



## STEPPED APPROACH TO TYPE 2 DIABETES

An electronic version of this document can also be viewed / downloaded from the North of Tyne Medicines Optimisation Website at

<http://medicines.necsu.nhs.uk/guidelines/north-of-tyne-guidelines/>

<b>Endorsed for use within North Tyneside, Northumberland, Newcastle and Gateshead by the North of Tyne APC</b>	
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Informed by existing NoT guideline and Durham guideline (Durham used Hartlepool and Stockton and South Tees CCGs type 2 diabetes guideline as part of their development process).	

Diabetes is a progressive condition: REINFORCE LIFESTYLE ADVICE, REVIEW COMPLIANCE STOP, DRUGS THAT ARE NOT EFFECTIVE

**Diagnosed Type 2 Diabetes**

Reconsider diagnosis if XS weight loss or symptoms of hyperglycaemia

**Refer to structured education**

**Reduced calories, Weight Loss, Increased Physical Activity**

Introduce STEP 1 when: 3 month HbA1c > 48mmol/mol OR consider earlier initiation of medication if symptomatic

At any phase of treatment if symptomatically hyperglycaemic, consider insulin and review treatment when blood glucose control achieved.

<b>SU</b>	Sulphonylurea
<b>TZD</b>	Thiazolidinedione (Glitazone)
<b>DPP4</b>	Dipeptylpeptidase 4 inhibitor (Gliptin)
<b>GLP-1</b>	Glucagon-Like-Peptide 1 Activator
<b>SGLT-2</b>	Sodium Glucose Co-Transporter 2 Inhibitor

**STEP 1 – START ONE OF:**

**METFORMIN\* - FIRST LINE** - only drug proven to reduce CV risk

IF CONTRAINDICATED

**SU (Second line)**

HbA1c target and glucose-lowering therapies must be individualized.

**STEP 2 – ADD ONE OF:**

**STEP 2 Treatment when HbA1c > 48mmol/mol at 3-12 monthly reviews, after reinforcing LIFESTYLE and checking COMPLIANCE**

Features of step 2 drugs
Priority for use
HbA1c reduction
Risk of hypoglycaemia
Weight
Side Effects
Cost*
NICE continuation criteria

SU
<b>FIRST LINE</b>
11-16.5mmol/mol (1-1.5%)
<b>High Gain</b>
<b>Hypoglycaemia</b>
~£30/year
n/a

OR if CI

TZD
<b>Alternative 1</b>
11-16.5mmol/mol (1-1.5%)
<b>Low Gain</b>
<b>Heart failure</b>
~£19/year
n/a

DPP4
<b>Alternative 2</b>
5.5-11mmol/mol (0.5-1%)
<b>Low Neutral</b>
<b>Rare</b>
~£430/year
Yes

SGLT-2
<b>Alternative 3</b>
6.6-13.2mmol/mol (0.6-1.2%)
<b>Low Loss</b>
<b>UTI/ genital inf</b>
~£475/year
Yes

SGLT-2 can only be used in a dual therapy regimen with metformin

**STEP 3 – ADD OR SUBSTITUTE WITH ONE OF:**

**STEP 3 Treatment when HbA1c > 58mmol/mol after reinforcing LIFESTYLE and checking COMPLIANCE**

OR IF INSULIN NOT ACCEPTED OR APPROPRIATE

Features of insulin / GLP-1
HbA1c reduction
Risk of hypoglycaemia
Weight
Side Effects
Cost*
NICE continuation criteria
Additional information on initiating

INSULIN especially if HbA1C > 110 mmol/mol
>11mmol/mol (>1%)
<b>High Gain</b>
<b>Hypoglycaemia</b>
£160-£1000/year
n/a
Stop TDZ, DPP4 and SU but continue metformin

GLP-1 do not use with gliptin**
11-16.5mmol/mol (1-1.5%)
<b>Low Loss</b>
<b>GI</b>
£650-£1400/year
Yes
If BMI > 35kg/m <sup>2</sup> or < 35kg/m <sup>2</sup> and insulin unacceptable

<b>SU</b>
<b>TZD</b>
<b>DPP4</b>
<b>SGLT-2 – canagliflozin or empagliflozin</b>

\*\*if DPP4 second line substitute GLP-1 for DPP4

\*prices from April 2015 drug tariff  
Metformin cost ~ £57/year

**Notes on medicines other than insulin**  
**See local formulary for individual drug choices**

Metformin	<p>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.</p> <p><b>Only oral agent associated with reduced CV risk and weight reduction.</b></p> <ul style="list-style-type: none"> <li>▶ Prescribe with caution for those at risk of sudden deterioration in kidney function and those at risk of eGFR falling below 45ml/min/1.73m<sup>2</sup></li> <li>▶ Reduce dose if eGFR below 45ml/min/1.73m<sup>2</sup></li> <li>▶ Stop if eGFR below 30ml/min/1.73m<sup>2</sup></li> </ul> <p>Counsel patients to stop temporarily if acutely unwell, particularly with vomiting and diarrhoea</p> <p>Metformin MR - only if intolerant (GI side effects) on standard release metformin</p>
Sulphonylurea	<p>Consider if patient not overweight, if metformin not tolerated or contra-indicated or if rapid response required because of hyperglycaemic symptoms.</p> <p>Do not prescribe gliclazide MR or tolbutamide</p> <p>Treat osmotic symptoms rapidly</p> <p>Contraindicated in pregnancy</p> <p>Risk of hypoglycaemia so patients will have to undertake home glucose monitoring. Educate about risk.</p> <p>No need to check BM routinely unless hypoglycaemia or driving.</p>
Thiazolidinedione (TZD)	<p>Pioglitazone:</p> <p>Contraindications: heart failure, active bladder cancer or history of bladder cancer, uninvestigated haematuria, pregnancy</p> <p>Cautions: Increased risk of bone fractures, particularly women</p> <p>Carries long term risk of limb fracture.</p> <p>Caution with liver disease.</p> <p>Rare reports of liver dysfunction – monitor liver function before and periodically during treatment.</p> <p>Start at 15-30mg daily and titrate to 45 mg daily according to response.</p> <p><b>NICE criteria: Discontinue if reduction in HbA1c is less than 0.5% (5.5 mmol/mol) after 6 months of treatment.</b></p>
DPP4 inhibitors (Gliptins)	<p>No long term safety data</p> <p>Low risk of hypoglycaemia – useful in patients at risk of hypoglycaemia. Appears to be weight neutral – useful if further weight gain would cause significant problems.</p> <p>Do not use in pregnancy and breastfeeding.</p> <p>Discontinue if symptoms of acute pancreatitis</p> <p>Consider stopping if NICE criteria for continuation not met.</p> <p><b>NICE criteria: Discontinue if reduction in HbA1c is less than 0.5% (5.5 mmol/mol) after 6 months treatment.</b></p>

GLP-1 mimetics	<p><b>Injected therapy</b></p> <p>Avoid in pregnancy and breastfeeding. Discontinue if pancreatitis suspected</p> <p>Main side effects GI disturbance (especially nausea) ~ 30% of patients</p> <p>Associated with weight loss</p> <p>GLP-1 used in combination with insulin <b>ONLY</b> in specialist care setting</p> <p><b>NICE criteria: Add as part of triple therapy ONLY if BMI is ≥ 35kg/m<sup>2</sup> 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/m<sup>2</sup> 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 sulphonylurea if either metformin, OR a sulphonylurea AND pioglitazone AND DPP-4 inhibitors contra-indicated or not tolerated (only liraglutide 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 than 3% weight loss after 6 months<sup>2</sup> (only HbA1c reduction required for dual therapy)</b></p>
SGLT-2	<p>Caution with thiazide or loop diuretic use.</p> <p><b>Volume depletion</b> - Correct hypovolaemia before starting treatment. Consider interrupting treatment if volume depletion occurs</p> <p><b>Determine renal function before treatment and annually thereafter.</b></p> <p><b>Dapagliflozin</b> – avoid if eGFR &lt;60ml/min/1.73m<sup>2</sup></p> <p><b>Canagliflozin</b> - monitor renal function at least twice a year in moderate impairment; avoid initiation if eGFR less than 60 mL/minute/1.73 m<sup>2</sup>; avoid in combination with metformin if eGFR less than 60 mL/minute/1.73 m<sup>2</sup>; reduce dose to 100 mg once daily if eGFR falls persistently below 60 mL/minute/1.73m<sup>2</sup> and existing canagliflozin treatment tolerated; avoid if eGFR less than 45 mL/minute/1.73m<sup>2</sup></p> <p><b>Empagliflozin</b> - avoid initiation if eGFR below 60 mL/minute/1.73 m<sup>2</sup>; reduce dose to 10 mg once daily if eGFR falls persistently below 60 mL/minute/1.73 m<sup>2</sup>; avoid if eGFR is persistently below 45 mL/minute/1.73 m<sup>2</sup></p> <p><b>NICE criteria:</b></p> <p><b>Dapagliflozin, canagliflozin or empagliflozin can be used in a dual therapy regimen in combination with metformin AND</b></p> <p><b>In combination with insulin with or without other antidiabetic drugs. Canagliflozin and empagliflozin can be used in a triple therapy regimen in combination with metformin and a sulphonylurea or a thiazolidinedione.</b></p> <p><b>Dapagliflozin is not recommended in triple therapy unless part of a clinical trial.</b></p> <p><b>Discontinue if reduction in HbA1c is less than 0.5% (5.5 mmol/mol) after 6 months treatment.</b></p>

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

### Group approach structured education 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 regime based on individual considerations

Option 1	Isophane insulin (basal) once or twice daily
Option 2	Pre-mixed insulin (human) twice daily. Most likely required initially if: Symptomatic Short history of diabetes BMI <25kg/m <sup>2</sup> HbA1c >75mmol/mol (9.0%) Start premixed insulin with breakfast and evening meal

**Insulin Dose:** 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:

**Needs to be individualised**

HbA1c <53mmol/mol (7%)

Blood glucose target

Fasting: 4 – 7mmol/l

Pre-meals: 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 daily isophane for elderly patients (stop Sulphonylurea)

### Basal bolus regime

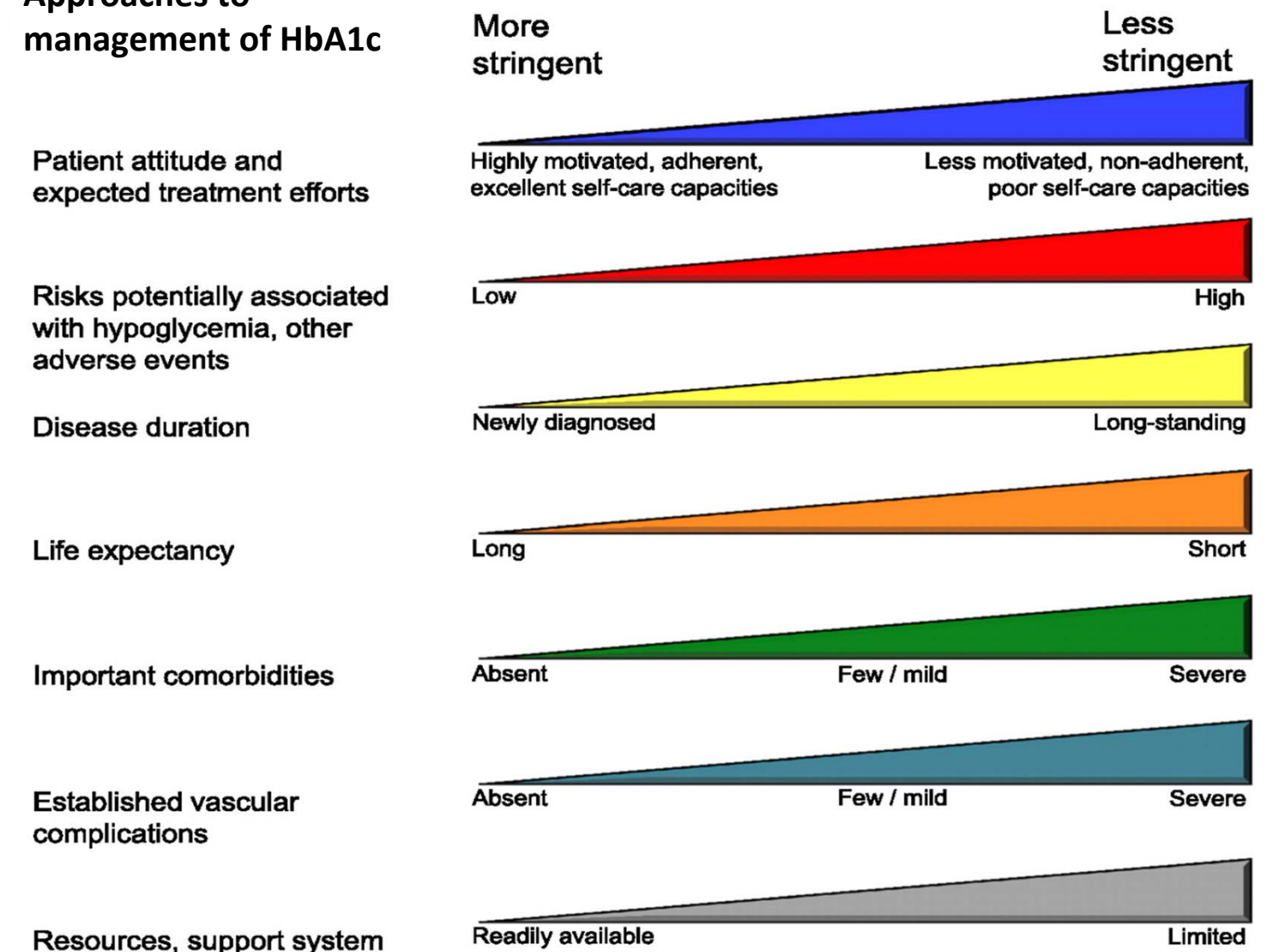
Not routinely used in the management of Type 2 diabetes – seek specialist advice

Isophane insulin	Premixed insulin	Long acting analogue
Insuman Basal Humulin I Insulatard	Insuman Comb Humulin M3	Levemir (Detemir) Lantus (Glargine)

### KEY POINTS

- HbA1c targets and glucose-lowering therapies must be individualized.
- 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 minimize 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.

### Approaches to management of HbA1c



Silvio E. Inzucchi et al. Dia Care 2012;35:1364-1379

The elements of decision making used to determine appropriate efforts to achieve HbA1c targets. Characteristics toward the left justify more stringent efforts to lower HbA1c, those toward the right are compatible with less stringent efforts. Where possible, decisions should be made in conjunction with the patient, reflecting his or her preferences, 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.