## STEPPED APPROACH TO TYPE 2 DIABETES

An electronic version of this document can also be viewed / downloaded from the North of Tyne, Gateshead and North Cumbria website at

http://www.northoftyneapc.nhs.uk/guidance/

<table>
<thead>
<tr>
<th>Review date</th>
<th>July 2019</th>
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</thead>
<tbody>
<tr>
<td>Membership of the guideline development group</td>
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</tbody>
</table>
**Diagnosed Type 2 Diabetes**

Refer for Structured Education

**Reduced calories, weight loss, increased physical activity**

**STEP 1 - when x2 3 monthly HbA1c > 48 mmol/mol or earlier if symptomatic**

Metformin – first line

~ £20/year – only drug with evidence for CV risk reduction

Gliclazide (SU)

**STEP 2 - When HbA1c reaches ≥58 mmol/mol @ 3-12 monthly reviews**

(Check success with lifestyle change and drug treatment)

Features of Step 2 drugs

- **Name(s)**
- **Priority**
- **HbA1c reduction**
- **Hypoglycaemia risk**
- **Weight**
- **Side effects**
- **Cost**
- **NICE continuation criteria**

- e.g. Gliclazide (SU)
  - FIRST LINE
  - 11-16.5 mmol/mol
  - Moderate Gain
  - Hypoglycaemia
  - ~£30 / year

- Pioglitazone (TZD)
  - Alternative 1
  - 11-16.5 mmol/mol
  - Low Gain
  - Hypoglycaemia
  - ~£19 / year

- Sitagliptin (DPP4)
  - Alternative 1
  - 5.5-11 mmol/mol
  - Low Neutral
  - UTI / genital infection
  - ~£430 / year

- Empagliflozin, Canagliflozin, Dapagliflozin (SGLT-2)
  - Alternative 3
  - 11-16.5 mmol/mol
  - Low
  - Heart failure
  - ~£440 / year

**STEP 3 - When HbA1c reaches >58 mmol/mol @ 3-12 monthly reviews**

(Check success with lifestyle change and drug treatment)

Consider dietitian review and exercise on referral. Use Shared Decision Making support tools

Features of Insulin / GLP-1

- **HbA1c reduction**
- **Hypoglycaemia risk**
- **Weight**
- **Side effects**
- **Cost**
- **NICE continuation criteria**
- **Additional Information**

- **INSULIN especially if HbA1c >110 mmol/mol**
  - > 11 mmol/mol
    - High
    - Gain
    - Hypoglycaemia
    - £160-1000/year
    - N/A
  - Continue metformin. Stop TZD, DPP4. Review need for SU, GLP-1, SGLT-2

- **e.g. Exenatide, Liraglutide, Lixisenatide (GLP-1)**
  - 11-16.5 mmol/mol
    - Low
    - Loss
    - Gl
    - £650-1400/year
    - Yes
  - Indication: BMI > 35kg/m2 / or >30kg/m2 and insulin not acceptable
  - DO NOT USE WITH GLIPTIN

**Insulin not tolerated or appropriate consider**

- **SU**
- **TZD**
- **DPP4**
- **GLP-1**
- **SGLT-2**

**Diabetes Key Considerations:**

- Reconsider diagnosis if excessive weight loss or symptoms of hyperglycaemia
- At any time if symptomatically hyperglycaemic, consider insulin and review treatment when blood glucose control achieved.
- HbA1c target and glucose lowering therapies should be individualised
## Notes on medicines other than insulin

**See local formulary and SPC for individual drug choice**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Key Points</th>
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<tbody>
<tr>
<td>Metformin</td>
<td>Benefits of increasing doses of metformin above 2g daily are limited and the BNF recommends a daily max of 2g. Specialist advice may support doses above this range in individual patients. Only oral agent associated with reduced CV risk and weight reduction. Prescribe with caution for those at risk of sudden deterioration in kidney function and those at risk of eGFR falling below 45ml/min/1.73m2 Reduce dose if eGFR below 45ml/min/1.73m2 Stop if eGFR below 30ml/min/1.73m2 Counsel patients to stop temporary if acutely unwell, particularly with vomiting and diarrhoea Metformin MR—only if intolerant (GI side effects) on standard release metformin</td>
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<tr>
<td>Sulphonylurea (SU)</td>
<td>Gliclazide first line choice. Consider if patient not over weight, if metformin not tolerated or contraindicated or if rapid response required because of hyperglycaemic symptoms. Do not prescribe gliclazide MR or tolbutamide Treat osmotic symptoms rapidly Contraindicated in pregnancy Risk of hypoglycaemia so patients will have to undertake home glucose monitoring. Educate about risk No need to check BM routinely unless hypoglycaemia or driving.</td>
</tr>
<tr>
<td>Thiazolidinedione (TZD)</td>
<td>Formulary choice—Pioglitazone Contraindications: heart failure, active bladder cancer or history of bladder cancer, uninvestigated haematuria, pregnancy Cautions: increased risk of bone fractures, particularly women Carries long term risk of limb fracture Caution with liver disease Rare reports of liver dysfunction—monitor liver function before and periodically during treatment Start at 15-30mg daily and titrate to 45mg daily according to response Discontinue if reduction in HbA1c is less than 0.5% (5.5mmol/mol) after 6 months treatment</td>
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<tr>
<td>DPP4 inhibitors (Gliptins)</td>
<td>Formulary choices include alogliptin, linagliptin and sitagliptin No long term safety data Low risk of hypoglycaemia—useful in patients at risk of hyperglycaemia Appears to be weight neutral—useful if further weight gain would cause significant problems Do not use in pregnancy and breastfeeding Discontinue if symptoms of acute pancreatitis Consider stopping if NICE criteria for continuation not met Discontinue if reduction in HbA1c is less than 0.5% (5.5mmol/mol) after 6 months treatment</td>
</tr>
<tr>
<td>GLP-1 mimetics</td>
<td>GLP-1 used in combination with insulin ONLY in specialist care setting Add as part of triple therapy ONLY if BMI is &gt;35kg/m2 in people of European descent (adjust for ethnic groups) and there are specific psychological or medical problems associated with high body weight, or BMI &lt;35kg/m2 and insulin is unacceptable because of occupational implications or weight loss would benefit other co-morbidities. Can be considered in dual therapy with metformin or a sulfonylurea if either metformin, OR a sulfonylurea AND pioglitazone AND DPP-4 inhibitors contra-indicated or not tolerated (only lirolutide and prolonged release exenatide considered by NICE for dual therapy). Consider stopping if reduction in HbA1c is less than 1% (11 mmol/mol) and there is less that 3% weight loss after 6 months 2 (only HbA1c reduction required for dual therapy)</td>
</tr>
<tr>
<td>SGLT-2</td>
<td>The formulary includes empagliflozin, canagliflozin and dapagliflozin in line with their NICE TAs. The guideline development group favoured Empagliflozin due to recent evidence of cardiovascular morbidity and mortality benefits Avoid initiation if eGFR below 60mL/minute/1.73m2; reduce dose to 10mg once daily if eGFR falls persistently below 60mL/minute/1.73 m2; avoid if eGFR is persistently below 45mL/minute/1.73m2 in case of conditions that may lead to fluid loss (e.g. gastrointestinal illness), careful monitoring of volume status (e.g. physical examination, blood pressure measurements, laboratory tests including haematocrit) and electrolyte is recommended for patients receiving empagliflozin. Temporary interruption of treatment with empagliflozin should be considered until the fluid loss is correct. Empagliflozin can be used in a dual therapy regimen in combination with metformin AND In combination with insulin with or without other antidiabetic drugs. Empagliflozin can be used in a triple therapy regimen in combination with metformin and sulphonylurea or a thiazolidinedione. Discontinue if reduction in HbA1c is less than 0.5% (5.5mmol/mol) after 6 months treatment</td>
</tr>
</tbody>
</table>

The element of decision making used to determine appropriate efforts to achieve HbA1c targets. Characteristics towards the left justify more stringent efforts to lower HbA1c, those towards the right are compatible with less stringent efforts. With possible, decision should be made in conjunction with the patient, reflecting his or her preference, needs and values. This “scale” is not designed to be applied rigidly but to be used as a broad construct to help guide clinical decisions.
KEY POINTS

- HbA1c targets and glucose-lowering therapies must be individualised
- Diet, exercise and education remain the foundation of any type 2 diabetes treatment program
- Unless there are prevalent contraindications, metformin is the optimal first-line drug
- After metformin, there are limited data to guide us. Combination therapy with an additional 1-2 oral or injectable agents is reasonable, aiming to minimise side effects where possible
- Ultimately, many patients will require insulin therapy alone or in combination with other agents to maintain glucose control
- All treatment decisions, where possible, should be made in conjunction with the patient, focusing on his/her preferences, needs and values
- Comprehensive cardiovascular risk reduction must be a major focus of therapy

Introduction of insulin for Type 2 diabetes for planned transfer via group sessions or 1:1

Group approach structured educational programme for insulin start

- Type 2 diabetes and insulin management
- Lifestyle change and healthy eating
- Management of hypoglycaemia and hyperglycaemia (sick days)
- Ongoing care
- 2 or 4 sessions according to local arrangements

Insulin regimes should be based on individual considerations

<table>
<thead>
<tr>
<th>Option</th>
<th>Isophane insulin (basal) once or twice daily</th>
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</thead>
<tbody>
<tr>
<td>Option 1</td>
<td>Pre-mixed insulin (human) twice daily. Most likely required initially:</td>
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<tr>
<td></td>
<td>• Symptomatic</td>
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<tr>
<td></td>
<td>• Short history of diabetes</td>
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<tr>
<td></td>
<td>• BMI &lt;25kg/m²</td>
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<td></td>
<td>• HbA1c &gt;75mmol/mol (9.0%)</td>
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<td>• Start premixed insulin with breakfast and evening meal</td>
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</tbody>
</table>

Insulin Dose: Suggested start with 8-10 units per dose

Titrate: Increase by 2-4 units per dose according to blood glucose profile every 3-7 days (provide written guide for dose titration)

Targets: Need to be individualised

- HbA1c <53mmol/mol (75%)
- Blood glucose target
  - Fasting: 4-7mmol/l
  - Pre-meal: 4-7mmol/l

Oral agents Stop TDZ, DPP4 and SU but continue metformin

Long acting analogues plus oral agents

- Can be used for elderly requiring community nursing support
- Or if problematic hypoglycaemia (use local guidelines)
- NB Could also use twice isophane for elderly patients (stop sulphonylurea)

Basal bolus regime - Not routinely used in the management of Type 2 diabetes—seek specialist advice

<table>
<thead>
<tr>
<th>Isophane insulin</th>
<th>Premixed insulin</th>
<th>Long acting analogue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insuman Basal</td>
<td>Insuman Comb</td>
<td>Levemir (Detemir)</td>
</tr>
<tr>
<td>Humulin I</td>
<td>Humulin M3</td>
<td>Lantus (Glargine)</td>
</tr>
<tr>
<td>Insulatard</td>
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