

## STEP 1 – Initial Drug Treatment – Monotherapy: Target HbA1c 48 mmol/mol

**Lifestyle advice + Referral to Good2Go ± Metformin** (consider 3 months lifestyle change first)  
*Consider trial of modified-release metformin in patients who experience gastrointestinal side effects with standard release metformin*

If Metformin contraindicated (CI) or intolerant and HbA1c 53 mmol/mol start monotherapy with:

1. Sulfonylurea (e.g. Gliclazide)-**Target HbA1c 48-53 mmol/mol**. *Blood glucose monitoring may be required initially in view of hypoglycaemia risk if commencing sulfonylurea\**
2. Or DPP4i (e.g. 'Gliptins')
3. Or SGLT2i (e.g. 'Dapagliflozin, canagliflozin or empagliflozin)- if above two options not suitable or if DPP4i is ineffective, before moving to Step 2.
4. Or Pioglitazone

**See page two for information on medication choice and when to stop**

\*Please refer to "[Who to Test, When to Test](#)" guidance

## STEP 2 – Dual Therapy: Target HbA1c 53 mmol/mol

**For non-obese patients:**  
Metformin + Sulfonylurea

**If Metformin intolerant or CI:**  
Sulfonylurea + DPP4i  
Or  
Sulfonylurea + Pioglitazone

*If BMI < 30 kg/m<sup>2</sup> and osmotic symptoms – consider straight to insulin as could be late onset Type 1 Diabetes*

**For obese patients (BMI ≥ 30 or over 27.5 if of Asian, Black African or African-Caribbean descent) or if hypo risk is a major issue consider:**

**Metformin +**

1. SGLT2i (or)
2. Or DPP4i (suitable for frailty) (or)
3. Or Pioglitazone

**Metformin intolerant or CI**

1. Sulfonylurea + DPP4i (or)
2. DPP4i + Pioglitazone (or)
3. Sulfonylurea + Pioglitazone (or)
4. If SGLT2i monotherapy consider adding a sulfonylurea or injectable (see below)

## STEP 3 – Triple Therapy: If HbA1c > 58 mmol/mol or individually agreed target

1. Metformin + Sulfonylurea + SGLT2i (or)
2. Metformin + Sulfonylurea + DPP4i (or)
3. Metformin + Sulfonylurea + Pioglitazone (or)
4. Metformin + Pioglitazone + SGLT2i (canagliflozin or empagliflozin only)

*If BMI > 25 kg/m<sup>2</sup> consider option 1 (ensure eGFR > 60 mL/min)*

*If BMI < 25 kg/m<sup>2</sup> consider option 2*

Metformin intolerant /CI:  
Likely to require injectable therapy therefore move to step 4

## STEP 4 – Injectable with combinations (refer to injectable pathway for further information)

### Option 1 – Oral Triple therapy with GLP1

Stop least effective in step 3 and replace with GLP-1  
Options include:  
Metformin + Sulfonylurea + GLP-1  
Metformin + SGLT2i + GLP1  
Sulfonylurea + SGLT2 + GLP1  
SGLT2 + GLP1

*Do not use DPP4 and GLP1 in combination*

### Option 2 – Oral Triple Therapy with Insulin

Consider once daily basal insulin in combination first  
Options include:  
Metformin + Sulfonylurea + Insulin  
Metformin + SGLT2i + Insulin  
Metformin + DPP4i + Insulin  
Sulfonylurea + DPP4i + Insulin  
Sulfonylurea + SGLT2i + Insulin  
SGLT2i + DPP4i + Insulin  
SGLT2i + Insulin

### Option 3 – GLP1 and Insulin

**Refer to community diabetes team for advice before initiation**

## Medication choice / decision making support

**Assess** the response of any drug at 3-6 months – if there is no reduction of at least 6mmol/mol in HbA1c in 6 months or weight loss if using GLP-1 or if there are any concerns regarding side effects **stop** the chosen medication and move to an alternative class. Metformin, empagliflozin, canagliflozin and liraglutide have shown to reduce cardiovascular risk, consider use in patients with high risk of CV events.

### Consult individual Summary of Product Characteristics for full prescribing information

Agent	Sulfonylurea Gliclazide	DPP4i 'Gliptins'	Glitazone Pioglitazone	SGLT2i Dapagliflozin, Canagliflozin, Empagliflozin
<b>Positive reasons to use this class</b>	<ul style="list-style-type: none"> <li>• Low cost</li> <li>• Rapid clinical effect</li> <li>• Long established profile</li> <li>• Agent of choice in MODY</li> </ul>	<ul style="list-style-type: none"> <li>• Low hypoglycaemia risk</li> <li>• Weight neutral</li> <li>• Licensed in people with CKD (may require dose reduction)</li> <li>• Fewer drug interactions</li> </ul>	<ul style="list-style-type: none"> <li>• Low hypoglycaemia risk</li> <li>• Reduces insulin resistance</li> <li>• Slower progression to insulin treatment</li> </ul>	<ul style="list-style-type: none"> <li>• Low hypoglycaemia risk</li> <li>• Weight loss</li> <li>• Proven cardiovascular benefits (empagliflozin and canagliflozin)</li> </ul>
<b>Reasons not to use this class</b>	<ul style="list-style-type: none"> <li>• Risk of hypoglycaemia (increased in CKD)</li> <li>• Potential need for blood glucose monitoring</li> <li>• Weight gain</li> </ul>	<ul style="list-style-type: none"> <li>• Relatively low potency and moderate cost</li> </ul>	<ul style="list-style-type: none"> <li>• Weight gain</li> <li>• Slow onset of action</li> <li>• Contraindicated in CCF, LVF</li> <li>• Risk of fractures (women)</li> <li>• Small increase in incidence of bladder cancer)</li> <li>• Moderate cost</li> <li>• Do not use with insulin</li> </ul>	<ul style="list-style-type: none"> <li>• If eGFR &lt;60</li> <li>• UTI, genital thrush</li> <li>• Relatively new class – unexpected long term side effects may yet to be recognised</li> <li>• Moderate cost</li> <li>• Risk of DKA</li> </ul>
<b>Good choice for</b>	<ul style="list-style-type: none"> <li>• Preferred to metformin for patients with osmotic symptoms</li> </ul>	<ul style="list-style-type: none"> <li>• In people whom further weight gain would cause or exacerbate significant problems associated with high body weight</li> <li>• Frail older people</li> <li>• Any person for whom hypoglycaemia is a particular concern</li> </ul>	<ul style="list-style-type: none"> <li>• Most likely to benefit people who wish to delay progression to insulin (e.g. group 2 LGV and C1 driving licence holders)</li> </ul>	<ul style="list-style-type: none"> <li>• Obese people</li> <li>• In those whom further weight gain would cause or exacerbate significant problems associated with high body weight</li> <li>• People for whom hypoglycaemia is a particular concern</li> </ul>
<b>Monitoring required</b>	<ul style="list-style-type: none"> <li>• Consider home glucose monitoring as per <a href="#">"Who to Test, When to Test"</a> guidance*</li> </ul>	<ul style="list-style-type: none"> <li>• Review U &amp; E annually</li> </ul>	<ul style="list-style-type: none"> <li>• Review urine dip for blood annually</li> <li>• Review LFTs annually</li> <li>• Stop if heart failure/fluid overload develops</li> </ul>	<ul style="list-style-type: none"> <li>• Review U &amp; E annually</li> </ul>

Repaglinide and nateglinide are 'Amber specialist recommendation' drugs, please speak to the diabetes specialist team before initiating.

**Consider referral to Community Diabetes Team for advice/support**  
**York - Tel: 01904 724938 (nurse) or 01904 724942 (consultant)**  
**Scarborough – Tel: 01653 609609**

## Injectable initiation pathway

### GLP initiation

#### When to consider initiation of a GLP-1

Treatment with GLP-1s is associated with the prevention of weight gain and possible promotion of weight loss:

GLP-1s should be considered in people with Type 2 diabetes and:

- a body mass index of 35 kg/m<sup>2</sup> or higher
- In those with a body mass index of less than 35 kg/m<sup>2</sup> where:
  - Insulin treatment would be unacceptable for significant occupational reasons
  - Where weight loss would benefit other significant obesity related co-morbidities

#### Considerations before initiating

- Persistent and severe abdominal pain with or without vomiting may be a sign of acute pancreatitis. If this is suspected, the GLP-1 should be stopped, and if confirmed, not be resumed
- Not recommended for individuals with severe gastro-intestinal problems.
- Individuals receiving a GLP-1 in combination with sulfonylurea may be at increased risk of hypoglycaemia, therefore consider a reduction in the dose of sulfonylurea
- There are no specific restrictions for drivers with Class 1 licences (cars and motorcycles) when being treated with a GLP-1. Normal precautions to avoid low blood glucose when driving apply.
- Not recommended during pregnancy or where pregnancy is planned, or for nursing mothers
- Liraglutide and dulaglutide can be used in severe renal impairment or eGFR down to 15 ml/min/1.73 m<sup>2</sup>)

#### Once daily options:

Lixisenatide (Lyxumia) 10mcgs for 2 weeks then 20mcgs daily thereafter

Liraglutide (Victoza) 0.6mgs daily for 1 week, increasing to 1.2mgs thereafter – option to increase to 1.8mgs if required  
*NB: Liraglutide has shown to reduce cardiovascular risk*

#### Once weekly options:

Dulaglutide (Trulicity) 1.5mgs once weekly

Exenatide extended release (Bydureaon) 2mgs once weekly

NICE recommends that treatment with GLP-1s is continued only if HbA1c has reduced by at least 11 mmol/mol [1%] and a weight loss of 3% is achieved within 6 months of commencing treatment

### Insulin initiation

#### When to consider initiation of insulin

- Fail to reach glycaemic targets using diet and non-insulin therapies
- If the individual is symptomatic, including weight loss, polyuria, nocturia
- In steroid induced diabetes, when hyperglycaemia persists following max oral hypoglycaemic agents
- In the individual who is intolerant to non- insulin therapies

#### Before insulin therapy

- Reinforce dietary advice and lifestyle issues including smoking, alcohol
- Consider driving or employment issues
- Check ability to self-administer own insulin or will need support
- Ensure patient understands how to monitor own blood glucose levels and understands management of hypoglycaemia (hypos) and sick day rules

#### Single injection of basal insulin with oral hypoglycaemics / GLP1

Isophane (NPH) injected at bedtime first choice e.g. Humulin I or Human Insulatard

Usual start dose 10 units pre bed

Recommended in:

- Overweight BMI >30
- Community care involvement
- Older person with no complications but where hypoglycaemia is unacceptable (see management of diabetes in over 75 age group)

#### Twice daily biphasic insulin regime with oral hypoglycaemics

*Consider discussion with diabetes team re oral therapies to continue*

Human Mixed Insulin first choice e.g. Humulin M3, Insuman Comb 25

Usual start dose 12 units AM, 8 units PM if not already on basal insulin. Basal insulin change – reduce total dose by 10%, then give 2/3<sup>rd</sup> AM, 1/3<sup>rd</sup> PM

Recommended in:

- Consider first line in pts with HbA1c > 75 mmol/mol
- Regular lifestyles, consistent dietary intake
- Patient symptomatic and / or normal weight
- Significant post prandial glucose rise

#### Basal Bolus regime

Refer to community diabetes nursing team for advice and support in initiation

#### Ongoing management on insulin should include:

- Management of hypos including causes, symptoms, treatment and driving advice
- Advice on titration of insulin
- Sick day rules / illness management
- Annual inspection of injection sites, and advice on rotation of insulin injections
- Safe disposal of sharps

## Management of Diabetes in the over 75 age group

<p style="text-align: center;"><b>Functionally Independent</b> People living independently with none / minimal care giver support</p>	<p style="text-align: center;"><b>Functionally Dependant</b> Impairment of activities of daily living e.g. bathing, dressing and personal cares. May need additional medical or social care</p>	<p style="text-align: center;"><b>Frail / Dementia</b> Increased risk of fall or institutionalization, restricted mobility and significant fatigue. Cognitive impairment, memory problems and unable to self-care</p>
<p style="text-align: center;"><b>Target HbA1c</b> <b>53 – 59 mmol/mol</b></p>	<p style="text-align: center;"><b>Target Hba1c</b> <b>53 – 64 mmol/mol</b></p> <p style="text-align: center;"><b>Capillary blood glucose target:</b> <b>6 – 12mmol/L</b></p>	<p style="text-align: center;"><b>Target HbA1c</b> <b>70 mmol/mol</b></p> <p style="text-align: center;"><b>Capillary blood glucose target:</b> <b>7 – 12mmol/L</b></p>
<p><b>As per Algorithm for management of type 2 diabetes but consideration around:</b></p> <p>Metformin 1<sup>st</sup> line unless renal impairment. Titrate slowly to avoid GI side effects.</p> <p>Sulfonylurea can be considered for acute illness or on steroids (blood glucose monitoring may be required)* Use in caution as may cause hypoglycaemia</p> <p>DPP4i next if not symptomatic with hyperglycaemia. Useful in renal impairment</p>	<p><b>Aim for top of target (64 mmol/mol) to reduce risk of hypoglycaemia. Follow guidelines as for functionally dependant but consideration around:</b></p> <p>Stop Sulfonylureas if Hba1c &lt; 53 mmol/mol as increased risk of hypoglycaemia in this group</p> <p>Consider simplifying regimens as third party may need to administer.</p> <p>Use oral agents with low risk of hypoglycaemia</p> <p>If insulin required, in type 2 diabetes, consider once daily in the morning. Intermediate (Isophane insulin) 1<sup>st</sup> choice for example Humulin I or Human Insulatard</p>	<p><b>Ensure simplifying regimens. Avoidance of hypoglycaemia a priority</b></p> <p>Consideration of education / support to care givers or if person with diabetes is institutionalized. Contact Community Diabetes team for advice</p> <p>If acutely unwell or hyperglycaemic and/or on steroids consider substituting all oral agents for insulin.</p> <p>Review use of insulin once acute event has passed</p> <p>For end of life care follow local guidelines.</p>