Algorithm for the Management of Type 2 Diabetes

York and Scarborough Medicines Commissioning Committee

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 + DDP4i
Or
Sulfonylurea + Pioglitazone
If BMI<30kg/m² 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 +		**Metformin intolerant or CI**
1. SGLT2i (or)		1. Sulfonylurea + DDP4i (or)
2. Or DPP4i (suitable for frailty)	(or)	2. DPP4i + Pioglitazone (or)
3. Or Pioglitazone		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 (canaglifozin or empagliflozin only)

If BMI > 25 kg/m² consider option 1 (ensure eGFR > 60mL/min)
If BMI < 25 kg/m² 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

Approved: March 2019 by York and Scarborough Medicines Commissioning Committee
Review: February 2021

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
Positive reasons to use this class	• Low cost • Rapid clinical effect • Long established profile • Agent of choice in MODY	• Low hypoglycaemia risk • Weight neutral • Licensed in people with CKD (may require dose reduction) • Fewer drug interactions	• Low hypoglycaemia risk • Reduces insulin resistance • Slower progression to insulin treatment	• Low hypoglycaemia risk • Weight loss • Proven cardiovascular benefits (empagliflozin and canagliflozin)
Reasons not to use this class	• Risk of hypoglycaemia (increased in CKD) • Potential need for blood glucose monitoring • Weight gain	• Relatively low potency and moderate cost	• Weight gain • Slow onset of action • Contraindicated in CCF, LVF • Risk of fractures (women) • Small increase in incidence of bladder cancer) • Moderate cost • Do not use with insulin	• If eGFR <60 • UTI, genital thrush • Relatively new class – unexpected long term side effects may yet to be recognised • Moderate cost • Risk of DKA
Good choice for	• Preferred to metformin for patients with osmotic symptoms	• In people whom further weight gain would cause or exacerbate significant problems associated with high body weight • Frail older people • Any person for whom hypoglycaemia is a particular concern	• Most likely to benefit people who wish to delay progression to insulin (e.g. group 2 LGV and C1 driving licence holders)	• Obese people • In those whom further weight gain would cause or exacerbate significant problems associated with high body weight • People for whom hypoglycaemia is a particular concern
Monitoring required	• Consider home glucose monitoring as per "Who to Test, When to Test" guidance*	• Review U & E annually	• Review urine dip for blood annually • Review LFTs annually • Stop if heart failure/fluid overload develops	• Review U & E annually

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

Approved: March 2019 by York and Scarborough Medicines Commissioning Committee
Review: February 2021

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/m2 or higher
- In those with a body mass index of less than 35 kg/m2 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 m2)

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 hypoglcaemics / 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 2/3rd AM, 1/3rd 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

Approved: March 2019 by York and Scarborough Medicines Commissioning Committee
Review: February 2021

Management of Diabetes in the over 75 age group

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

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Review: February 2021