatitis is suspected.
- If pancreatitis in a patient using a GLP-1 agonist is confirmed, appropriate supportive treatment should be initiated and the patient carefully monitored until recovery. GLP-1 agonist should not be restarted.
Algorithm for using GLP-1 agonist in type 2 diabetes

Lixisenatide - 1st line GLP1 in new patients

Individualised target not achieved
Treat: other vascular risk factors & complications of T2DM
Review: education, lifestyle, diet
Optimise: metformin and sulfonylurea doses

HbA1c?

Individualised target achieved

Individualised target not achieved

BMI?

≥ 35 kg/m² in those of European descent, with appropriate adjustment in tailoring this advice for other ethnic groups or
< 35 kg/m² if therapy with insulin has significant occupational implications or weight loss would benefit other significant obesity-related co-morbidities.

Lixisenatide – 1st line
Check SPC for exclusions, contraindications and cautions

Record initial weight and HbA1c

Start lixisenatide 10 micrograms once daily subcutaneously for 14 days
Give up to 60 minutes before first meal of the day or evening meal

Review at 2 weeks

Adverse reaction or persistent nausea or vomiting?

Yes

Stop treatment

No

Increase dose to 20 micrograms once daily on day 15
(Consider not increasing in elderly patients or those with a low eGFR)

Reduce dose e.g lixisenatide 10 micrograms once daily (local expert opinion)

Review at 6 months

Lixisenatide not appropriate for the patient or failed trial of lixisenatide
Check SPC for exclusions, contraindications and cautions

Consider an alternative GLP-1 agonist

Record initial weight and HbA1c

Review as appropriate

No

Titrate dose as appropriate

A response is defined as decrease in initial bodyweight of at least 3% AND a decrease in HbA1c ≥ 11mmol/mol (1.0% point)

If individualised target not achieved or no response - stop GLP-1 agonist and consider other treatment.

Management of Type 2 Diabetes
First produced: June 2009  Updated: July 2018
Review date: June 2020
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Patient agreement form- GLP-1 agonists for Type 2 diabetes

At your appointment today we have agreed to start treatment with one of the following medicines to help manage your type 2 diabetes:

- Lixisenatide (Lyxumia)
- Exenatide (Byetta)
- Liraglutide (Victoza)
- Dulaglutide (Trulicity)
- Exenatide MR (Bydureon)
- Semaglutide (Ozempic)

These medicines all work in a very similar way and are sometimes known as GLP-1 agonists. Further information on how to use the device and any side-effects you should be aware of is included in the patient information provided with your medicine supply.

Although these medicines are given as an injection, they work in a different way to insulin. However they should help reduce your blood glucose levels and may also help you lose weight, especially if you follow a healthy diet and take regular exercise.

Please ask your diabetes nurse if you would like further information on the use of these medicines to treat type 2 diabetes or help and support with losing weight.

These injections do not work for everyone and if left unchecked may not be the best use of NHS resources. We therefore need to regularly monitor whether they are being effective.

In order to do this, we follow the guidance from the National Institute of Health and Clinical Excellence (NICE). This states that treatment with these medicines should only be continued after 6 months if a patient sees a reduction in their HbA1c (measurement of long term blood sugar control) of 11mmol/mol (in the old number system that is about 1% HbA1c) and a reduction in their weight of 3% or more.

If the GLP-1 agonist injection we have agreed to start today does not provide these beneficial outcomes after 6 months, we will need to consider alternative options to manage your condition and stop the GLP1 agonist injection.

If treatment is continued after 6 months, we will continue to monitor your HbA1c and weight on a regular basis. If the beneficial effects are not maintained, then again we will need to consider alternative options to manage your condition and then stop the GLP 1 agonist injection.

PATIENT AGREEMENT:
The information overleaf has been explained to me and I understand that treatment with lixisenatide, liraglutide or exenatide will be stopped and alternative options considered if the beneficial effects on my weight and HbA1c are not achieved after 6 months, or continued long-term.

<table>
<thead>
<tr>
<th>Weight (3% loss needed by 6 months)</th>
<th>Today</th>
<th>6 month’s target</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (11mmol/mol (1%) reduction needed by 6 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR (to check your kidney function)</td>
<td>To be measured in 6 months</td>
<td></td>
</tr>
</tbody>
</table>

Patient Name: ___________________  Patient Signature: ___________________

Clinician Name: ___________________  Clinician Signature: ___________________

Date: ___/___/____  Date of 6 month review: ___/___/____

If you have any questions or problems with your treatment, please contact:

Name: _____________________________

Contact number: ___________________

Please give a copy to the patient and keep a copy in the patient’s record. If treatment is started by hospital clinicians, please also send a copy to the patient’s GP
Appendix 4

Reporting units for HbA1c
Glycated haemoglobin (HbA1c) is the recommended method of measuring long term control of blood glucose in people with both type 1 and type 2 diabetes. Previously the results were reported as a percentage (%). This has changed to millimoles/mole (mmol/mol) where people with diabetes will receive their HbA1c measurement in mmol/mol only.

<table>
<thead>
<tr>
<th>HbA1c (new units)</th>
<th>HbA1c (old units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mmol/mol</td>
<td>%</td>
</tr>
<tr>
<td>20</td>
<td>4.0</td>
</tr>
<tr>
<td>31</td>
<td>5.0</td>
</tr>
<tr>
<td>42</td>
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<td>64</td>
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<tr>
<td>75</td>
<td>9.0</td>
</tr>
<tr>
<td>86</td>
<td>10.0</td>
</tr>
</tbody>
</table>

A 0.5% difference in HbA1c is equivalent to a difference of about 5.5mmol/mol, and a 1% difference is equivalent to a difference of about 11mmol/mol. Note these are rounded equivalents.

Appendix 5 - STAR (Stop Think Assess Review)

Titrating insulin doses
This strategy provides a guide for increasing insulin and should be supported by the expertise of suitably experienced clinicians. To prevent excessive doses clinicians need to be competent in understanding the variations in insulin delivery by the products and interpreting glycaemic control in relation of food and timing. Each patient should have a care management plan. Diabetes specialists have produced this systematic approach to the initiation of insulin in type II diabetes and subsequent management based upon currently available evidence. It is intended as a guide to management, and as such will be appropriate to most groups of people starting insulin in primary care. It is intended to:
1. Provide a standardised systematic approach.
2. To use a personalised care planning approach to support goals and actions, using a discovery diary to support people starting on insulin.
3. Introducing appropriate educational program addressing knowledge and lifestyle issues prior to the commencement of insulin.
4. Achieve glycaemic control using the least possible amount of insulin to prevent the consequences of hyper-insulinaemia such as weight gain, hypoglycaemia, adverse lipids, and raised blood pressure.
5. Provide a cost-effective program for insulin management with appropriate choice of insulin matched to clinical need.
7. Make effective use of blood glucose monitoring.

At each stage explain insulin initiation will occur in a series of stages, each increase in insulin will happen over 2 to 3 weeks followed by a period of stabilisation. The person will need to monitor their blood glucose during each increase in insulin and discuss their results with their health care professional at the next appointment. Monitor blood glucose before breakfast and before bedtime, plus pre meals to see if OHA are working. Phone call support from the initiating clinician is recommended during this period.
### Stage 1 0-20 units
Initiate Human NPH (isophane) insulin 10 units at night time (or teatime if more convenient). Increase insulin by 2 to 4 units every three days up to 20 units.
At 20 units complete two day discovery diary (record of insulin, blood glucose 4 times each day, weight, and any episode of hypoglycaemia)

**Starting Insulin of choice will be dependent on individual patient see regimen of choice in guidelines**

### Stage 2 20-40 units (2 weeks after commencing insulin)
**Stop Think assess review**
Do not increase insulin further until review of discovery diary with HCP and patient. Review current insulin and allow reflection of lifestyle changes and goals.
- Review personalised care plan what has happened to the person during this time. What questions do they have?
- Review the person’s own knowledge and understanding of use of insulin.
- Review progress towards lifestyle goals

**Consider:**
- if the person is putting on weight
- have they had any hypoglycaemia?
- review blood glucose, has insulin made any difference?
If weight is increasing but blood glucose not responding, do not progress to higher doses of insulin until lifestyle issues have been reviewed and new goals set.
Consider hypoglycaemia risk.
Seek advice from the local DSN if required.
If some response of blood glucose to insulin, continue with Human NPH (isophane) insulin until target reached or 40 units whichever is lower, increasing in 4 units every 3 or 4 days.
If sugars dropping overnight but steady all day, consider split dose (Human NPH (isophane) insulin)
If no response, consider change to mixed human insulin, or a basal bolus regimen.
(see insulin charts)

**Education is key at all stages to support in self-management.**

Increase insulin further as part of agreed plan with the patient.
Increase insulin by 4 units every 3 days, up to 40 units or until fasting blood glucose target is reached **without overnight drop**, or any **signs of hypoglycaemia**.
At 40 units complete two day discovery diary (record of insulin, blood glucose 4 times each day, weight, and hypoglycaemia)

### Stage 3 40-60 units (6 to 8 weeks after commencing insulin)
**Stop think assess review**
Do not increase insulin further until review of discovery diary with HCP and patient.

Review current insulin and allow reflection of lifestyle changes and goals.
- Review personalised care plan, what has happened to the person during this time? What questions do they have?
- Review the person’s own knowledge and understanding of use of insulin.
- Review progress towards lifestyle goals.

**Consider:**
- If the person is putting on weight
- Have they had any hypoglycaemia?
- Review blood glucose, has insulin made any difference?
If weight is increasing but blood glucose not responding, do not progress to higher doses of insulin until lifestyle issues have been reviewed and new goals set.
Consider hypoglycaemia risk, see checklist/screening tool
Seek advice from the local DSN if required.
If some response of blood glucose to insulin, continue with Human NPH (isophane) insulin until target reached 60 units whichever is lower, increasing in 4 units every 3 or 4 days.

If still only on long acting insulin, change to mixed insulin or basal bolus. (BBR) (Consider reducing dose by approximately 10% while changing insulin).

Increase twice daily insulin by 2 units each morning or evening every 3 or 4 days depending on blood test results. ONLY CHANGE ONE AT A TIME TO SEE KNOCK ON EFFECT. (Unless having HYPOS) Stop increasing insulin if blood glucose test before the next meal has reached target. Sometimes one test may be at target and another not if on a fixed mix of insulin the mix of insulin or regimen will need to be reviewed.

At 60 units complete two day discovery diary (record of insulin, blood glucose 4 times each day, weight and hypoglycaemia).

Stage 4  60-80 units
Stop think assess review. Do not increase insulin further until review of discovery diary with HCP and patient.

Review current insulin and allow reflection of lifestyle changes and goals.
- Review personalised care plan, what has happened to the person during this time? What questions do they have?
- Review the person's own knowledge and understanding of use of insulin.
- Review progress towards lifestyle goals.

Consider:
- If the person is putting on weight
- Have they had any hypoglycaemia?
- Review blood glucose, has insulin made any difference?

If weight is increasing but blood glucose not responding, do not progress to higher doses of insulin until lifestyle issues have been reviewed and new goals set.

Consider hypoglycaemia risk, see checklist/screening tool.
Seek advice from the local DSN if required.

If some response of blood glucose to insulin, continue with MIX/ BBR until target reached or 80 units whichever is lower, increasing in 4 units every 3 or 4 days.

Stage 5
Do not increase insulin further until review of discovery diary with HCP and patient.

Review current insulin and allow reflection of lifestyle changes and goals.
- Review personalised care plan, what has happened to the person during this time? What questions do they have?
- Review the person's own knowledge and understanding of use of insulin.
- Review progress towards lifestyle goals.

Consider:
- If the person is putting on weight
- Have they had any hypoglycaemia?
- Review blood glucose, has insulin made any difference?

If weight is increasing but blood glucose not responding, do not progress to higher doses of insulin until lifestyle issues have been reviewed and new goals set.

Consider hypoglycaemia risk, http://www.trend-uk.org/resources.php
Seek advice from the local DSN if required.

Stop think and review
Consider reducing insulin, the useful effective dose may already have been passed.
Consider adding other agents e.g. pioglitazone to reduce insulin resistance.
Consider seeking further advice, or referral to insulin support group.

Hypoglycaemia
Hypoglycaemia is more frequent in patients taking insulin with impaired renal function compared to those with normal renal function.
Patients should be questioned closely about hypoglycaemia (frequency, severity and awareness) and consideration given to reduce the doses of insulin and if necessary change the insulin regimen order to reduce the risks of hypoglycaemia. Patients experiencing severe episodes of hypoglycaemia, defined as requiring help from a third party should be referred to the specialist diabetes team.

**Oral agent combination therapy with insulin**

When starting basal insulin therapy, continue with metformin and gliclazide (and acarbose, if used) However review sulfonylureas:

I. If hypoglycaemia occurs

II. When mealtime quick acting insulin injections or mixed insulin’s are started, sulfonylureas should be discontinued, or tapered and then discontinued, since they are not considered synergistic with these insulin types

When starting pre-mixed insulin therapy (or mealtime plus basal insulin regimens):

I. Continue with metformin

II. Consider combining pioglitazone with insulin therapy if patient:
   a) has previously had a marked glucose-lowering response to thiazolidinedione therapy
   b) on high-dose insulin therapy and blood glucose is inadequately controlled. This may need specialist guidance.

Warrn the person to discontinue pioglitazone if clinically significant fluid retention develops.

**Insulin delivery devices**

- Offer education to patients or carers about using an injection device that they and/or their carer find easy to use.
- Appropriate local arrangements should be in place for the disposal of sharps.
- Only insulatard® and insulin detemir (levemir®) can be used with the Innolet® device.
- Innolet device is useful for patients with dexterity and visual impairment problems.
- Consider any manual or visual disability a patient may have that affects their ability to use a device. Offer a device or adaptation that:
  - Takes into account the patients individual needs
  - The patient can use successfully.

**Advice for the safe administration of insulin (NPSA/2010/RRR013)**

- All regular and single insulin (bolus) doses are measured and administered using an insulin syringe or commercial insulin pen device. Intravenous syringes must never be used for insulin administration.
- The term ‘units’ is used in all contexts. Abbreviations, such as ‘U’ or ‘IU’, are never used.
- All clinical areas and community staff treating patients with insulin have adequate supplies of insulin syringes and subcutaneous needles, which staff can obtain at all times.
- A training programme should be put in place for all healthcare staff (including medical staff) expected to prescribe, prepare and administer insulin. An e-learning programme is available from: www.diabetes.nhs.uk/safe_use_of_insulin

**Adult patients passport to safer insulin use (NPSA/2011/PSA003) 30 March 2011**

- Adult patients on insulin therapy receive a patient information booklet and an Insulin Passport to help provide accurate identification of their current insulin products and provide essential information across healthcare sectors.
- Healthcare professionals and patients are informed how the Insulin Passport and associated patient information can be used to improve safety.
- When prescriptions of insulin are prescribed, dispensed or administered, healthcare professionals cross-reference available information to confirm the correct identity of insulin products.
- Systems are in place to enable hospital inpatients to self-administer insulin where feasible and safe.

More detailed information to support the implementation of this guidance is available at: www.nrls.npsa.nhs.uk/alerts Email: medicationteam@npsa.nhs.uk

Supplies of the Insulin Passport and patient booklet will be obtained from Primary Care Support England (PCSE) through the following link http://pcse.england.nhs.uk/ using your practice log in details.

If you have access to the electronic ordering system you can place your orders via www.nhsforms.co.uk
### Appendix 6 – Cost comparison chart (Doses given do not imply therapeutic equivalence)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Traffic light status</th>
<th>Daily dose range</th>
<th>28 day cost</th>
<th>Annual cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>GREEN 1st line</td>
<td>2g per day or 3g per day</td>
<td>£3.00</td>
<td>£39</td>
</tr>
<tr>
<td>Metformin MR</td>
<td>GREEN 2nd line</td>
<td>2g per day or 3g per day</td>
<td>£8.52</td>
<td>£111</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>GREEN 1st line</td>
<td>80-320mg daily</td>
<td>£0.71-2.84</td>
<td>£9.23-36.92</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>BROWN</td>
<td>45mg daily</td>
<td>£3.17</td>
<td>£41.21</td>
</tr>
<tr>
<td>Alogliptin</td>
<td>GREEN 1st line DPP4i</td>
<td>25mg daily</td>
<td>£26.60</td>
<td>£349</td>
</tr>
<tr>
<td>Linagliptin</td>
<td>GREEN alternative 1st line choice in renal and hepatic impairment</td>
<td>5mg daily</td>
<td>£33.26</td>
<td>£433</td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>BROWN</td>
<td>5mg daily</td>
<td>£31.60</td>
<td>£411</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>BROWN</td>
<td>100mg daily</td>
<td>£33.26</td>
<td>£433</td>
</tr>
<tr>
<td>Vildagliptin</td>
<td>BROWN</td>
<td>50mg BD</td>
<td>£33.35</td>
<td>£434</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>GREEN 1st line SGLT2i</td>
<td>10mg daily ↑25mg daily</td>
<td>£36.59</td>
<td>£476</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>BROWN</td>
<td>100mg daily ↑300mg daily</td>
<td>£36.59</td>
<td>£476</td>
</tr>
<tr>
<td>Dapagliflozin</td>
<td>BROWN</td>
<td>10mg daily</td>
<td>£36.59</td>
<td>£476</td>
</tr>
<tr>
<td>Ertugliflozin</td>
<td>BROWN</td>
<td>5-15mg daily</td>
<td>£31.50</td>
<td>£378</td>
</tr>
<tr>
<td>Lixisenatide</td>
<td>GREEN 1st line GLP1 agonist</td>
<td>20microg daily</td>
<td>£57.93</td>
<td>£753</td>
</tr>
<tr>
<td>Exenatide</td>
<td>BROWN</td>
<td>10mcg BD</td>
<td>£81.89*</td>
<td>£983</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>BROWN</td>
<td>1.2mg daily</td>
<td>£78.48*</td>
<td>£1020</td>
</tr>
<tr>
<td>Dulaglutide</td>
<td>BROWN (when weekly preparation is indicated)</td>
<td>750microg once weekly ↑1.5mg once weekly</td>
<td>£73.25</td>
<td>£952</td>
</tr>
<tr>
<td>Semaglutide</td>
<td>BROWN (weekly preparation; positive cardiovascular outcomes in clinical trials.</td>
<td>250microg once weekly ↑1mg once weekly</td>
<td>£73.25</td>
<td>£952</td>
</tr>
<tr>
<td>Exenatide MR</td>
<td>BROWN (when weekly preparation is indicated)</td>
<td>2mg once weekly</td>
<td>£73.36</td>
<td>£954</td>
</tr>
<tr>
<td>Albiglutide</td>
<td>Unclassified</td>
<td>30mg once weekly ↑50mg once weekly</td>
<td>£71</td>
<td>£923</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>BROWN (limited for use in early diabetes)</td>
<td>Starting dose is 0.5 mg with main meals. Maximum single dose is 4 mg taken with main meals. 'Total maximum daily dose should not exceed 16 mg.</td>
<td>£14.63 (maximum dose 16mg)</td>
<td>£190</td>
</tr>
</tbody>
</table>

*30 day cost ; Price as per Drug Tariff July 2018; semaglutide cost as per MIMs February 2019
Appendix 7 – structured education programmes - further resources

Southern Derbyshire and Erewash CCG
X-pert diabetes programme. (Referral form include below)
Contact telephone number: 01773 525 029,
DCHS new referral email: DCHST.XPertdiabeteseducation@nhs.net

| Referral to the X-Pert Diabetes Programme Structured Patient Education for Patients with TYPE 2 Diabetes |
|---|---|---|---|
| **Title** | **Full Name** | **Date of Birth** | **Gender** | **M** | **F** | **NHS No.** | **Address** | **Postcode** | **Email address** | **Home-phone** | **Mobile phone** | **Consent to leave voicemail?** | **Yes** | **No** | **Preferred contact method** | **Phone Text** | **Email Post** | **Best time to contact client** | **AM** | **PM** | **EVE** | **GP Name** | **GP Surgery** | **Diagnosis date** | **Referral date** | **Preferred language** | **Please give details of any reasonable adjustments required for this person to attend this education programme.** |
| **Weight (cm)** | **Weight (Kg)** | **BMI (Kg/m²)** | **Waist circumference (cm)** | **Blood Pressure (mmHg)** | **HbA1c (mmol/mol)** | **Blood Glucose Level** | **Total cholesterol (mmol/l)** | **Diabetes medication** | **YES** | **NO** |
| **I confirm the reason for the referral has been explained and the person has consented to be contacted by the X-Pert Diabetes Education team** | **Yes** | **No** |
| I confirm that this person has consented to share this health data with the X-Pert Diabetes Education Service for monitoring purposes and that they consent to similar data being shared from their next annual diabetes review meeting | **Yes** | **No** |

Please send this referral to the Type 2 X-Pert Diabetes Education Service
Erewash and Southern Derbyshire CCG areas
Email address: DCHST.XPertdiabeteseducation@nhs.net  Tel: 01773 525029
Derbyshire Diabetic Retinopathy Screening Programme & Derbyshire Community Health Service

Notification of New Diabetic Referral form

Please copy and paste the following email addresses into your NHS mail address ‘To’ box dhft.diabetic@nhs.net; DCHST.DiabetesandYou@nhs.net

Please fill in the below table and either copy and paste the table into your email text box or send this whole document as an email attachment once complete.

<table>
<thead>
<tr>
<th>NHS Number</th>
<th>Title</th>
<th>Forename</th>
<th>Surname</th>
<th>Address</th>
<th>Town</th>
<th>County</th>
<th>Postcode</th>
<th>Home telephone number</th>
<th>Mobile telephone number</th>
<th>Date of Birth</th>
<th>Gender</th>
<th>GP</th>
<th>GP Address</th>
<th>Diabetes Type</th>
</tr>
</thead>
</table>

*To refer to a Diabetes & You programme please continue overleaf*
**Derbyshire Community Health Service**

**Diabetes & You Programme**

Suitable for people diagnosed with Type 2 Diabetes who would benefit by attending the education programme

**Please note:** this programme is not suitable for people on insulin or who have been diagnosed with Type 1 Diabetes.

Please provide the following information to enable patients to plan and set goals for their Diabetes management whilst attending the course, and for audit purposes.

| Date Diagnosed with Type 2 Diabetes: |  
| Requires invitation to ‘Diabetes and you’ | Yes | No |
| Is patient aware of referral? Please tick | Yes | No |

**Please tick if patient has given consent to share their personal information with the Diabetic Education Team.** This information will be used within the structured education programme to allow patients to set their individual goals, as part of the individuals self-management plan.

<table>
<thead>
<tr>
<th>Item</th>
<th>Date</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>Date</td>
<td>Result</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Date</td>
<td>Result</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>Date</td>
<td>Result</td>
</tr>
<tr>
<td>Waist circumference (if known)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main Language</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Name and contact no of person making referral</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PLEASE EMAIL THIS COMPLETED FORM TO:**

DCHST.DiabetesandYou@nhs.net

**Diabetic Retinopathy Screening:** Tel: 01332 254977 Fax: 01332 783713

**Diabetes and You Education Programme:** Tel: 01246 515170