Type 2 Diabetes Patient

Objectives

Stopping Smoking

↓

BMI > 25 kg m²

↓

Control BP to <140/80
(<130/80 if kidney, eye or cerebrovascular damage)

↓

Initiate Simvastatin 40mg ON

↓

Aim to reduce total cholesterol to <4mmol/l & LDL-cholesterol< 2mmol/l.
Switch to Atorvastatin 40mg daily if after 3-6 months of treatment cholesterol is not at target.

+ Dietary Advice
Consider early referral to DESMOND or X-PERT programme.
Check HbA1C + fasting glucose in 3-6 months.
If HbA1C > 6.5% (48 mmol/mol) after lifestyle interventions.

Consider referral to smoking cessation

Refer to obesity pathway

See NHS Rotherham hypertension guidelines

All diabetic patients over 40 can be considered to have a CVD risk > 20%. All other patients should be risk accessed annually using UKPDS risk engine see: www.dtu.ox.ac.uk/index.php?maindoc=/riskengine/

Aim to reduce total cholesterol to <4mmol/l & LDL-cholesterol< 2mmol/l.
Switch to Atorvastatin 40mg daily if after 3-6 months of treatment cholesterol is not at target.

Triglycerides
Consider management if TG remains > 4.5mmol/litre (despite optimised glycaemic control & statin therapy).

Initiate Metformin

Refer to the DESMOND / X-PERT programme or an approved structure patient education programme.
Newly Diagnosed Type 2 Diabetes Patient

Objectives (continued)

Metformin
Initiate 500mg daily titrated slowly to maximally tolerated dose.

Current maximum BNF recommended dose = 2g daily. In divided doses

→ Unless Blood Glucose controlled with diet and weight loss.

Ramipril 10mg OD
(Irbesartan 150mg increased to 300mg OD if ramipril not tolerated).

↓

If microalbuminuria/proteinuria present.

+/−

Aspirin 75mg OD
Only if patient has had an MI or has symptoms of cardiovascular disease (Secondary prevention).

↓

Unless contra-indicated
(If dyspepsia or increased risk or GI bleeding add Lansoprazole 15mg daily).
(If aspirin allergic consider Clopidogrel 75mg daily see clopidogrel guidelines).

Control Blood Glucose

• HbA1C to be below 6.5% (48 mmol/mol).
• Fasting glucose < 6mmol/L (Venous sample).
## Overview

Controlling Blood Glucose in a patient with Type 2 Diabetes

### Objectives

- HbA1C to be below 6.5% (48mmol/mol).
- Fasting glucose < 6mmol/l (venous sample).
- Patients must not experience frequent episodes of hypoglycaemia.
- In the very elderly or frail, symptom control alone may be the priority.

### Treatment

Review HbA1C every 3-6 months if not at target, every 12 months once at target.

- **Diet and Weight Loss**
  Consider referral to the DESMOND/ X-PERT programme
  If HbA1C above 6.5%, (48mmol/mol) fasting glucose above 6mmol/l and/or BMI >25 initiate metformin.

### Oral treatment to lower blood glucose

**Step 1**

- **METFORMIN**
  (SEE NOTE 1)

**Step 2**

- **GLICLAZIDE**
- **SITAGLIPTIN**
  (SEE NOTE 2)

**Step 3**

- **SITAGLIPTIN**
  (SEE NOTE 2)
- **EXENATIDE**
  (SEE NOTE 3)
- **GLICLAZIDE**
  (SEE NOTE 4)
- **PIOGLITAZONE**

### Targets for glycaemic control

**HbA1C Control (QOF Targets)**

<table>
<thead>
<tr>
<th>HbA1C Control</th>
<th>&lt; 7.0%</th>
<th>7.0-8.0%</th>
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<tbody>
<tr>
<td></td>
<td>=53 mmol/mol</td>
<td>=53-64 mmol/mol</td>
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If HbA1C is 1% above a patient’s individual target consider whether an adjustment in diet or medication is needed to restore optimal glucose control.
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<th>Oral Diabetes Treatment Pathways</th>
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Step 1 Treatment of Type 2 Diabetes; **METFORMIN**

**Aims of treatment**
- HbA1C to be below 6.5% (48 mmol/mol)
- Fasting glucose < 6mmol/l (venous sample)
- In the very elderly or frail, symptom control alone may be the priority

**Targets for glycaemic control**

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If HbA1C is 1% above a patient’s individual target consider whether an adjustment in diet or medication is needed to restore optimal glucose control restore optimal glucose control.

**Blood Glucose Monitoring**
Patient blood glucose monitoring may not be necessary at this stage. Patients are very unlikely to experience hypoglycaemia on Metformin, consider blood glucose monitoring if the patient reports hypoglycaemia like symptoms. Effectiveness can be monitored using HbA1C measurements.

**Initiate Metformin**
- Start with 500mg daily for 1-2 weeks, then 500mg twice a day for 1-2 weeks then increase to 500mg TDS (unless glycaemic target is reached).
- Then titrate every 1-3 months to achieve glycaemic target until maximum dose is prescribed (2g daily in divided doses)
- Tablets should be taken with or immediately after a meal.
- Diarrhoea occurs in up to 20%, this usually resolves after 3-5 days or may be dose dependent and may resolve on dose reduction.
- Consider FBC if any signs of B12 deficiency.

**Avoid Metformin**
- In patients with creatinine >150 micromol/l, eGFR ≤ 30 mls/min/1.73-m2
- Hepatic impairment
- Respiratory failure
- Recent MI < 6 weeks
- Sepsis
- History of ketoacidosis

**Caution Review dose**
- In patients with creatinine >130 micromol/l, eGFR ≤ 45 mls/min/1.73-m2

**Metformin for All**
UKPDS 34 found that 10 years of treatment in obese patients, metformin reduced rates of MI, diabetes related deaths and mortality. For every 14 patients treated with Metformin, one of them would have their life extended. A recent study found metformin was as effective for non-obese diabetic patients. Therefore metformin should be first line for all type 2 diabetic patients.

**Review 3-6 months after initiation and following a dose increase**
- If glycaemic targets met → Review in 6-12 months
- If glycaemic targets not met → Patient is taking the maximum Or maximum tolerated metformin dose
  
  Check compliance → Consider adding Gliclazide or Sitagliptin

**Consider titrating more slowly or a prolonged release formulation for patients unable to tolerate metformin due to GI problems**
Step 2 Treatment of Type 2 Diabetes; GLICLAZIDE (Sulphonylurea)

Patient has:
- A contraindication to metformin.
- Failure to tolerate metformin despite a reasonable trial and a slow initiation
- Failure of metformin to control diabetes

| Diabetes Control | • HbA1C below 7.5% (48 mmol/mol)  
|                 | • Fasting glucose < 6mmol/l (venous sample)  
|                 | • Patients must not experience frequent episodes of hypoglycaemia  

- In the very elderly or frail, symptom control alone may be the priority

**Initiate Gliclazide**
- 40mg-80mg daily with breakfast and subsequently with evening meal.
- Titrate by 40-80mg steps, every 1-3 months to achieve glycaemic target or until:
  - Maximum daily dose is reached = 320mg daily, given as 160mg BD
  - Or maximum tolerated dose is reached.
- **Side effects** are generally mild and infrequent and include hypoglycaemia, gastro-intestinal disturbances, such as nausea, vomiting, diarrhoea and constipation. Hypersensitivity occurs rarely and usually in the first 6-8 weeks of therapy, and usually manifest as allergic skin reactions.

**Avoid Gliclazide**
- Severe hepatic disease
- Severe renal impairment eGFR ≤30 mls/min/1.73-m²
- Porphyria
- Pregnancy and Breast feeding
- Presence of ketoacidosis

**Weight Gain**
A 2-4kg weight gain is recognised as a consequence of sulphonylurea therapy; in some patients this may exceed 10kg. Patients should be re-assessed and dietary compliance reaffirmed before initiation.

Review 3-6 months after initiation and following a dose increase

- If glycaemic targets met → Review in 6-12 months
- If glycaemic targets not met → Patient is taking the maximum Or maximum tolerated metformin and/or gliclazide dose

Check compliance → Consider adding Exenatide, Sitagliptin if not added at step 2 or pioglitazone if alternatives inappropriate.

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If HbA1C is 1% above a patient’s individual target consider whether an adjustment in diet or medication is needed to restore optimal glucose control.

Refer to Rotherham PCT Blood Glucose Monitoring Guidelines
Step 2 or 3 Treatment of Type 2 Diabetes; SITAGLIPTIN

Sitagliptin as a third line agent to metformin and gliclazide if the patient has;
- Failure of metformin and/or gliclazide to control diabetes

Sitagliptin should be considered as a second line agent in addition to Metformin if the patient;
- Is at significant risk of hypoglycaemia or its consequences, consider work and social circumstances (e.g., older person, people working with machinery or at heights or living alone).
- Has a contraindication or cannot tolerate gliclazide.
- Further weight gain would be undesirable.

Sitagliptin can be used in combination with gliclazide as a second line agent if the patient;
- Has a contraindication or cannot tolerate metformin despite a reasonable trial

| Diabetes Control | • HbA1C below 7.5% (58 mmol/mol)   |
|                 | • Fasting glucose < 6mmol/l (venous sample) |
|                 | • Patients must not experience frequent episodes of hypoglycaemia |
- In the very elderly or frail, symptom control alone may be the priority

**Initiate Sitagliptin**
- 100mg once daily
- The dose of metformin to be maintained
- The dose of gliclazide may need lowering if hypoglycaemia is a concern.
- No dose adjustment is required for patients with mild renal insufficiency, mild to moderate hepatic insufficiency or in the elderly.

**Side effects.** Hypersensitivity reactions include anaphylaxis, angioedema, and exfoliate skin conditions and stevens-johnson have been reported usually in the first 3 months of treatment. Nausea, flatulence and constipation have been reported when used in conjunction with other hypoglycaemic agents.

**Avoid Sitagliptin**
- Moderate or worse renal failure
- Pregnancy
- If eGFR <50mls/min/1.73 m²

Sitagliptin is a new drug and is subject to intensive monitoring by the CHM and MHRA its adverse effect profile may not fully known.

Review 3-6 months after initiation and following a dose increase
- If glycaemic targets met → Review in 6-12 months
- If glycaemic targets not met → Patient is taking the maximum
  Or maximum tolerated metformin and/or sitagliptin/gliclazide dose
  ↓
  Check compliance → Consider adding exenatide or initiating Insulin or pioglitazone

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If HbA1Cis 1% above a patient’s individual target consider whether an adjustment in diet or medication is needed to restore optimal glucose control

Refer to Rotherham PCT Blood Glucose Monitoring Guidelines
**Step 3 Treatment of Type 2 Diabetes; EXENATIDE**

Exenatide should be considered as a third line agent in addition to Metformin and gliclazide if there is a.

- Failure of metformin and/or gliclazide/sitagliptin to control diabetes
- Weight loss is desirable (BMI ≥ 35 kg/m²)

**Diabetes Control**

- HbA1C below 7.5% (58 mmol/mol)
- Fasting glucose < 6mmol/l (venous sample)
- Patients must not experience frequent episodes of hypoglycaemia
- In the very elderly or frail, symptom control alone may be the priority

**Initiate Exenatide**

- 5 micrograms by subcutaneous injection into the thigh abdomen or upper arm, twice daily
- Increased after at least one month to 10micrograms twice daily if or when necessary.
- Doses to be given within 1 hour before the 2 main meals with doses at least six hours apart.
- No dosage adjustment is required in mild renal failure or hepatic failure.
- There have been rare reports of pancreatitis, which may or may not be associated with exenatide. Patients should informed of the characteristic symptom of acute pancreatitis (persistent, severe abdominal pain)

**Caution;** Dose adjustments should be made with caution in patients over 70, experience is limited in patients over 75.

**Side effects;** Nausea can be a problem, other GI disturbances such as vomiting, diarrhoea, dyspepsia, abdominal pain, distension, GI reflux. Also decreased appetite, headache, dizziness, asthenia, hypoglycaemia, increased sweating. Very rarely anaphylactic reactions have also been reported.

**Avoid Exenatide**

- History of Ketocidosis
- Severe gastro-intestinal disease
- Pregnancy
- If eGFR < 30 mls/min/1.73 m²

Exenatide is a new drug and is subject to intensive monitoring by the CHM and MHRA its adverse effect profile may not fully know.

Exenatide delays gastric emptying this may affect the effectiveness of drugs with a narrow therapeutic range or drugs that have gastro-resistant formulations

**Refer to the Exenatide pathway for further details**

Review 3-6 months after initiation and following a dose increase

- If glycaemic targets met → Review in 6-12 months
- If glycaemic targets not met → Patient is taking the maximum

Or maximum tolerated metformin and/or gliclazide dose and exenatide or insulin is inappropriate

Check compliance → Consider adding initiating Insulin or pioglitazone

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If HbA1Cis 1% above a patient’s individual target consider whether an adjustment in diet or medication is needed to restore optimal glucose control.

Refer to Rotherham PCT Blood Glucose Monitoring Guidelines


**Step 3** Treatment of Type 2 Diabetes; **PIOGLITAZONE**

Pioglitazone should only be considered if:
- There is a failure of tolerate metformin and/or gliclazide to control diabetes
- The patient considers human insulin and or exenatide to be an unacceptable option

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<th>Initiation Criteria</th>
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**Initiate Pioglitazone**

15-30mg Once daily
Increased to 45mg Once daily according to response (it takes several weeks (up to 6 months) before the full therapeutic effect becomes obvious.

**Side effects**
Gastro-intestinal disturbances, weight gain, oedema, fractures at atypical sites, anaemia, headache, visual disturbances, dizziness, arthralgia, hypoaesthesia, haematuria, impotence, macular oedema.

*less commonly*
hypoglycaemia, fatigue, insomnia, vertigo, sweating, altered blood lipids, proteinuria

**Avoid Pioglitazone**

- Hepatic impairment
- Heart Failure
- Pregnancy
- Breast feeding
- In patients considered to be at high risk of fractures.

**Liver Toxicity**
Due to rare reports of liver dysfunction. Liver function should be checked before and after initiation and at all reviews.

Review 3-6 months after initiation or following a dose increase

- If glycaemic targets met → Review in 6-12 months
- If glycaemic targets not met → Patient is taking the maximum
  Or maximum tolerated metformin and/or gliclazide and/or pioglitazone

Check compliance → Consider Initiating Insulin

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Review Date May 2012