NHS
Newcastle Gateshead
Clinical Commissioning Group

Stepped Approach to Type 2 Diabetes

Implementation date: June 2015

Review date: June 2017

This guideline has been prepared and approved for used within Gateshead in consultation with Gateshead CCG and Secondary Care Trusts.

Approved by:

Committee	Date
Gateshead Medicines Management Committee	12/11/2014
Newcastle Gateshead Alliance CCGs Optimisation of Medicines, Pathways and Guidelines Committee	20/11/2014

This guideline is not exhaustive and does not override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Full details of contra-indications and cautions for individual drugs are available in the BNF or in the Summary of Product Characteristics (available in the Electronic Medicines Compendium) www.emc.medicines.org.uk

NORTH EAST AND CUMBRIA
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/

Approved on behalf of the:	
North of Tyne Medicines Guidelines and Use Group	
North of Tyne Area Prescribing Committee	
Review date	June 2017
Organisations signed up to this guideline	
Membership of the guideline development group	Nicky Leech (NuTH) Stuart Bennett (NHCT) Barbara Palmer (Newcastle West CCG) Chris Jones-Unwin (Newcastle North and East CCG) Helen Ramsey (Gateshead CCG) Lou Shearer (Northumberland CCG, co-chair of the Diabetes Network in Northumberland) Narayanan Kilimangalam (Gateshead Health NHS Foundation Trust) Rebecca Haines (NHS Gateshead CCG) Anne-Marie Bailey (North of England Commissioning Support) Sarah Tulip (North of England Commissioning Support) Caroline Sprake (North Tyneside CCG)
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

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

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

SU	Sulphonylurea
TZD	Thiazolidinedione (Glitazone)
DPP4	Dipeptylpeptidase 4 inhibitor (Gliptin)
GLP-1	Glucagon-Like-Peptide 1 Activator
SGLT-2	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 LIFESYTLE and checking COMPLIANCE

Features of step 2 drugs	SU	→ OR if CI → TZD	DPP4	SGLT-2
Priority for use	FIRST LINE	Alternative 1	Alternative 2	Alternative 3
HbA1c reduction	11-16.5mmol/mol (1-1.5%)	11-16.5mmol/mol (1-1.5%)	5.5-11mmol/mol (0.5-1%)	6.6-13.2mmol/mol (0.6-1.2%)
Risk of hypoglycaemia	High	Low	Low	Low
Weight	Gain	Gain	Neutral	Loss
Side Effects	Hypoglycaemia	Heart failure	Rare	UTI/ genital inf
Cost*	~£30/year	~£19/year	~£430/year	~£475/year
NICE continuation criteria	n/a	n/a	Yes	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

Features of insulin / GLP-1	INSULIN especially if HbA1C >110 mmol/mol	GLP-1 do not use with gliptin**
HbA1c reduction	>11mmol/mol (>1%)	11-16.5mmol/mol (1-1.5%)
Risk of hypoglycaemia	High	Low
Weight	Gain	Loss
Side Effects	Hypoglycaemia	GI
Cost*	£160-£1000/year	£650-£1400/year
NICE continuation criteria	n/a	Yes
Additional information on initiating	Stop TDZ, DPP4 and SU but continue metformin	If BMI>35kg/m^2 or <35kg/m^2 and insulin unacceptable

OR IF INSULIN NOT ACCEPTED OR APPROPRIATE

- SU
- TZD
- DPP4
- SGLT-2 – canagliflozin or empagliflozin

**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	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 temporarily if acutely unwell, particularly with vomiting and diarrhoea Metformin MR - only if intolerant (GI side effects) on standard release metformin
Sulphonylurea	Consider if patient not overweight, if metformin not tolerated or contra-indicated 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.
Thiazolidinedione (TZD)	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 45 mg daily according to response. **NICE criteria: Discontinue if reduction in HbA1c is less than 0.5% (5.5 mmol/mol) after 6 months of treatment.**
DPP4 inhibitors (Gliptins)	No long term safety data 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. Do not use in pregnancy and breastfeeding. Discontinue if symptoms of acute pancreatitis Consider stopping if NICE criteria for continuation not met. **NICE criteria: Discontinue if reduction in HbA1c is less than 0.5% (5.5 mmol/mol) after 6 months treatment.**
GLP-1 mimetics	**Injected therapy** Avoid in pregnancy and breastfeeding. Discontinue if pancreatitis suspected Main side effects GI disturbance (especially nausea) ~ 30% of patients Associated with weight loss GLP-1 used in combination with insulin **ONLY** in specialist care setting **NICE criteria: Add as part of triple therapy ONLY if BMI is ≥ 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<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 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 months2 (only HbA1c reduction required for dual therapy)**
SGLT-2	Caution with thiazide or loop diuretic use. **Volume depletion** - Correct hypovolaemia before starting treatment. Consider interrupting treatment if volume depletion occurs **Determine renal function before treatment and annually thereafter.** **Dapagliflozin** – avoid if eGFR <60ml/min/1.73m^2 **Canagliflozin** - monitor renal function at least twice a year in moderate impairment; avoid initiation if eGFR less than 60 mL/minute/1.73 m^2; avoid in combination with metformin if eGFR less than 60 mL/minute/1.73 m^2; reduce dose to 100 mg once daily if eGFR falls persistently below 60 mL/minute/1.73m^2 and existing canagliflozin treatment tolerated; avoid if eGFR less than 45 mL/minute/1.73m^2 **Empagliflozin** - avoid initiation if eGFR below 60 mL/minute/1.73 m^2; reduce dose to 10 mg once daily if eGFR falls persistently below 60 mL/ minute/1.73 m^2; avoid if eGFR is persistently below 45 mL/minute/1.73 m^2 **NICE criteria:** **Dapagliflozin, canaglifloxin or empagliflozin can be used in a dual therapy regimen in combination with metformin** **AND** **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 thiazolodinedione.** **Dapagliflozin is not recommended in triple therapy unless part of a clinical trial.** **Discontinue if reduction in HbA1c is less than 0.5% (5.5 mmol/mol) after 6 months treatment.**

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/m2** **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)

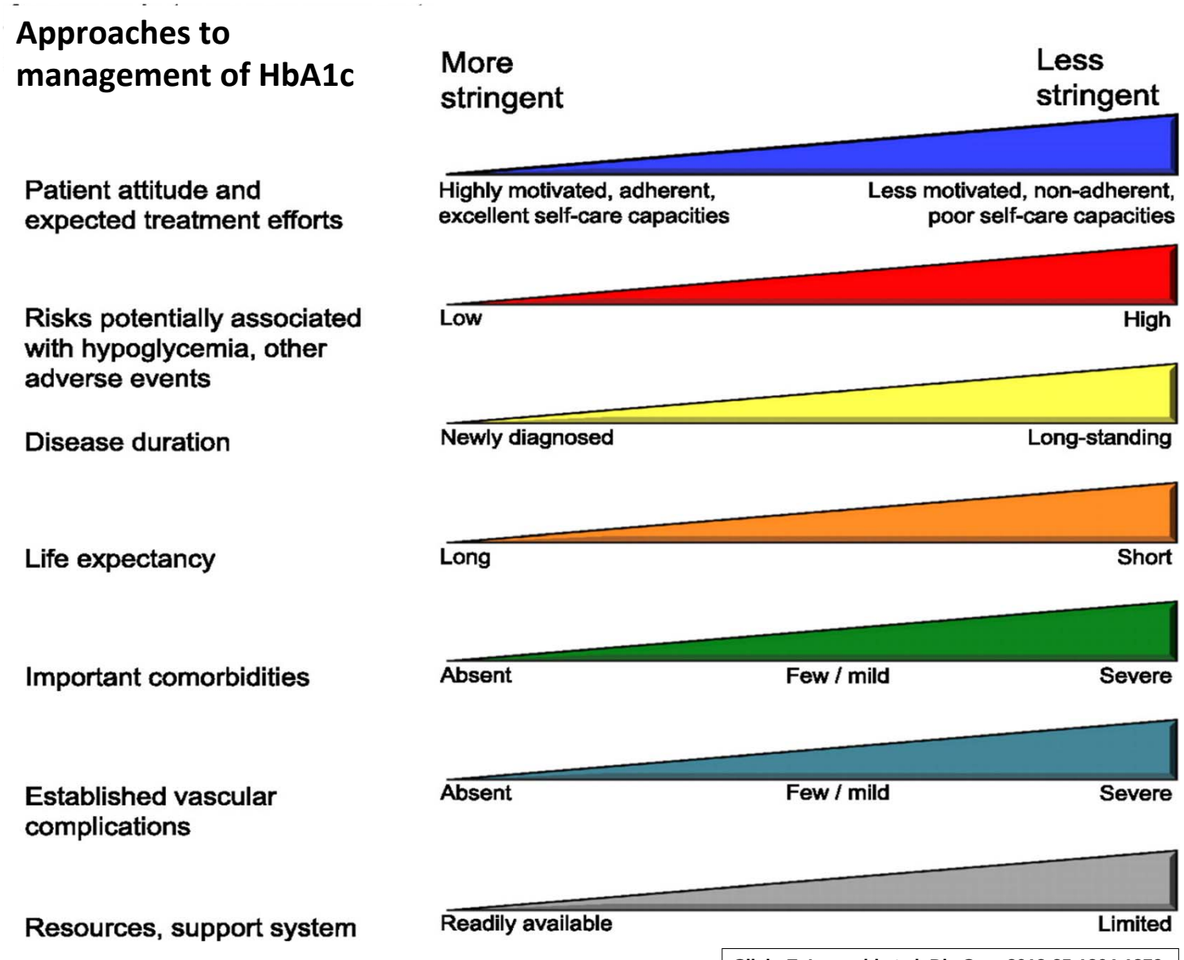
Basal bolus regime

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.



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.