Diabetes Pathway

Contact
Tel: 023 8028 6401
Fax: 023 8028 6407
Mon-Fri 9.00am-5.00pm
Email: hp-tr.diabetes@nhs.net
Consultants email: kate.fayers@southernhealth.nhs.uk
    hermione.price@southernhealth.nhs.uk

Produced by West Hampshire Community Diabetes Service
October 2015
Adapted from Leicester Diabetes Guidelines 2013
Type 2 Diabetes - Referral Criteria to Specialist Services

**Secondary Care referral criteria**
1. Antenatal
2. Ophthalmology
3. Insulin pumps
4. Foot clinic
5. Specialist joint renal clinic (GFR <30)
6. Bariatric Service

**Same day secondary care referrals**

Newly diagnosed Children with Diabetes - refer to Paediatric Services. **All children suspected of diabetes need to be referred to secondary care urgently**

Newly diagnosed Type 1 Diabetes urgent in those who present with ketonuria and/or vomiting

Patients with infected, necrotic or gangrenous foot ulceration or suspected Charcot Foot

Sudden loss of vision contact local eye casualty

**Secondary Care Services: urgent referrals**

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Emergency</th>
<th>DSNs</th>
<th>Secretary/Admin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winchester RHCH</td>
<td>McGill ward</td>
<td>01962 825 700/5701, 01962 863 535</td>
<td>01962 825 097</td>
</tr>
<tr>
<td></td>
<td>bleep 131</td>
<td>Fax: 01962 825 300</td>
<td></td>
</tr>
<tr>
<td>Basingstoke NHH</td>
<td>AAU via switchboard</td>
<td>01256 313 613</td>
<td>01256 313 613</td>
</tr>
<tr>
<td></td>
<td>On call medical doctor</td>
<td>Fax: 01256 313 419</td>
<td></td>
</tr>
<tr>
<td>Southampton UHS</td>
<td>EMAU 023 8074 0999, 01256 313 613</td>
<td>01256 313 613</td>
<td>023 8120 4165</td>
</tr>
<tr>
<td></td>
<td>x3761 bleep 1199</td>
<td>Fax: 023 8120 5203</td>
<td></td>
</tr>
<tr>
<td>Salisbury</td>
<td>9.00am-7.00pm</td>
<td>01722 425 176</td>
<td>01722 425 143</td>
</tr>
<tr>
<td></td>
<td>01722 336 262</td>
<td>Fax: 01722 425143</td>
<td></td>
</tr>
<tr>
<td></td>
<td>bleep medical reg</td>
<td>1361</td>
<td></td>
</tr>
<tr>
<td>Bournemouth</td>
<td>Switchboard</td>
<td>01202 704 888</td>
<td>01202 704 888</td>
</tr>
<tr>
<td></td>
<td>01202 303 626 ask for Medical admissions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Paediatric services**
- Salisbury Hospital: 01722 366 262
- Southampton: 023 8077 7222 x6893
- Winchester: 01962 824 283
- Portsmouth: 023 922 83331

**Multidisciplinary Foot Care services**
- Basingstoke NHH Mon pm: 01256 313 648
- Winchester RHCH Weds am: 01962 825 097
- Andover War Memorial Hospital: 01962 825 097
- Royal Bournemouth Hospital: 01202 404 811
- Solent Health Podiatry: 0300 300 2011
- (Portsmouth & Southampton): 01722 429 229

**Antenatal clinics**
- Florence Portal, RHCH. Winchester: 01962 825 162
- Tues am: 01962 825 162
- Basingstoke NHH Thurs pm: 01256 313 648
- Southampton General Hospital: 07775 715 930
- Salisbury Tues am: 01722 429 229
- Royal Bournemouth Hospital Fri am: 01202 704 681

Date of preparation: October 2015. Review: April 2017
Primary care referral criteria to West Hampshire Community Diabetes Service

Patient Education
- Type 1
- Type 2

Suboptimal glycaemic control, despite titration of medication according to NICE guidance

Patients with complications:
1. Stage 3b CKD
2. Diabetic Retinopathy* (active ophthalmology FU)
3. Painful Diabetic Neuropathy
4. Previous Amputation
5. Active foot ulceration*
6. Active macrovascular disease (MI/unstable angina/CVA/TIA within the last year)
7. Other diabetic related complications
 (*with no access to active secondary care specialist service)

Others where specialist advice may be considered

Referral to West Hampshire Community Diabetes Service (WHCDS)
- Recurrent hypoglycaemia and impaired hypo-awareness
- Poor glycaemic control despite intensive management
- Persistent hypertension and/or hyperlipidaemia despite intensive management as per guidelines
- Painful neuropathy not responding to treatment (refer to Specialist Care)
- People with Type 1 Diabetes with previous failure to attend but now receptive to specialist referral
- Patients CKD 3 for optimisation of glucose, BP and lipids if control suboptimal
- Patients for type 1 carbohydrate counting education
- Patients in whom insulin pump therapy is being considered (refer for assessment)

Emergency Eye Departments

<table>
<thead>
<tr>
<th>Area</th>
<th>Contact Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Southampton UHS</td>
<td>023 8120 6592</td>
</tr>
<tr>
<td>Salisbury</td>
<td>01722 366 262 ext 4327</td>
</tr>
<tr>
<td>Basingstoke NHH</td>
<td>01256 315 572</td>
</tr>
<tr>
<td>Royal Bournemouth Hospital</td>
<td>01202 704 181</td>
</tr>
<tr>
<td>Portsmouth</td>
<td>02392 286 162</td>
</tr>
</tbody>
</table>

Hampshire Eye Screening Services

Southampton Diabetic Eye Screening Service
(Southampton and Isle of Wight)
Royal South Hants Hospital
Brintons Terrace
Southampton
SO14 0YG
0300 123 3937

Salisbury & North Hampshire Diabetic Eye Screening Programme
Block 8
Salisbury NHS Foundation Trust
Salisbury District Hospital
Odstock Road
Salisbury
SP2 8BJ
01722 425 022
t.screening1@nhs.net

Portsmouth and South East Hampshire Diabetic Eye Screening Service
Patient Management Centre
27 Guildhall Walk
Portsmouth
PO1 2RY
Tel: 0333 9992597
Email: CUK.drgpu@nhs.net
**Type 2 Diabetes - Diagnosis and screening**

**Whom to test**
- At least half of people with Type 2 diabetes are asymptomatic.
- Diabetes is often missed in the elderly.
- Glycosuria on its own does not confirm diabetes.
- Finger prick capillary results can not be used to diagnose diabetes.
- It is very important to identify diabetes as early as possible: 50% of newly presenting people with Type 2 diabetes already have 1 or more complications at diagnosis (1).

**How to test**
- An HbA1c of ≥48mmol/l (6.5%) is diagnostic of diabetes in most situations. It can be used to diagnose diabetes in asymptomatic patients. It should not be used in certain patient groups including children, pregnancy, suspected type 1 diabetes and acute illness. Measurement can be misleading in patients with haemoglobinopathies, anaemia or renal failure.

**Predetermined risk of diabetes**
- Coronary Heart Disease
- Women who have had Gestational Diabetes (screen at 6 weeks and one year post-partum, and then yearly)
- Those known to have impaired glucose tolerance, HbA1c 6.0-6.4% (42–47mmols/mol) or oral glucose tolerance test 2-hour value between 7.8mmol/l and 11.1 mmol/l impaired glucose regulation (IGR) or fasting glucose 6.1-6.9mmol/l (Impaired fasting glucose IFG)

**High risk for diabetes**
- White European people aged over 40 and people from Black, Asian and minority ethnic groups aged over 25 with
  - first degree relative with diabetes
  - BMI of 25-30 (i.e. are overweight) and who have a sedentary lifestyle >23 in South Asian people
  - BMI >30
  - Women with polycystic ovary syndrome
  - Cerebrovascular disease, peripheral vascular disease or hypertension/ hyperlipidaemia
  - Patients on prolonged steroid therapy
  - Patients on atypical anti-psychotic drugs

(3) The Expert Committee on the diagnosis and Classification of Diabetes Mellitus
Principles of Treatment

• Offer structured education The National Recommended Criteria from DoH on Structured Education 2004) to include diet/lifestyle advice to everyone. Usually wait 6-12 weeks before glucose lowering agents are introduced.

However:
Introduce oral hypoglycaemic agents early if fasting plasma glucose >15mmol/l and symptomatic.

• In patients with suspected type 1 diabetes or very raised glucose levels, (HbA1c>100mmols/mol) and symptomatic, Blood glucose monitoring is recommended and consider early treatment with insulin. In these patients ensure they are shown how to monitor their own diabetes, and know what to do if results do not fall in the target range. Consider referral to Specialist if type 1 Diabetes is suspected – See flow chart.

• Regular monitoring will identify the need to actively titrate treatment.

• Measure HbA1c every 2-6 months.

• Target HbA1c 48mmol/mol/6.5% in newly diagnosed Type 2 diabetes and those on up to two oral hypoglycaemic agents unless individual target more appropriate or at risk of hypoglycaemia. Involve the person in discussions about individual HbA1c target.

• In South Asian people BMI underestimates adiposity. Waist measurements need to be considered. Range for healthy weight is BMI 18.5-22.9 in South Asian people.

### Treatment decision tree for early insulin initiation

1. **Symptoms of hyperglycaemia and a diagnostic blood glucose (random ≥11.1 mmol/l)**
   - **YES**
   - **NO**

2. **Is the patient ill (vomiting, semiconscious or clinically dehydrated)?**
   - **YES**
   - **NO**

3. **Does the urine test show moderate/heavy ketonuria?**
   - **YES**
   - **NO**

4. **Are one or more of the following present?**
   - Severe osmotic symptoms (nocturia x 3-4)
   - Short history (weeks)
   - Marked weight loss (irrespective of absolute weight)
   - A first degree relative with Type 1 Diabetes
   - A personal history of autoimmune disease
   - **YES**
   - **NO**

5. **Is the patient under 30 years of age?**
   - **YES**
   - **NO**

6. **There is no immediate need for insulin. Give dietary advice on healthy eating. Provide regular review.**

7. **Arrange direct admission to hospital**

8. **Very likely to need insulin. Discuss with specialist team within 24 hours.**

9. **Two or more are a strong indication for insulin**

10. **First degree relative on diet or tablets consider Maturity Onset Diabetes of the Young (MODY)**
**Aims of dietary management:**
- Achieve normal glycaemia
- Reduce and or/maintain weight and waist measurements within healthy ranges
- Manage dyslipidaemia
- Manage hypertension
- Manage hypoglycaemia

**Dietary basics:**
1. Regular, well balanced meals (three meals/day) based on the Eatwell Plate. Snacks are not necessary unless treating or preventing hypoglycaemia. Portion sizes should be appropriate to the individual and their activity level. A useful guide is to use the clenched fist as a standard carbohydrate portion, the palm of the hand for the protein portion and as many vegetables as could be fitted into two cupped hands.
2. Reduce saturated fat intake by changing type of fat from saturated to unsaturated, preferably monounsaturated (olive or rapeseed based spreads and oils) and removing visible fat from food e.g. chicken skin, bacon rind. Fat is the most energy dense nutrient and should be reduced if weight loss is desired.
3. Eat at least 5 portions each day of fruit and vegetables, a portion is roughly what can be held in the hand e.g one apple, 6 strawberries, 2 apricots. Eating vegetables more than fruit is preferable for weight loss or improved blood sugar control and only one portion of fruit at a time due to high natural sugar content. Temperate/home-grown fruits (e.g. apples, pears, plums, berries) are preferable to tropical varieties (e.g. bananas, grapes, mango) as they have a lower glycaemic index. Including beans or lentils will increase fibre content and reduce the glycaemic effect of meals.
4. Choose low glycaemic index carbohydrates e.g. those with wholegrains, oat-based cereals and breads, as they cause a more gradual and sustained rise in blood sugar levels
5. Avoid sugary drinks e.g. regular varieties of cordials, fizzy drinks or adding sugar to hot drinks. Low sugar varieties are available.
6. Reducing salt and salty foods will help control hypertension. Foods labelled as less than 0.3g or salt or 0.1g sodium per 100g are considered to be low salt. Choose alternative flavourings for foods e.g. curry, pepper, lemon rather than adding salt. Maximum daily intake 6g of salt or less is recommended.
7. Eat 1-2 portions of oily fish per week for the benefit of omega-3 fats
8. Diabetic foods and drinks have no special benefit and are not necessary in a healthy diabetic diet
9. All carbohydrates will affect blood glucose levels. Educating people with diabetes about carbohydrate contents can help them achieve consistent carbohydrate intake for stable blood sugars or to be able to adjust the doses of their rapid acting insulin if on basal-bolus insulin regimens
10. Regular moderate activity each day will reduce insulin resistance and reduce weight

**BMI relates to an individual’s weight in relation to their height. For most adults, an ideal BMI is in the 18.5-24.9 range. BMI is not a useful measure in people of muscular build e.g. military personnel, sports people.**

<table>
<thead>
<tr>
<th>BMI</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>Underweight</td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>Desirable</td>
</tr>
<tr>
<td>25-29.9</td>
<td>Overweight</td>
</tr>
<tr>
<td>30-39.9</td>
<td>Obese</td>
</tr>
<tr>
<td>40+</td>
<td>Morbidly obese</td>
</tr>
</tbody>
</table>

**Waist circumference is most useful in people with BMI 25-35. It provides an additional measure and indicator of risk. Waist circumference measurement for men and women at which there is an increased relative risk is:**

<table>
<thead>
<tr>
<th>Increased risk</th>
<th>Substantially increased risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men &gt;=94 cm (37&quot;)</td>
<td>&gt;=102 cm (40&quot;)</td>
</tr>
<tr>
<td>Women &gt;=80 cm (31.5&quot;)</td>
<td>&gt;=88 cm (34.5&quot;)</td>
</tr>
</tbody>
</table>
Type 2 Diabetes - Monitoring Glycaemic control

National Service Framework for Diabetes- Standard 4

Key principles of practice

- 95% of the care people with diabetes receive is self-care and all patients should have access to high quality structured education programmes.
- The ability to monitor their own glucose level gives people with diabetes the feedback they need in order to learn how to manage their condition optimally.
- Monitoring should be based on the individual’s clinical needs and in the context of diabetes education and self management.
- People should receive appropriate training in the technique and the actioning of the results.
- The frequency of testing will be different for different people and will change with their circumstances. Any guidelines can only be used as a framework and then adapted to meet individual needs.
- People may move between different methods of monitoring dependent on their needs at that time.
- Equipment used for monitoring should follow local guidelines and policies.

HbA1c (Glycated haemoglobin)

At least once a year, your doctor should check your long-term diabetes control by taking a blood sample from your arm.

**HbA1c**

The most common test is the HbA1c test, which indicates your blood glucose levels for the previous two to three months. The HbA1c measures the amount of glucose that is being carried by the red blood cells in the body. Ref Diabetes UK

**Haemoglobin A1c**

Ideal targets are <53mmol/mol (7.0%) in Type 1 Diabetes and <48mmol/mol (6.5%) in newly diagnosed and short duration Type 2 Diabetes. Although we need to strive for these levels, targets should be set with the individual patient. Should not be measured more frequently than two monthly, except in pregnancy, and should be measured at least 6-12 monthly. Avoid pursuing highly intensive management to levels of <48mmol/mol (6.5%).

- HbA1c levels between 6.5% (48mmol/mol) to 48mol/mol (6.5%) are recommended by NICE (1)
- A MeREC review (2) states “...If appropriate and achievable in an individual, reducing blood glucose to HbA1c levels of around 7.5% would seem optimal based on current evidence. Lower levels may be appropriate for individuals with early disease...”
- NICE note that (1):
  - when setting a target glycated haemoglobin (HbA1c):
    - involve the person in decisions about their individual HbA1c target level, which may be above that of 6.5%(48mmol/mol) set for people with type 2 diabetes in general
    - encourage the person to maintain their individual target unless the resulting side effects (including hypoglycaemia) or their efforts to achieve this impair their quality of life
    - offer therapy (lifestyle and medication) to help achieve and maintain the HbA1c target level
    - inform a person with a higher HbA1c that any reduction in HbA1c towards the agreed target is advantageous to future health

### HbA1c conversion table

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

Patient education

All people newly diagnosed with type 2 diabetes (and/or their carer) should be offered referral to a structured education programme. Inform people and their carers that structured education is an integral part of diabetes care. West Hampshire Community Diabetes Service has a range of patient education programmes and workshops. For more details view the People Living with Diabetes Education Prospectus at www.southernhealth.nhs.uk/diabetes
Type 2 Diabetes - Monitoring Glycaemic control

**Type 2 Diabetes - Diet & lifestyle management only**
Self blood glucose monitoring is not recommended as part of routine care if HbA1c is within target but may be useful as an educational tool to understand lifestyle interventions. Urine testing may be adequate provided HbA1c targets are achieved. Measure HbA1c 3 monthly until target is reached, then monitor 6 monthly. If self-monitoring of blood glucose is considered appropriate, possible regime is: A

**Type 2 Diabetes – Oral therapy**
Re-assess patient needs if not achieving target HbA1c level, or if there is risk of hypoglycaemia which cannot be addressed by using an alternative diabetes treatment.
Consider self blood glucose monitoring. Frequency of testing should be agreed with patient and adequate training provided.
Some patients benefit from blood testing for short periods of time and then stop or return to urine testing, e.g. when oral medication is changed or adjusted.
Continue to measure HbA1c 3-6 monthly.
Possible regimes: A B C

**Type 2 Diabetes – Insulin with/ without oral agents**
Self blood glucose monitoring is recommended. Regular testing is required at initiation and during adjustment of doses. Frequency may be reduced when glycaemic target reached. Increased testing may be required during intercurrent illness and when there is risk of hypoglycaemia. Adequate training must be provided.
Those unable to self-monitor blood glucose may find urine testing helpful or may require more frequent HbA1c measurement.
HbA1c should be measured 3-6 monthly
Possible regimes: B C D

**Self-monitoring of plasma glucose should be available:**
- to those on insulin treatment
- to those on oral glucose-lowering medications to provide information on hypoglycaemia
- to assess changes in glucose control resulting from medications and lifestyle changes
- to monitor changes during intercurrent illness
- to ensure safety during activities, including driving

**Assess at least annually and in a structured way:**
- self-monitoring skills
- quality and appropriate frequency of testing
- use made of the results obtained
- impact on quality of life
- continued benefit
- equipment used
- if self-monitoring is appropriate but blood glucose monitoring is unacceptable
- to the individual, discuss the use of urine glucose monitoring
ref: Type 2 diabetes NICE clinical guideline 87

**Typical Self-Monitoring Regimens**

A Periodic testing to meet needs at that time
B 1-2 tests daily, varying times of testing including pre meal and post meal
C 4 tests per day x 2 week
D 4 tests per each day
E 7 tests per day pre & post meals

**Pregnancy**
Gestational Diabetes, type 2 diabetes and type 1 diabetes
Will need to monitor both pre meal and 1 hour post meal glucose levels and frequency will depend on treatment
Possible regimes: D E

**Type 1 Diabetes**
It is recommended that all people with Type 1 Diabetes monitor their blood glucose levels.
Self-monitoring may be used to adjust insulin doses prior to meals (eg basal bolus therapy and carbohydrate counting, pump therapy, during pregnancy) and so frequent daily testing will be required up to 4-7 tests per day. In more stable Type 1 Diabetes less frequent monitoring may be acceptable depending on patients daily routine.
Children with Diabetes or their parents may need to do frequent testing and this will be decided between themselves and the specialist paediatric team but could range from 1-7 tests per day.
HbA1c should be measured 3-6 monthly in all Type 1 Diabetes Patients.
Possible regimes: B C D E

**Targets for Self-blood glucose monitoring (SBGM)**
These should be set with the individual patient taking into account age, infirmity, and clinical factors.
Recommended targets for the general adult population are:
Type 2 diabetes
- Pre-meals: 4-7 mmol/l
- 2 hours post prandial: <8.5 mmol/l
Type 1 diabetes
- Pre meal 4-7mmol/l
- 2 hours post prandial <9mmol/l
Driving – recommended >5mmols is safe to drive
Type 2 Diabetes - Treatment Algorithm

Initiation of lifestyle interventions

Refer to structured education programme

Metformin (with active dose titration)

Efficacy (↓HbA1c): high, ↓CV events
Hypoglycaemia: low
Weight: neutral/ loss (~0-5kg)
Side effects: GI. See notes on lactic acidosis and renal impairment
Cost (£): low

If HbA1c target not achieved after ~3 months at maximum tolerated dose, proceed to dual therapy (order not intended to denote preference-choose according to patient- and disease- specific factors). NB. Combination tablets not recommended. Consider beginning at this stage if very high HbA1c (eg. ≥ 75 mmol/mol)

Metformin + Gliclazide
Efficacy (↓HbA1c): high
Hypoglycaemia: moderate
Weight: gain (~1.5-2kg)
Side effects: hypoglycaemia
Cost (£): low

Metformin + DPP-4 inhibitor
Efficacy (↓HbA1c): mid
Hypoglycaemia: low
Weight: neutral
Side effects*: rare
Cost (£): high

Metformin + SGLT2 inhibitor**
Efficacy (↓HbA1c): mid
Hypoglycaemia: low
Weight: loss (~2kg)
Side effects*: GU infections, dehydration
Cost (£): high

Metformin + Pioglitazone
Efficacy (↓HbA1c): high
Hypoglycaemia: low
Weight: gain (~4-5kg)
Side effects: oedema, HF, fractures
Cost (£): high

Metformin + GLP-1 agonist**
Efficacy (↓HbA1c): highest
Hypoglycaemia: high
Weight: gain (~4-5kg)
Side effects: hypoglycaemia
Cost (£): variable

Metformin + Insulin***
(usually basal)

If HbA1c target not achieved after ~3 months at maximum tolerated dose, proceed to triple therapy (order not intended to denote preference-choose according to patient- and disease- specific factors)

Metformin + Gliclazide
+ DPP-4 inhibitor
or SGLT2 inhibitor**
or pioglitazone or GLP-1 agonist**
or insulin***

Metformin + DPP-4 inhibitor
+ pioglitazone or insulin***

Metformin + SGLT2 inhibitor
+ pioglitazone or insulin***

Metformin + Pioglitazone
+ DPP4 inhibitor or SGLT2 inhibitor** or GLP-1 agonist**

Metformin + GLP-1 agonist
+ basal insulin***

Metformin + Insulin
+ DPP4 inhibitor or GLP-1 receptor agonist** or SGLT2 inhibitor**

If HbA1c target (and weight loss target for patients on GLP-1 agonists) not achieved after 3-6 months at maximum tolerated dose, proceed to a more complex insulin strategy, usually in combination with one or two non-insulin agents

Insulin (multiple daily doses)**

- ▼ Side effect profile still being established
- **GLP-1 agonists & SGLT2 inhibitors should be initiated in line with NICE TAs- see medicine notes
- ***Consider referral to structured education programme for patients initiated on insulin

West Hampshire Community Diabetes Team Oct 15, adapted from Nottinghamshire Health Community Treatment guideline for the Management of Type 2 diabetes.
# Biguanides - Metformin
(Metformin is the only available biguanide)
Decreases gluconeogenesis and increases peripheral utilisation of glucose.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
<th>Formulary choice</th>
<th>Precautions/ Contra-indications/ Patients with complex disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Metformin has a cardioprotective effect</td>
<td>First choice</td>
<td>Actively titrate the dose of metformin (i.e. increase to the maximum tolerated dose). This must be done over several weeks to minimise risk of gastrointestinal (GI) side effects. (NICE CG87). If adding metformin to gliclazide, it may be appropriate to decrease the gliclazide dose in order to titrate the metformin. HbA1c target for patients on metformin plus gliclazide should not be lower than 59mmol/ml. Renal impairment (NICE CG87): Review the dose of metformin if the serum creatinine exceeds 130 micromol/litre or the estimated glomerular filtration rate (eGFR) is below 45 ml/minute/1.73-m2. • Stop the metformin if the serum creatinine exceeds 150 micromol/litre or 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 45 ml/minute/1.73-m2. Liver or cardiac 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.</td>
</tr>
<tr>
<td></td>
<td>NICE guidance (CG87): Start metformin treatment in a person who is overweight or obese (tailoring the assessment of body-weight-associated risk according to ethnic group) and whose blood glucose is inadequately controlled by lifestyle interventions (nutrition and exercise) alone. Consider metformin as an option for first-line glucose-lowering therapy for a person who is not overweight. Continue with metformin if blood glucose control remains or becomes inadequate and another oral glucose-lowering medication (usually a sulfonylurea) is added. NICE guidance (PH38): Use clinical judgement on whether (and when) to offer standard-release metformin to support lifestyle change for people whose HbA1c or fasting plasma glucose blood test results have deteriorated if: this has happened despite their participation in an intensive lifestyle-change programme, or they are unable to participate in an intensive lifestyle-change programme.</td>
<td></td>
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</tr>
<tr>
<td>Metformin MR</td>
<td>Consider a trial of extended-absorption metformin tablets where GI tolerability prevents continuation of metformin therapy. (NICE CG87)</td>
<td>Second choice (for patients with proven GI intolerance)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Price per month: 1g twice daily £6.32 Sept 2015</td>
<td></td>
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<tr>
<td></td>
<td>Price per month: 2g daily: £10.64 Sept 2015</td>
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### Sulfonylureas - Gliclazide

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

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
<th>Formulary choice</th>
<th>Precautions/ Contra-indications/ Patients with complex disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gliclazide</td>
<td>Prescribe gliclazide when a sulfonylurea is indicated.</td>
<td>First choice</td>
<td>Educate the person about the risk of hypoglycaemia, particularly if they have renal impairment.</td>
</tr>
<tr>
<td></td>
<td>NICE guidance (CG87): Consider a sulfonylurea as an option for first-line glucose-lowering therapy if:</td>
<td></td>
<td>Increase dose every 4-6 weeks to achieve glycaemic target (do not exceed maximum dose). Check blood glucose (finger prick) before each titration to reduce risk of causing hypoglycaemia.</td>
</tr>
<tr>
<td></td>
<td>• the person is not overweight</td>
<td></td>
<td>HbA1c results of less than 48mmol/ml in patients on gliclazide should prompt a review of therapy due to a risk of symptomatic hypoglycaemia.</td>
</tr>
<tr>
<td></td>
<td>• the person does not tolerate metformin (or it is contraindicated)</td>
<td></td>
<td>If adding metformin to gliclazide, it may be appropriate to decrease the gliclazide dose in order to titrate the metformin.</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td></td>
<td>HbA1c target for patients on gliclazide plus metformin should not be lower than 59mmol/ml.</td>
</tr>
<tr>
<td></td>
<td>• a rapid response to therapy is required because of hyperglycaemic symptoms.</td>
<td></td>
<td>Gliclazide can cause weight gain (a few kilograms).</td>
</tr>
<tr>
<td></td>
<td>Add a sulfonylurea as second-line therapy when blood glucose control remains or becomes inadequate with metformin.</td>
<td></td>
<td>Advice for drivers:</td>
</tr>
<tr>
<td>Price per month (Nov14):</td>
<td></td>
<td></td>
<td>For Group 1 drivers (car/motorcycle) it may be appropriate to monitor blood glucose regularly and at times relevant to driving to enable the detection of hypoglycaemia. Group 2 drivers (bus/lorry) on sulfonylureas are required by law to monitor glucose level at least twice daily and at times relevant to driving.</td>
</tr>
<tr>
<td>80mg daily- 160mg twice daily</td>
<td></td>
<td></td>
<td>For more information about driving with diabetes see the Government guidance for drivers with diabetes and advice for drivers on the Diabetes UK website. DVLA also has info- see guidance for professionals.</td>
</tr>
<tr>
<td>£1.32- £5.28</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Glitptins (also known as DPP-4 inhibitors)
Inhibit dipeptidylpeptidase-4 to increase insulin secretion and to lower glucagon secretion.

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Formulary choice</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Alogliptin</td>
<td>Combinations approved for use locally:</td>
<td>First choice glitin for new patients and dose changes</td>
<td>See sitagliptin entry for MHRA warning regarding pancreatitis (applies to all gliptins). No long term safety data available for these agents.</td>
</tr>
<tr>
<td>rice per month (May15): 6.25mg-25mg daily £26.60</td>
<td>• Dual therapy with metformin, sulfonylurea or pioglitazone.</td>
<td></td>
<td>Renal impairment (CrCl, SPC):</td>
</tr>
<tr>
<td></td>
<td>• Triple therapy with metformin &amp; pioglitazone.</td>
<td></td>
<td>&gt;50ml/min – no dose adjustment</td>
</tr>
<tr>
<td></td>
<td>• Insulin (with or without metformin).</td>
<td></td>
<td>30-50ml/min – 12.5mg daily</td>
</tr>
<tr>
<td></td>
<td>NB there is currently limited data regarding use of alogliptin when used as triple therapy with metformin and a sulphonylurea</td>
<td></td>
<td>&lt;30ml/min – 6.25mg daily</td>
</tr>
<tr>
<td></td>
<td>Licensed in combination with:</td>
<td></td>
<td>No dose adjustment is necessary based on age. However, dosing of alogliptin should be conservative in patients with advanced age due to the potential for decreased renal function.</td>
</tr>
<tr>
<td></td>
<td>other glucose lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Sitagliptin | Low risk of hypoglycaemia and are weight neutral.                    | Continue glitin therapy only if there is a reduction of ≥5.5mmol/mol (0.5%) in HbA1c in 6 months. | No long term safety data available for these agents. |
|            | NICE guidance (CG87): Consider adding a glitin instead of a sulfonylurea as second-line therapy to first-line metformin when control of blood glucose remains or becomes inadequate (HbA1c ≥ 48mmol/mol, or other higher level agreed with the individual) if: |                                                                 | Renal impairment (CrCl, SPC):                                   |
|            | • the person is at significant risk of hypoglycaemia or its consequences (for example, older people and people in certain jobs [for example, those working at heights or with heavy machinery] or people in certain social circumstances [for example, those living alone], or |                                                                 | >50ml/min – no dose adjustment                                |
|            | • the person does not tolerate a sulfonylurea or a sulfonylurea is contraindicated.       |                                                                 | 30-50ml/min – 50mg daily                                    |
|            | Consider adding a glitin as second-line therapy to first-line sulfonylurea monotherapy when control of blood glucose remains or becomes inadequate (HbA1c ≥ 48mmol/mol, or other higher level agreed with the individual) if: |                                                                 | <30ml/min – 25mg daily                                      |
|            | • the person does not tolerate metformin, or metformin is contraindicated.                |                                                                 | No dose adjustment is necessary based on age. Limited safety data is available in patients ≥ 75 years of age and care should be exercised. Applies to all gliptins: |
|            | Consider adding a glitin as third-line therapy to first-line metformin and a second-line sulfonylurea when control of blood glucose remains or becomes inadequate (HbA1c ≥ 59mmol/mol or other higher level agreed with the individual) and insulin is unacceptable or inappropriate. |                                                                 | Discuss the potential benefits and risks of treatment with a glitin with the person to enable them to make an informed decision. |
|            | Licensed combinations:                                                   |                                                                 | Increased risk of pancreatitis associated with all gliptins. Patients should be informed of the characteristic symptoms of acute pancreatitis – persistent, severe abdominal pain (sometimes radiating to the back) – and encouraged to tell their healthcare provider if they have such symptoms. Link to MHRA warning |
|            | • Dual therapy with metformin, sulfonylurea or pioglitazone.               |                                                                 |                                                                 |
|            | • Triple therapy with metformin & sulfonylurea or pioglitazone.            |                                                                 |                                                                 |
|            | • Insulin (with or without metformin)                                      |                                                                 |                                                                 |
## Gliptins (also known as DPP-4 inhibitors)
*Inhibit dipeptidylpeptidase-4 to increase insulin secretion and to lower glucagon secretion.*

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Linagliptin</td>
<td>Licensed combinations:</td>
<td></td>
<td>See sitagliptin entry for MHRA warning regarding pancreatitis (applies to all gliptins). No long term safety data available for these agents.</td>
</tr>
<tr>
<td></td>
<td>• Dual therapy with metformin</td>
<td></td>
<td>Renal impairment (SPC): Does not require dose reduction in renal impairment,</td>
</tr>
<tr>
<td></td>
<td>• Triple therapy with metformin &amp; sulfonylurea</td>
<td></td>
<td>No dose adjustment is necessary based on age. However, clinical experience in patients &gt; 80 years of age is limited and caution should be exercised when treating this population.</td>
</tr>
<tr>
<td></td>
<td>• Insulin (with or without metformin)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Price per month (Nov14):**
- Linagliptin: 5mg daily £33.26
Thiazolidinediones (also known as Glitazones) (Pioglitazone is the only available thiazolidinedione) 
Reduces peripheral insulin resistance, leading to a reduction of blood glucose concentration

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Pioglitazone</td>
<td>NICE guidance (CG87): Consider adding pioglitazone instead of a sulfonylurea as second-line therapy to first-line metformin when control of blood glucose remains or becomes inadequate (HbA1c ≥ 48mmol/mol, or other higher level agreed with the individual) if: • the person is at significant risk of hypoglycaemia or its consequences (for example, older people and people in certain jobs [for example, those working at heights or with heavy machinery] or people in certain social circumstances [for example, those living alone]), or • a person does not tolerate a sulfonylurea or a sulfonylurea is contraindicated. Consider adding a pioglitazone as second-line therapy to first-line sulfonylurea monotherapy when control of blood glucose remains or becomes inadequate (HbA1c ≥ 48mmol/mol, or other higher level agreed with the individual) if: • the person does not tolerate metformin or metformin is contraindicated. Consider adding pioglitazone as third-line therapy to first-line metformin and a second-line sulfonylurea when control of blood glucose remains or becomes inadequate (HbA1c ≥ 59mmol/mol, or other higher level agreed with the individual) and insulin is unacceptable or inappropriate. Consider combining pioglitazone with insulin therapy for a person: • who has previously had a marked glucose-lowering response to thiazolidinedione therapy (pioglitazone), or • who is on high-dose insulin therapy and whose blood glucose is inadequately controlled. Licensed combinations: • Dual therapy with metformin or sulfonylurea. • Triple therapy with metformin &amp; sulfonylurea. • Insulin (if metformin not appropriate)</td>
<td>Pioglitazone is the only thiazolidinedione available</td>
<td>Continue pioglitazone therapy only if there is a reduction of ≥ 5.5mmol/mol (0.5%) in HbA1c in 6 months Do not start or continue pioglitazone in people who: • have heart failure (NYHA class I-IV) • are at a higher risk of fracture • macula oedema • a history of bladder cancer or in patients with uninvestigated macroscopic or microscopic haematuria. Risk of bladder cancer: MHRA safety update MHRA guide on patient selection and risk minimisation. 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. Risk of cardiac failure when combined with insulin: MHRA safety update Pioglitazone can cause weight gain. Discuss the potential benefits and risks of treatment with pioglitazone with the person to enable them to make an informed decision. Pioglitazone may be preferable to a gliptin if: • the person has marked insulin insensitivity, or • a gliptin is contraindicated, or • the person has previously had a poor response to, or did not tolerate, a gliptin. Renal impairment (SPC): No dose adjustment is necessary in patients with impaired renal function (creatinine clearance &gt; 4 ml/min). Do not use if hepatically impaired. No dose adjustment is necessary for elderly patients. Start with the lowest available dose and increase gradually, particularly when used in combination with insulin.</td>
</tr>
</tbody>
</table>
**GLP-1 (Glucagon-like peptide-1) Agonists**

**Increase insulin secretion, suppress glucagon secretion, and slow gastric emptying**

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Precautions/ Contra-indications/ Patients with complex disease</th>
</tr>
</thead>
</table>
| Lixisenatide | Once daily subcutaneous injection  
- Lixisenatide is currently the GLP-1 agonist with the lowest acquisition cost.  
- Start 10micrograms daily increasing to 20micrograms daily after 2 weeks if tolerated  
Dual / Triple therapy:  
As per exenatide (Byetta®)  
Licensed in combination with:  
oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, do not provide adequate glycaemic control.  
(See exenatide for local patient group comments on use with basal insulin)  
There is no specific NICE guidance for lixisenatide.                                                                 | Prescriber to decide most appropriate GLP-1 agonist after discussion with patient.  
If all other patient factors are equal prescribe the GLP-1 agonist with the lowest acquisition cost. | Dual therapy - continue lixisenatide only if the person has a reduction in HbA1c of ≥11mmol/mol (1%) after 6 months.  
Triple therapy - continue lixisenatide only if the person has a reduction in HbA1c of ≥11mmol/mol (1%) and a 3% loss of initial bodyweight after 6 months.  
No long term safety data available.  
Renal impairment (CrCl, SPC):  
50-80ml/min – no dose adjustment  
30-50ml/min – use with caution  
<30ml/min – not recommended  
No dose adjustment required based on age, but limited therapeutic experience in patients > 75yrs.  
See exenatide for information on hypoglycaemia and pancreatitis risk (applies to all GLP-1 agonists). |
| Exenatide    | Twice daily subcutaneous injection  
NICE guidance (CG87): Dual / Triple therapy:  
Can be used in dual or triple therapy regimens when control of blood glucose remains or becomes inadequate (HbA1c ≥ 59mmol/mol or agreed individualised target). Patients should be on maximally tolerated doses of oral hypoglycaemic agents and have a BMI;  
- ≥ 35.0 kg/m2 in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight, or  
- < 35.0 kg/m2, and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.  
Licensed indications:  
Dual therapy with metformin, a sulfonylurea or pioglitazone. Triple therapy with metformin & a sulfonylurea or metformin & pioglitazone.  
In combination with insulin:  
Exenatide (Byetta®) is licensed for addition to patient currently receiving insulin +/- metformin and/or pioglitazone in adults who have not achieved adequate glycaemic control with these agents.  
The local patient group indicated to receive this combination the person must fulfill the following criteria:  
- BMI >35 and HbA1c > 75mmol/mol and currently using insulin. | Prescriber to decide most appropriate GLP-1 agonist after discussion with patient.  
If all other patient factors are equal prescribe the GLP-1 agonist with the lowest acquisition cost. | Dual therapy - continue exenatide only if the person has a reduction in HbA1c of ≥11mmol/mol (1%) after 6 months.  
Triple therapy - continue exenatide only if the person has a reduction in HbA1c of ≥11mmol/mol (1%) and a 3% loss of initial bodyweight after 6 months.  
No long term safety data available.  
Renal impairment (CrCl, SPC):  
50-80ml/min – no dose adjustment  
30-50ml/min – dose escalation from 5 mcg to 10 mcg should proceed conservatively  
<30ml/min – not recommended  
Use with caution and dose from 5 mcg to 10 mcg should proceed conservatively in patients >70 years. The clinical experience in patients >75 years is very limited.  
Applies to all GLP-1 agonists:  
- Discuss the potential benefits and risks of treatment with a GLP-1 agonist with the person to enable them to make an informed decision.  
- 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.  
- 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. (MHRA warning). |
**GLP-1 (Glucagon-like peptide-1) Agonists**
Increase insulin secretion, suppress glucagon secretion, and slow gastric emptying

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
<th>Formulary choice</th>
<th>Precautions/ Contra-indications/ Patients with complex disease</th>
</tr>
</thead>
</table>
| **Exenatide prolonged release (Bydureon®)**<br>Price per month (Nov14): 2mg weekly: £73.36 | Once weekly subcutaneous injection  
- Use as per NICE TA248.  
- Exenatide MR is NOT licensed in combination with insulin.  
NICE TA248 – Exenatide prolonged release:<br>Dual therapy: (Met or Glic) + Exenatide MR  
Prolonged-release exenatide in dual therapy regimens (that is, in combination with metformin or a sulfonylurea) is recommended as a treatment option for people with type 2 diabetes, as described in ‘Liraglutide for the treatment of type 2 diabetes mellitus’ (NICE technology appraisal 203); that is, only if:  
- the person is intolerant of either metformin or a sulfonylurea, or a treatment with metformin or a sulfonylurea is contraindicated, and  
- the person is intolerant of thiazolidinediones and dipeptidyl peptidase-4 (DPP-4) inhibitors, or a treatment with thiazolidinediones and DPP-4 inhibitors is contraindicated.  
Triple therapy: Met + (Glic or Pio) + Exenatide MR  
Prolonged-release exenatide in triple therapy regimens (that is, in combination with metformin and a sulfonylurea, or metformin and a thiazolidinedione) is recommended as a treatment option for people with type 2 diabetes as described in ‘Type 2 diabetes: the management of type 2 diabetes (NICE clinical guideline 87); that is, when control of blood glucose remains or becomes inadequate (HbA1c ≥ 59 mmol/mol or agreed individualised target), and the person has:  
- a body mass index (BMI) ≥ 35 kg/m² in those of European family origin (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight or  
- a BMI < 35 kg/m², and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.  
Licensed combinations:  
- Dual therapy with metformin, a sulfonylurea or pioglitazone.  
- Triple therapy with metformin & sulfonylurea or metformin & pioglitazone. | Prescriber to decide most appropriate GLP-1 agonist after discussion with patient.  
If all other patient factors are equal prescribe the GLP-1 agonist with the lowest acquisition cost | Dual therapy - continue exenatide MR only if the person has a reduction in HbA1c of ≥11mmol/mol (1%) after 6 months.  
Triple therapy - continue exenatide MR only if the person has a reduction in HbA1c of ≥11mmol/mol (1%) and a 3% loss of initial bodyweight after 6 months.  
No long term safety data available.  
Renal impairment (CrCl, SPC):  
50-80ml/min – no dose adjustment  
<50ml/min – not recommended  
No dose adjustment required based on age, but limited therapeutic experience in patients > 75yrs.  
See exenatide for information on hypoglycaemia risk and warning about pancreatitis risk (applies to all GLP-1 agonists). |
**GLP-1 (Glucagon-like peptide-1) Agonists**

*Increase insulin secretion, suppress glucagon secretion, and slow gastric emptying*

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Formulary choice</th>
<th>Precautions/ Contra-indications/ Patients with complex disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liraglutide</td>
<td>Once daily subcutaneous injection</td>
<td>Prescriber to decide most appropriate GLP-1 agonist after discussion with patient.</td>
<td>Dual therapy - continue liraglutide only if the person has a reduction in HbA1c of ≥11mmol/mol2 (1%) after 6 months.</td>
</tr>
<tr>
<td></td>
<td>Use as per NICE TA203.</td>
<td></td>
<td>Triple therapy - continue liraglutide only if the person has a reduction in HbA1c of ≥11mmol/mol2 (1%) and a 3% loss of initial bodyweight after 6 months.</td>
</tr>
<tr>
<td></td>
<td>0.6mg daily for 2 weeks, increasing to 1.2mg daily if tolerated.</td>
<td></td>
<td>No long term safety data available.</td>
</tr>
<tr>
<td></td>
<td>Liraglutide 1.8 mg daily is not recommended for the treatment of people with type 2 diabetes. (NICE TA203)</td>
<td></td>
<td>Renal impairment (CrCl, SPC):</td>
</tr>
<tr>
<td></td>
<td>NICE TA203 – Liraglutide</td>
<td></td>
<td>30-90ml/min - no dose adjustment</td>
</tr>
<tr>
<td></td>
<td>Dual therapy: (Met or Glic) + Liraglutide</td>
<td></td>
<td>&lt;30ml/min – not recommended</td>
</tr>
<tr>
<td></td>
<td>Liraglutide 1.2 mg daily in dual therapy regimens (in combination with metformin or a sulfonylurea) is recommended as an option for the treatment of people with type 2 diabetes, only if:</td>
<td></td>
<td>No dose adjustment required based on age, but limited therapeutic experience in patients &gt; 75yrs.</td>
</tr>
<tr>
<td></td>
<td>• the person is intolerant of either metformin or a sulfonylurea, or treatment with metformin or a sulfonylurea is contraindicated, and</td>
<td></td>
<td>See exenatide for information on hypoglycaemia risk and warning about pancreatitis risk (applies to all GLP-1 agonists).</td>
</tr>
<tr>
<td></td>
<td>• the person is intolerant of thiazolidinediones and dipeptidyl peptidase-4 (DPP-4) inhibitors, or treatment with thiazolidinediones and DPP-4 inhibitors is contraindicated.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triple therapy: Met + (Glic or Pio) + Liraglutide</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Liraglutide 1.2 mg daily in triple therapy regimens (in combination with metformin + sulfonylurea, or metformin + thiazolidinedione) is recommended as an option for the treatment of people with type 2 diabetes, only if used as described for exenatide in NICE CG87; that is, when control of blood glucose remains or becomes inadequate (HbA1c ≥ 59mmol/mol, or agreed individualised target), and the person has BMI:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• ≥ 35 kg/m2 in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight, or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• &lt; 35 kg/m2, and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Licensed in combination with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, do not provide adequate glycaemic control.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correct at time of print. For most up to date version see www.southernhealth.nhs.uk/diabetes or the West Hampshire Community Diabetes Service App
**GLP-1 (Glucagon-like peptide-1) Agonists**

*Increase insulin secretion, suppress glucagon secretion, and slow gastric emptying*

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</tr>
</thead>
</table>
| Dulaglutide | Once weekly subcutaneous injection  
NICE advice [ESN59] June 2015  
Dulaglutide is licensed for improving glycaemic control in adults with type 2 diabetes mellitus as:  
Monotherapy: 0.75mg weekly, when diet and exercise alone do not provide adequate glycaemic control in people for whom the use of metformin is considered inappropriate due to intolerance or contraindications.  
Add on therapy: 1.5mg weekly, in combination with other glucose lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.  
The SPC and PIL are not specific in listing exactly which combinations are included in the product licence, the combinations that were used to support this indication in clinical trials were:  
Dulaglutide plus metformin  
Dulaglutide plus metformin and sulphonylurea  
Dulaglutide plus metformin and pioglitazone  
Dulaglutide plus metformin and prandial insulin (N.B. not with basal insulin)  
Dulaglutide and prandial insulin (N.B. not with basal insulin) | May be used in mild to moderate renal impairment.  
May be of benefit for patients with compliance problems, such as dexterity with other devices or dosing regimens | Elderly patients > 75 years recommended starting dose 0.75 mg weekly  
Renal impairment - No dosage reduction in mild to moderate. There is limited experience in severe renal failure or end stage renal disease so its use is not recommended.  
Hepatic impairment – No dosage adjustment required  
See exenatide for information on hypoglycaemia risk and warning about pancreatitis risk (applies to all GLP-1 agonists). |
**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.

### Sodium Glucose Co-Transporter 2 (SGLT2) Inhibitor Formulary

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin</td>
<td>NICE TA288: Dual therapy: Met + Dapagliflozin (as per glitptins): Dapagliflozin in a dual therapy regimen in combination with metformin is recommended as an option for treating type 2 diabetes, only if it is used as described for glitptins in Type 2 diabetes: the management of type 2 diabetes (NICE clinical guideline 87). Dapagliflozin + insulin: Dapagliflozin in combination with insulin with or without other antidiabetic drugs is recommended as an option for treating type 2 diabetes. The NICE TA states that dapagliflozin is not recommended for triple therapy. However, this is considered acceptable practise locally if dapagliflozin is used in combination with metformin and gliclazide. Licensed in combination with: other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.</td>
</tr>
</tbody>
</table>

### Precautions/Contra-indications/Patients with complex disease

- **Formulary choice**
  - Prescriber to decide most appropriate SGLT2 inhibitor after discussion with patient.
  - If all other patient factors are equal prescribe the SGLT2 inhibitor with the lowest acquisition cost.

- **Precautions/Contra-indications/Patients with complex disease**
  - No long term safety data available.
  - Licensed for initiation in adults between 18 and 75 years only.
  - Renal impairment (eGFR or CrCl SPC): >60ml/min – no dose adjustment <60ml/min – not recommended
  - Due to its mechanism of action, patients taking dapagliflozin are at increased risk of urinary tract infection and will test positive for glucose in their urine.
  - Increases diuresis associated with a modest decrease in blood pressure (more pronounced in patients with very high blood glucose concentrations).
  - Not recommended for patients receiving loop diuretics or who are volume depleted e.g. due to acute illness (such as gastrointestinal illness).
  - While a causal relationship between dapagliflozin and bladder cancer is unlikely, as a precautionary measure, dapagliflozin is not recommended for use in patients concomitantly treated with pioglitazone.
  - When treating patients who are taking an SGLT2 inhibitor (canagliflozin, dapagliflozin or empagliflozin): Test for raised 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
    - 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 (see below); advise them to get immediate medical help if these occur
    - be aware that SGLT2 inhibitors are not approved for treatment of type 1 diabetes
    - please continue to report suspected side effects to SGLT2 inhibitors or any other medicines on a Yellow Card

### Signs and symptoms

- Thirst
- Feeling tired and lethargic
- Blurry vision
- Abdominal pain, nausea, vomiting
- Breathing changes (deep sighing breaths)
- Ketones present Collapse/unconsciousness.
## 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.

### Drug

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
<th>Formulary choice</th>
<th>Precautions/ Contra-indications/ Patients with complex disease</th>
</tr>
</thead>
</table>
| Canagliflozin | • For use as per NICE TA315  
• Note that although canagliflozin is licensed for monotherapy, the APC have only approved it for use as per NICE TA315.  
NICE TA315:  
Dual therapy: Met + Canagliflozin  
Canagliflozin in a dual therapy regimen in combination with metformin is recommended as an option for treating type 2 diabetes, only if:  
• a sulfonylurea is contraindicated or not tolerated or  
• the person is at significant risk of hypoglycaemia or its consequences.  
Triple therapy: Met + (Glic or Pio) + Canagliflozin  
Canagliflozin in a triple therapy regimen is recommended as an option for treating type 2 diabetes in combination with:  
• metformin and a sulfonylurea or  
• metformin and a thiazolidinedione.  
Canagliflozin + insulin:  
Canagliflozin in combination with insulin with or without other antidiabetic drugs is recommended as an option for treating type 2 diabetes.  
Licensed in combination with:  
other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control. | Prescriber to decide most appropriate SGLT2 inhibitor after discussion with patient.  
If all other patient factors are equal prescribe the SGLT2 inhibitor with the lowest acquisition cost. | No long term safety data available.  
Licensed for adults aged over 18 years only. For patients over 65 years renal function and risk of volume depletion should be taken into account.  
Renal impairment (eGFR or CrCl, SPC):  
60-89ml/min – no dose adjustment.  
<60ml/min – do not initiate canagliflozin. Max dose 100mg daily if eGFR or CrCl persistently falls below 60ml/min whilst on canagliflozin.  
<45 ml/min- discontinue canagliflozin if eGFR or CrCl persistently falls below 45ml/min whilst on canagliflozin.  
Due to its mechanism of action, patients taking canagliflozin are at increased risk of urinary tract infection and will test positive for glucose in their urine.  
When treating patients who are taking an SGLT2 inhibitor (canagliflozin, dapagliflozin or empagliflozin):  
• test for raised 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  
• 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 (see below); advise them to get immediate medical help if these occur  
• be aware that SGLT2 inhibitors are not approved for treatment of type 1 diabetes  
• please continue to report suspected side effects to SGLT2 inhibitors or any other medicines on a Yellow Card. |
**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.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
<th>Formulary choice</th>
<th>Precautions/ Contra-indications/ Patients with complex disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empagliflozin</td>
<td>• For use as per NICE TA336: NICE TA315: Dual therapy: Met + Empagliflozin Empagliflozin in a dual therapy regimen in combination with metformin is recommended as an option for treating type 2 diabetes, only if: • a sulfonylurea is contraindicated or not tolerated or • the person is at significant risk of hypoglycaemia or its consequences. Triple therapy: Met + (Glic or Pio) + Empagliflozin Empagliflozin in a triple therapy regimen is recommended as an option for treating type 2 diabetes in combination with: • metformin and a sulfonylurea or • metformin and a thiazolidinedione. Empagliflozin + insulin: Empagliflozin in combination with insulin with or without other antidiabetic drugs is recommended as an option for treating type 2 diabetes. Licensed in combination with: other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.</td>
<td>Prescriber to decide most appropriate SGLT2 inhibitor after discussion with patient. If all other patient factors are equal prescribe the SGLT2 inhibitor with the lowest acquisition cost. 1st line SGLT2 inhibitor in established CV disease.</td>
<td>No long term safety data available. No dose adjustment is recommended based on age. In patients 75 years and older, an increased risk for volume depletion should be taken into account. In patients aged 85 years and older, initiation of empagliflozin therapy is not recommended due to the limited therapeutic experience. Renal impairment (eGFR or CrCl, SPC): 60-89ml/min – no dose adjustment. &lt;60ml/min – do not initiate empagliflozin. Max dose 10mg daily if eGFR or CrCl persistently falls below 60ml/min whilst on empagliflozin. &lt;45 ml/min- discontinue empagliflozin if eGFR or CrCl persistently falls below 45ml/min whilst on empagliflozin Due to its mechanism of action, patients taking empagliflozin are at increased risk of urinary tract infection and will test positive for glucose in their urine. When treating patients who are taking an SGLT2 inhibitor (canagliflozin, dapagliflozin or empagliflozin): • test for raised 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 • 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 (see below); advise them to get immediate medical help if these occur • be aware that SGLT2 inhibitors are not approved for treatment of type 1 diabetes • please continue to report suspected side effects to SGLT2 inhibitors or any other medicines on a Yellow Card</td>
</tr>
</tbody>
</table>
## Other Antidiabetic Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes</th>
<th>Formulary choice</th>
<th>Precautions/ Contra-indications/ Patients with complex disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acarbose</td>
<td>Useful in the occasional overweight patient.</td>
<td></td>
<td>Usage by limited by gastrointestinal intolerance.</td>
</tr>
<tr>
<td></td>
<td>NICE guidance (CG87): Consider acarbose for a person unable to use other oral glucose-lowering medications.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Licensed indication: Acarbose tablets are recommended for the treatment of non-insulin dependent (NIDDM) diabetes mellitus in patients inadequately controlled on diet alone, or on diet and oral hypoglycaemic agents.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibits intestinal alpha glucosidases (delays digestion and absorption of starch and sucrose)</td>
<td>Price per 28 days (Nov 14): 50mg-200mg three times daily £9-£30.65</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Insulin treatment

- If other measures do not keep HbA1c to <59 mmol/mol (or other agreed target), discuss benefits and risk of insulin treatment.
- Initiate with a structured programme including patient education and management plan. 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®) taken at bedtime or twice daily according to need.
- There is no evidence of a clinical benefit of analogue insulins over human insulins in type 2 diabetes.
- Consider twice-daily biphasic human insulin (pre-mix) regimens in particular where HbA1c >75 mmol/mol. 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 excursions.
- Recurrent symptomatic hypoglycaemia should prompt a re-examination of the current insulin regimen, injection sites, a search for other co-morbidities (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.
- If a patient requires once a day insulin administration because a carer or healthcare professional is needed to administer the insulin injection, and once daily NPH insulin does not provide sufficient control, then consider a trial of basal analogue insulin.
- Note that insulin tresiba may only be initiated by consultant diabetologist/endocrinologist (see Formulary for more detail).
- Monitor a person using a basal insulin regimen (NPH or a long-acting insulin analogue [insulin lantus/levemir]) 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 insulins (such as Humulin S®, Actrapid®, 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.
- Always prescribe insulin by brand to avoid the risk of error at the point of dispensing. Pay particular attention to the strength of the insulin as concentrated insulins are now available. The DPC has not yet approved the use of concentrated insulins in primary care. MHRA
- 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 insulins, if blood glucose control remains inadequate.
Oral agent combination therapy with insulin

- When starting basal insulin therapy:
  - Continue with metformin and gliclazide (and acarbose, if used)
  - Review the use of gliclazide if hypoglycaemia occurs.

- When prandial quick or rapid acting insulin injections or mixed insulins are started, gliclazide should be discontinued, or tapered and then discontinued, since it is not considered synergistic when with administered insulin.

- When starting pre-mixed insulin therapy (or mealtime plus basal insulin regimens):
  - Continue with metformin
  - Consider combining an SGLT2 inhibitor with insulin therapy if:
    - An SGLT2 inhibitor has previously had a marked glucose lowering effect, or
    - Blood glucose control is inadequate with high dose insulin.

Use of GLP1 analogues in combination with insulin

- Exenatide (Byetta®), lixisenatide and liraglutide are licensed for addition to patients currently receiving insulin.
- The patient group indicated to receive this combination must fulfill the following criteria: morbidly obese (BMI >35) and HbA1c >75mmol/mol and currently using insulin.
- This regimen must be initiated by a specialist.
- Continue the GLP1 in combination with insulin only if the person has a reduction in HbA1c of ≥11mmol/mol and a 3% loss of initial body weight in 6 months.

Intensifying the insulin regimen

- Monitor those using basal insulin regimens for the need for short acting insulin before meals or pre-mixed insulin.
- Monitor those using premixed insulin once or twice daily for need for further injections of short acting insulin before meals or change to mealtime plus basal regimen.

Insulin delivery devices

- Offer education to a person who requires insulin on using an injection device (usually a pen injector and cartridge or a disposable pen) to ensure that they and/or their carer find it easy to use.
- Appropriate local arrangements should be in place for the disposal of sharps.
- If a person has a manual or visual disability and requires insulin, offer a device or adaptation that:
  - takes into account his or her individual needs
  - he or she can use successfully.

With thanks to: Jill Theobald and Lynne Kennell, Specialist Interface & Formulary Pharmacists, Nottinghamshire APC for allowing us to adapt their guidelines.

Adapted by Emma Smithson Medicines Management Pharmacist West Hants CCG, Dr Kate Fayers Consultant Diabetologist SHFT, Dr Hermoine Price Consultant Diabetologist SHFT, October 2015

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- Dr Sadpreet Shota, Diabetes Consultant, SHFT
- Dr Renee Page, Diabetes & Endocrinology Consultant, NUH
- Dr Kamal Chokkalingham (Nottingham University Hospitals NHS Trust)
- Diabetes Specialist Nurses, SHFT

CityCare Diabetes Specialist Nurse via Panchmatia Shailesh - Head of Medicines Management
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- Aynge Jeremy, Practice Pharmacist / Independent Prescriber for Diabetes, Nottingham City CCG

Additional comments received from:
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- Diabetes Specialist Nurses, City Campus NUH
- Diabetes Specialist Nurses in County CCGs
- West Hampshire Community Diabetes Specialist Nurses, Southern Health NHS Foundation Trust

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- Dr Simon Page (Diabetes and Endocrinology Clinical Lead, Nottingham NHS Treatment Centre)
- Nottinghamshire County Clinical Commissioning Groups & Medicines Management teams
- Nottingham City Clinical Commissioning Group & Medicines Management team

With thanks to Jan Hammerton and Carra Smith, Southern Health NHS Foundation Trust

References:
- Derbyshire APC Guideline – Glucose control in type 2 diabetes May 2011
- MHRA Drug Safety Update March 2009
- NICE Clinical Guideline 87 Type 2 Diabetes May 2009
- NICE Technology Appraisal – Leaguide for the treatment of Type 2 Diabetes Mellitus October 2010
- NICE Technology Appraisal – Dapagliflozin combination therapy June 2013
- NICE Technology Appraisal – Canagliflozin combination therapy June 2014
- NICE Technology Appraisal Diabetes (Type 2) – Erbstatin (prolonged release) February 2012
- Nottinghamshire Diabetes Guidelines
- Type 2 Diabetes mellitus and renal impairment – dosing guidelines. Author; Dr Simon Page (Diabetes and Endocrinology Clinical Lead, Nottingham NHS Treatment Centre)
- NICE evidence summary Diaglutide June 2015
## Type 2 Diabetes - Medications

### Worsening renal function or Hepatic impairment

#### Worsening renal function (GFR range in ml/min)

<table>
<thead>
<tr>
<th>Drug</th>
<th>CKD stage 1 (GFR &gt;90)</th>
<th>2 (60-80)</th>
<th>3a (59-45)</th>
<th>3b (44-30)</th>
<th>4 (29-15)</th>
<th>5 (≤ 15 or RRT)</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acarbose</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (GFR &lt;25ml/min)</td>
<td>✓</td>
<td>✓ Contraindicated</td>
</tr>
<tr>
<td>Metformin / Metformin MR</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (review regularly)</td>
<td>✓</td>
<td>✓ Contraindicated in hepatic insufficiency</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (Use lowest effective dose)</td>
<td>✓</td>
<td>✓ Contraindicated</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>100mg</td>
<td>50mg (GFR&lt;50ml/min)</td>
<td>25mg</td>
<td>✓</td>
<td>✓</td>
<td>✓ No dose adjustment required, but clinical experience is lacking in hepatic impairment</td>
<td></td>
</tr>
<tr>
<td>Linagliptin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ Not studied in severe hepatic impairment</td>
</tr>
<tr>
<td>Alogliptin</td>
<td>25mg</td>
<td>12.5mg (GFR&lt;50ml/min)</td>
<td>6.25mg</td>
<td>✓</td>
<td>✓</td>
<td>✓ No dose adjustment required, but clinical experience is lacking in hepatic impairment</td>
<td></td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (not if dialysis)</td>
<td>✓ Contraindicated</td>
</tr>
<tr>
<td>Lisixenatide</td>
<td>✓</td>
<td>✓</td>
<td>✓ (Cautions if GFR &lt;50ml/min)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ Contraindicated</td>
</tr>
<tr>
<td>Exenatide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (Conservative dose escalation)</td>
<td>✓</td>
<td>✓ Contraindicated</td>
</tr>
<tr>
<td>Exenatide MR</td>
<td>✓</td>
<td>✓</td>
<td>✓ (not if GFR&lt;50ml/min)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ Contraindicated</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ No recommended</td>
<td>✓ Not recommended</td>
</tr>
<tr>
<td>Dulaglutide</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ Contraindicated</td>
</tr>
<tr>
<td>Dapagliflozin</td>
<td>✓</td>
<td>✓</td>
<td>✓ (Do not initiate if GFR &lt;60ml/min, max dose 100mg od if GFR persistently falls below 60ml/min after initiation)</td>
<td>✓</td>
<td>✓</td>
<td>✓ Start at 5mg, increase to 10mg if well tolerated</td>
<td></td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>✓</td>
<td>✓</td>
<td>✓ (Do not initiate if GFR &lt;60ml/min, max dose 100mg od if GFR persistently falls below 60ml/min after initiation)</td>
<td>✓</td>
<td>✓</td>
<td>✓ No recommended</td>
<td></td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>✓</td>
<td>✓</td>
<td>✓ (Do not initiate if GFR &lt;60ml/min, max dose 100mg od if GFR persistently falls below 60ml/min after initiation)</td>
<td>✓</td>
<td>✓</td>
<td>✓ No recommended</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ Requirements may be reduced in severe renal impairment - monitor and adjust dose accordingly</td>
<td>✓ Requirements may be altered in hepatic impairment - monitor and adjust dose accordingly</td>
</tr>
</tbody>
</table>
## Type 2 Diabetes - Medications

### Dual therapy combination table

<table>
<thead>
<tr>
<th>Type 2 diabetes mellitus treatments – Dual therapy combination table</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alphabetical</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td><strong>Metformin</strong></td>
</tr>
<tr>
<td><strong>Metformin MR</strong></td>
</tr>
<tr>
<td><strong>Glicazide</strong></td>
</tr>
<tr>
<td><strong>Alogliptin</strong></td>
</tr>
<tr>
<td><strong>Linagliptin</strong></td>
</tr>
<tr>
<td><strong>Sitagliptin</strong></td>
</tr>
<tr>
<td><strong>Pioglitazone</strong></td>
</tr>
<tr>
<td><strong>Exenatide</strong></td>
</tr>
<tr>
<td><strong>Exenatide MR</strong></td>
</tr>
<tr>
<td><strong>Lixisenatide</strong></td>
</tr>
<tr>
<td><strong>Liraglutide</strong></td>
</tr>
<tr>
<td><strong>Canagliflozin</strong></td>
</tr>
<tr>
<td><strong>Dapagliflozin</strong></td>
</tr>
<tr>
<td><strong>Empagliflozin</strong></td>
</tr>
<tr>
<td><strong>Acarbose</strong></td>
</tr>
<tr>
<td><strong>Insulin</strong></td>
</tr>
</tbody>
</table>

**Key**

- **L**: Not licensed
- **NICE**: Licensed, but not NICE approved
- **LOCAL**: Licensed, but not approved for use locally
- **Y**: Combination can be used as per guideline
- **NICE***: Combination can be used as per guideline, but outside of NICE

Correct at time of print. For most up to date version see www.southernhealth.nhs.uk/diabetes or the West Hampshire Community Diabetes Service App

Date of preparation: October 2015. Review: April 2017
## Type 2 Diabetes - Medications

### Triple therapy combination table

**Type 2 diabetes mellitus treatments – Triple therapy combination table**

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Met + Gliclazide</th>
<th>Met + Pioglitazone</th>
<th>Met + Sitagliptin</th>
<th>Met + Exenatide</th>
<th>Met + Liraglutide</th>
<th>Met + Sotagliflozin</th>
<th>Met + Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Metformin MR</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Alogliptin</td>
<td>LOCAL</td>
<td>NICE</td>
<td>LOCAL</td>
<td>NICE</td>
<td>NICE*</td>
<td>NICE</td>
<td>NICE*</td>
</tr>
<tr>
<td>Linagliptin</td>
<td>Y</td>
<td>LOCAL</td>
<td>NICE*</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td>Sitagliptin</td>
<td>Y</td>
<td>LOCAL</td>
<td>NICE*</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>Y</td>
<td>NICE*</td>
<td>L</td>
<td>Y</td>
<td>L</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Exenatide</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Exenatide MR</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Lixisenatide</td>
<td>Y</td>
<td>Y</td>
<td>L</td>
<td>Y</td>
<td>L</td>
<td>NICE</td>
<td>NICE</td>
</tr>
<tr>
<td>Lisinaglutide</td>
<td>Y</td>
<td>NICE*</td>
<td>L</td>
<td>NICE</td>
<td>NICE</td>
<td>Y</td>
<td>L</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>Y</td>
<td>NICE</td>
<td>L</td>
<td>NICE</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Dapagliflozin</td>
<td>NICE*</td>
<td>L</td>
<td>L</td>
<td>NICE</td>
<td>Y</td>
<td>L</td>
<td>Y</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>Y</td>
<td>Y</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>Y</td>
<td>L</td>
</tr>
<tr>
<td>Acarbose</td>
<td>Y</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>NICE</td>
<td>NICE</td>
</tr>
<tr>
<td>Insulin</td>
<td>Y</td>
<td>NICE*</td>
<td>NICE*</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

**Correct at time of print. For most up to date version see www.southernhealth.nhs.uk/diabetes or the West Hampshire Community Diabetes Service App.**
Type 2 Diabetes - Cardiovascular Risk

See Algorithm for Blood Pressure Management

There is now no need to estimate cardiovascular risk in those with diabetes before deciding whether to intervene to improve individual cardiovascular risk factors in people with either Type 1 or Type 2 diabetes. All people with diabetes are considered to be at high cardiovascular risk. All require lifestyle advice and multifactorial risk factor intervention.

### Lifestyle intervention

**Smoking cessation**
should be encouraged, with use of Stop Smoking clinics as required.

**Dietary intervention**
- Should include weight loss for those with high waist circumferences
  - >94cm in Northern European White male
  - >80cm in Northern European White females
  - >90cm in South Asian males
  - >80cm in South Asian females
- and, for all should include advice about a low fat diet high in fruit and vegetables (at least 5 portions per day).
- Should include advice to decrease total dietary fat to <30% of total energy intake
- Should include advice to decrease saturated fats to <10% of total fat intake.
- Should include advice about lowering salt intake to be less than 6g of salt (=2.4 g sodium chloride) per day.
- Alcohol intake should be discussed, with the advice for males to limit to 21 units per week and females to 14 units/week.
- Regular intake of oily fish and other sources of omega 3 fatty acids (at least 2 portions of fish per week)

**Exercise**
The benefits of regular exercise should be explained and patients should be advised to perform regular aerobic activity. Clinical studies show that walking for 30 minutes every day has cardiovascular benefits.

**Smoking**
Please assess patients for smoking status and refer to Smoking Cessation Teams for patient support.

To access the service please visit the Quit4Life website to find a session local to you, call the Quitline for support wherever you are on 0845 602 4663, or text QUIT to 60123. You can also email the Quit4Life advisors at quit4life@nhs.net

### Blood pressure

All patients with diabetes (Type 1 or Type 2) should be treated to a target of 140/80 with a combination of lifestyle intervention (see above) and drug therapy. If kidney, eye or cerebrovascular damage set a target <130/80.

Up to half the patients with Type 2 diabetes will need 3 or more antihypertensive agents, and it is important for patients to be made aware of this when discussion around hypertension occurs. ACE inhibitors and ARBs are preferred first line therapy in people with any degree of nephropathy (micro- or macroalbuminuria).

In all patients measure renal functions and electrolytes 1-2 weeks after initiation of ACE inhibitors and ARBs and with each increase in dose.

The British Hypertension Society’s Guidelines should be followed. Assess blood pressure at least 3 monthly until targets are achieved, and monitor every 4-6 months once targets are achieved.

Patients who do not achieve target should be referred for further management. Remember that, if the patient does not achieve target despite greatest efforts by the multidisciplinary team, any improvement towards the target is better than the patient’s baseline.

In females who are planning a pregnancy or who are pregnant these drugs should be withheld until breast feeding has ceased.
Type 2 Diabetes - Cardiovascular Risk

See Algorithm for Lipid and Diabetes Management

**Lipids**

**Whom to consider for treatment:**
- All those who are aged 40 or more with either Type 1 or Type 2 diabetes
- Those aged 18-39 with either Type 1 or Type 2 diabetes who have at least one of the following with poor CV risk factor profile:
  - Significant retinopathy (pre-proliferative, proliferative or maculopathy)
  - Any degree of nephropathy (micro- or macroalbuminuria)
  - HbA1c > 75 mmol/mol (9%)
  - Requirement of antihypertensive therapy (see above)
  - Total cholesterol >5 mmol/l
  - Family history of premature cardiovascular disease in a first degree relative (<55 years in males, <65 years in females)
  - Features of metabolic syndrome (increased waist circumference, increased triglycerides, decreased HDL and hypertension)

**Optimal HDL levels are:**
- Males >1.0 mmol/l
- Females >1.2 mmol/l

**Fasting Triglyceride target:**
- Males <1.7 mmol/l
- Females <1.7 mmol/l

It is important to note that the target triglyceride level is a fasting target, so an individual with a non-fasting result >2.3 mmol/l should be invited back to have a fasting triglyceride estimation. HDL and triglyceride interventions include lifestyle (predominantly weight loss and exercise) and drug therapies. The drug of choice is a fibrate, usually Fenofibrate 160mg. If using a combination lipid lowering regimen, monitoring of ALT and CK is appropriate.

**Treatment targets**

Dietary interventions alone only reduce cholesterol by <10%. To reach targets, often drug therapy will be required. The initial target is to achieve a total cholesterol of <4.0 mmol/l and an LDL of <2.0 mmol/l. Statins are first line drugs for this indication. In accordance with NICE guidelines, low cost statins should be first choice e.g. Simvastatin 40mgs. The dose of the statin should be increased until these targets are achieved. If targets are not achieved a more potent statin such as Atorvastatin should be considered. If Atorvastatin is not tolerated consider using Rosuvastatin, and then the addition of a second agent Ezetimibe. Monitor LFTs 6 weeks post initiation of statin. If normal check annually.

In females who are planning a pregnancy or who are pregnant these drugs should be withheld until breast feeding has ceased.

**Anti-Platlet Agents**

Aspirin 75 mg daily is indicated for all patients with diabetes who have any form of cardiovascular disease. In those who are hypertensive the blood pressure should be controlled to 145/90 or below before commencement of aspirin. If aspirin is not tolerated or is contraindicated, clopidogrel 75 mg daily should be considered.

Fibrates should not be commenced if eGFR is <45. They should be discontinued with deterioration of renal function.
NSF key intervention
Regular surveillance for diabetic retinopathy in adults with Diabetes and early laser treatment of those identified as having sight threatening retinopathy can reduce the incidence of new visual impairment and blindness in people with Diabetes.

Screening
Examine eyes of people with Type 2 Diabetes at diagnosis and at least annually thereafter, including those blind and partially sighted, and all those with Type 1 Diabetes from 12 months after diagnosis.

Algorithm for the early management of diabetic retinopathy in Type 2 Diabetes

On diagnosis of Type 2 Diabetes, examine eyes:
- Check visual acuity, corrected with spectacles or pinhole - if problem, including cataract, seek ophthalmologic opinion.
- Examine for diabetic retinopathy following dilation of pupils with tropicamide or take a photograph with a digital camera of sufficient specification.

Is retinopathy present?
- No
- Yes

Maintain good blood glucose control (HbA1c below 6.5-7.5%, according to individual's target) and good blood pressure control (below 130/80 mmHg)

Manage retinopathy as follows:
- Sudden loss of vision
- Retinal detachment
- New vessels
- Pre-retinal and/or vitreous haemorrhage
- Rubeosis iridis
- Unexplained drop in visual acuity (which may indicate macular oedema)
- Hard exudates within 1 disc diameter of fovea
- Macular oedema
- Unexplained retinal findings
- Pre-proliferative or severe retinopathy
- Occurrence or worsening of lesions since previous examination
- Scattered exudates more than 1 disc diameter from fovea
- People at high risk of progression

Referral
Arrange referral for specialist opinion within 4 weeks

Early referral
Emergency referral to ophthalmology specialist / Eye Casualty
Same day referral

Urgent referral to ophthalmology specialist
Arrange referral within 1 week

Routine Care
Arrange recall and annual review

Background points
- Diabetic retinopathy is the most common cause of blindness in people of working age. (1)
- About 38% of Type 2 diabetics have retinopathy at diagnosis.(2)
- Progresses over the years: after 15 years, at least two thirds of patients may have background retinopathy.

All patients with Diabetes should be on a register and minimum data should include annual measures for microvascular disease. Please see Cardiovascular Risk for additional requirements.


Type 1 and Type 2 Diabetes - Preventing specific complications - Retinopathy
NICE CG66 Type 2 Diabetes
Obesity is a major modifiable risk factor in the development of type 2 diabetes. Decrease in weight in those who are obese can improve diabetes control enormously without the need for escalation in therapy. **Weight loss can be effective enough to cure type 2 diabetes.**

**Guidance**
Those people with diabetes whose adipose tissue mass is likely to contribute to the progression of their diabetes control should be offered the opportunity to discuss their weight. The benefits to the patient of weight loss should be made clear. If the individual does not wish to consider making any changes then this should be reviewed at future consultations. Any choice of weight loss intervention should be negotiated between patient and health care professional. Consideration of what has been tried before is important.

**Interventions**
Interventions include lifestyle advice, specific drug therapy and obesity surgery.

**General Points**
Realistic targets for weight loss should be discussed
- Maximum weekly weight loss of 0.5 – 1kg
  
  Aim to lose 5-10% of original weight

Realistic targets for exercise will vary greatly depending on the individual. Ideally, individuals should be encouraged to take up to 45 minutes of exercise per day, 5 times per week. Encouragement to join a commercial weight loss organisation can be beneficial.

**Lifestyle intervention**
This is the main stay of obesity management. Any advice offered is more likely to be accepted by the patient if we as health care professionals offer the advice in an enthusiastic manner. Ideally, a combination of reduction of calorie intake and an increase in energy expenditure should be considered.

**Obesity Surgery**
Bariatric surgery is recommended as a treatment option for adult with obesity and recent onset diabetes (within last 10 years) if all the following local criteria are fulfilled:

1. they have type 2 diabetes and a BMI of 35 kg/m2 or more as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent)
2. all appropriate non-surgical measures have been tried but have failed to achieve or maintain adequate, clinically beneficial weight loss for at least 6 months
3. the person has been receiving or will receive intensive management in a specialist obesity service
4. the person is generally fit for anaesthesia and surgery
5. the person commits to the need for long-term follow-up.

Assessments for bariatric surgery should be considered for people with a BMI of 30–34.9 (or lower BMI for people of Asian family origin) who have recent-onset and poorly controlled type 2 diabetes as long as they are also receiving or will receive assessment in a tier 3 service (or equivalent). Bariatric surgery is also recommended as a first-line option (instead of lifestyle interventions or drug treatment) for adults with a BMI of more than 50 kg/m2 in whom surgical intervention is considered appropriate.
Obesity - drug therapy

Before deciding to start treatment, and choosing the drug, discuss with the patient the potential benefits and limitations, including the mode of action, adverse effects and monitoring requirements, and their potential impact on the patient’s motivation.

- When prescribing, make arrangements for appropriate healthcare professionals to offer information, support and counselling on additional diet, physical activity and behavioural strategies.
- Give information on patient support programmes.
- Follow the drug’s summary of product characteristics.

Drug therapy
Pharmacological agents are only to be used once lifestyle interventions have been instigated and the patient has reached a plateau in their weight loss but still wishes to lose more weight. It is important to set achievable targets for weight loss of no more than 10% of body weight.

When considering the use of pharmacological agents to aid weight loss, ensure that the patient:
1. wishes to lose weight (the benefits of weight loss should be discussed)
2. is prepared to make changes to their calorie intake following appropriate dietary advice, preferably from a dietitian with an interest in obesity
3. is prepared to increase the level of physical activity (if able), preferably up to 45 minutes of moderate exercise at least 5 times per week
4. is prepared to consider joining a commercial weight loss programme.
5. Understands that, if the drug is deemed not to be successful then it will be withdrawn.

All studies showing the greatest benefit with the weight loss drugs involved lifestyle intervention as part of the management.

Continued prescribing and withdrawal
- Review regularly, to monitor the effect of drug treatment, and to reinforce lifestyle advice and need for adherence.
- Drug treatment may be used to help people to maintain weight loss, as well as to continue to lose weight.
- Consider withdrawing drug treatment if the person does not lose enough weight.

Agree goals with the person and review regularly
- If concerned about micronutrient intake, consider giving a supplement providing the reference nutrient intake for all vitamins and trace elements, particularly for vulnerable groups such as older people, who may be at risk of malnutrition.
- If withdrawing a person’s drug treatment, offer support to help maintain weight loss because their self-confidence and belief in their ability to make changes may be low.

Specific advice on orlistat
(NICE guidance available)
- Use only in those with diabetes or endocrine conditions who have a BMI >28kg/m2
- Continue beyond 3 months of therapy only if the patient has lost at least 5% of their body weight.
- Continue beyond 12 months for weight maintenance only after discussion of potential benefits and limitations with the patient.

Type 2 Diabetes - Preventing specific complications - Obesity
Nephropathy screening and management

**Background points**

Diabetic nephropathy or diabetic kidney disease affects nearly 20-30% individuals with Type 2 diabetes. The earliest sign of kidney involvement in Type 2 diabetes is abnormal amounts of albumin excretion in the urine which is assessed by laboratory measurement of the albumin creatinine ratio (ACR). Depending on this measure, individuals are categorized into the stages of microalbuminuria or proteinuria.

**Definition of higher-risk urine albumin excretion**

<table>
<thead>
<tr>
<th>ACR</th>
<th>Protein concentration</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microalbuminuria</td>
<td>2.5 male 3.5 female to 30</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Proteinuria (low)</td>
<td>30-70</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Proteinuria (high)</td>
<td>&gt;70</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>

**Assessment of individual with Diabetic nephropathy**

- Take a full history. List all medications taken
- Physical examination, evaluate for presence of cardiovascular disease
- Urine analysis (ACR), assess kidney function (GFR), Full Blood Count to exclude anaemia, kidney imaging studies and other investigations as appropriate
- Look for presence of retinopathy, peripheral vascular disease, other diabetes complications including erectile dysfunction
- The presence of haematuria, red cell casts on urine microscopy, vasculitis, nephrotic range proteinuria or rapid deterioration in GFR in the absence of long standing diabetes should raise suspicion of non-diabetic kidney disease (refer to nephrology for advice/management).

**Management of individual with Diabetic nephropathy**

- Tight Blood Glucose control - Target HbA1c 48 - 53 mmol/mol (6.5% - 7%) (individualisation of targets is recommended in partnership with the patient)
- Maintain blood pressure below 130/80 mm Hg
  1. ACE inhibitors or Angiotensin II receptor blockers (ARB’s) are recommended first line drugs (unless contraindicated)
  2. Calcium channel blocker (non-dihydropyridine class) drugs and low dose thiazide diuretics are useful second line agents
  3. Loop diuretics are useful in the presence of volume overload (e.g.leg edema)
  4. Additional antihypertensive therapy may be required.
  5. Combination therapy with ACE inhibitor and ARB has superior anti-proteinuric effect, however watch out for hypertensive symptoms (syncop) and hyperkalemia.
- Treat dyslipidemia (serum cholesterol, LDL cholesterol and serum triglycerides treated to targets)
- Aspirin therapy if indicated
- Lifestyle changes, weight loss and smoking cessation should be advised
- Dietary protein restriction is not routinely advised however in the face of overt nephropathy and or established kidney failure, restriction to 0.6-0.8 gm protein/kg/day has been recommended
- Patient education is an integral part of overall management.

**Classification of CKD according to GFR**

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt; 90</td>
<td>Normal or increased GFR, with other evidence of kidney damage</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>Slight decrease in GFR, with other evidence of kidney damage</td>
</tr>
<tr>
<td>3A</td>
<td>45-59</td>
<td>Moderate decrease in GFR, with or without other evidence of kidney damage</td>
</tr>
<tr>
<td>3B</td>
<td>30-44</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>Severe decrease in GFR with or without other evidence of kidney damage</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>Established renal failure</td>
</tr>
</tbody>
</table>

**Starting ACE inhibitor or ARB therapy**

- Caution in individuals with impaired kidney function
- Assess kidney function and electrolytes 1-2 weeks after initiating therapy, watch out for hyperkalemia
- Assess kidney function after any subsequent increase in dose
- Small rise in creatinine or a mild fall in eGFR values is expected with therapy
- STOP therapy - If serum creatinine rises by >30% or >25% fall in estimated GFR seek specialist advice (to exclude possible renovascular disease).
Nephropathy screening and management

When using the nephropathy algorithm it is important to understand that this is not designed to be used in isolation from the other diabetes-related guidelines. In particular, cardiovascular risk is not discussed in the nephropathy algorithm simply because it is assumed that the guidance on lipid lowering, anti-platelet therapy and blood pressure are being followed in tandem.

Nephropathy may not necessarily be due to diabetes but could, instead, be secondary to other pathologies such as hypertension.

If protein is detected in the urine on simple dipstick testing (proteinuria) this should be repeated after one or two weeks. If this subsequent test is positive, and the patient has persistent proteinuria the result should then be further quantified by requesting a laboratory measured “protein:creatinine ratio”. Persons with any degree of proteinuria should be offered treatment with an ACE inhibitor or ARB regardless of their initial blood pressure. See renal guidelines about starting ACE or ARB and subsequent monitoring of eGFR. Metformin should not be started if eGFR <45, and should be stopped if eGFR <30.

Patients with CKD1 and CKD2 should have annual review of their renal status. Patients with CKD3 should have 6 monthly assessment of their renal status and review of their medication to ensure that prescription of potentially nephrotoxic drugs is avoided as much as possible.

Patients with CKD4 and CKD5 should be referred to nephrology for an assessment.

Patients with CKD5 should also be under the care of the Diabetes Specialist Team.

If the urine is negative for proteinuria, an early morning urine specimen should be sent to the laboratory for an “albumin:creatinine ratio”. A positive test (>2.5 mg/mmol in men, >3.5 mg/mmol in women) should be confirmed by a second test one or two weeks later. If this second test is positive, the patient has persistent microalbuminuria. These patients should then be offered an ACE inhibitor or ARB regardless of their initial blood pressure. See renal guidelines about starting ACE or ARB and subsequent monitoring of eGFR.
**Background points**

People with Diabetes identified as at increased risk of developing lower limb complications can reduce this by participating in a foot care programme that provides education, podiatry and, where required, protective footwear.

- In those with Diabetes who develop foot ulceration, prompt intervention can minimise the risk of subsequent disability and amputation.

**Principal recommendations**

**Foot care for all people with Diabetes**

- Arrange recall and annual review of complications and their risk factors, by trained and competent personnel
- Examine feet and lower legs as part of annual review to detect risk factors for ulceration
- Include: - testing of foot sensation using a 10g monofilament or 128 Hz tuning fork
  1. palpation of foot pulses
  2. inspection of foot shape and footwear.
- Classify foot risk as: low current risk or at risk or high risk or ulcerated foot.

**Foot care for the low current risk foot** (normal sensation, palpable pulses)

- In the absence of Foot Pathology, patient can be seen routinely
- Agree a management plan including foot care education with each person.

**Foot care for the at risk foot** (neuropathy or absent pulses or other risk factor)

- In the absence of Foot Pathology, can be managed routinely.
- If Foot Pathology - needs specialist review
  - If previous foot ulcer or deformity or skin changes manage as High Risk
  - Enhance foot care education
  - Inspect feet 3-6 monthly
  - Advise on appropriate footwear
  - Review need for vascular assessment
  - Low threshold for further referral.

**Foot care for the high risk foot** (risk factor + deformity or skin changes or previous ulcer)

- Arrange frequent review (1-3 monthly) from specialised podiatry/foot care team.
- At each regular Diabetes review, evaluate the provision of:
  - intensified foot care education
  - specialist footwear and insoles
  - frequent (according to need) skin and nail care
- Review education/footwear/vascular status as for the AT RISK foot.
- Ensure special arrangements for those people with disabilities or immobility.

**Foot care for the ulcerated foot**

- Urgently arrange foot ulcer care to specialist multi-disciplinary clinic (NICE Guidelines 2004). (See referral sheet for contact details)
- Expect that team to ensure, as a minimum:
  - investigation and treatment of vascular sufficiency.
  - local wound management, appropriate dressings, and debridement as indicated
  - systematic antibiotic therapy for cellulitis or bone infection
  - effective means of distributing foot pressures, including specialist footwear, casts or scotch cast boot
  - tight blood glucose control

**Foot care emergency** (new ulceration, cellulitis, discoloration)

- Refer to specialised podiatry/foot care team within 24 hours

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All patients with Diabetes should be on a register and minimum data should include annual measures for microvascular disease. Please see Cardiovascular Risk for additional requirements.
### Neuropathic pain

#### Background points
Neuropathic pain in people with diabetes is common and often goes undiagnosed or may not be associated with their diabetes. It can be extremely debilitating and can have physical and psychosocial implications. All clinicians involved in the care of people with diabetes are responsible for the diagnosis, treatment and monitoring of neuropathic symptoms. Some patients will require referral to specialist diabetes care or pain service at UHL for advice and treatment plan.

#### Other Neuropathic Complications

##### Erectile Dysfunction
- Review annually as part of complication screening and care planning
- Discuss causes and contributory factors
- Discuss treatment options available
- Medical treatment
- Surgery
- Psychological support
- Involve partner where appropriate
- Consider referral to erectile dysfunction clinic.

##### Autonomic Neuropathy
If any of the following symptoms exist consider autonomic neuropathy as a possible cause:
- Unexplained gastric bloating or vomiting
- Loss of warning signs for hypoglycaemia
- Unexpected diarrhoea especially at night
- Unexpected bladder emptying problems

#### Management
Further investigations are required to exclude other causes and diseases. Requires referral to specialist services if uncertainty about diagnosis and management.

### Neuropathic pain management

**Questions regarding the presence of neuropathic symptoms should be a formal part of the diabetes annual review.**

- Take a detailed history of symptoms
- Exclude systemic disease. If present treat or refer if appropriate

**Symptoms**
- Pins & needles, prickling or tingling, often worse at night
- Abnormally sensitive skin with tight/stretch sensations
- Shock-like ‘jumping pain’
- Burning pain/cold or numb

If normal consider neuropathic pain management below in line with NICE guidelines: The Management of Type 2 Diabetes May 2009.

**Symptoms present**
- Discuss cause and prognosis of neuropathic symptoms (other causes excluded)
- Agree appropriate treatment options and review at each clinical contact
- Assess glycaemic control and how it may be impacting/causing painful neuropathy and agree management plan
- Explore psychosocial consequence and offer support depending on individual

**Symptoms uncontrolled**

- Tricyclic drugs - These may be used to treat neuropathic discomfort (Nortriptyline is an alternative to amitriptyline if the latter is too sedating)
  - Start with low doses and titrate as tolerated up to 75mg per day to minimise side effects
  - Discuss the timing of taking the medication to have the most benefit and least side effects
  - Advise this is a trial of therapy

**Symptoms uncontrolled**
- Offer trial of Duloxetine, Gabapentin or Pregabalin in addition to tricyclic drugs. Stop tricyclic drugs if not tolerated.
- Trial should be stopped if ineffective at maximum tolerated dose
- Try another of the drugs if side effects limit titration of doses

**Symptoms controlled**
- Discuss with person and consider referral to specialist diabetes service/pain management team

**Consider stopping/reducing dose following discussion with patient**