Interim Guidance-Pharmacological treatment of type 2 diabetes in adults

NHS Basildon and Brentwood Clinical Commissioning Group

NHS Thurrock Clinical Commissioning Group

Adult with type 2 diabetes who can take metformin

If HbA1c rises to 48 mmol/mol (6.5%) on lifestyle interventions:

- Offer **standard-release metformin**
  -Gradually titrate and optimise dose
- Agree an individual HbA1c level on a case by case basis

If standard-release metformin is not tolerated after an appropriate trial, consider modified-release metformin.
-Titrate and optimise dose

FIRST INTENSIFICATION
If insufficient response:

- Consider dual therapy with:

-**metformin** and a **SU (gliclazide)**

- If SU contraindicated or not tolerated, consider dual therapy with:

-**metformin** and a **DPP-4i (alogliptin)**

- Support the person to aim for their individual HbA1c level

SECOND INTENSIFICATION
If insufficient response:

- Consider:

-triple therapy with:

- **metformin**, **gliclazide** and **alogliptin**

-if not effective stop alogliptin, consider:

- **metformin**, **gliclazide** and an **SGLT-2i (empagliflozin)**

-or **insulin-based treatment**

- Support the person to aim for their individual HbA1c level

If triple therapy is not effective, not tolerated or contraindicated,

- Discontinue DPP-4i or SGLT-2i
- Consider:

-combination therapy with **metformin**, **gliclazide** and a **GLP-1 mimetic (lixisenatide)**
-for adults with type 2 diabetes who:
-have a BMI of 35 kg/m^2 or higher (adjust accordingly for people from black, Asian and other minority ethnic groups) **and** specific psychological or other medical problems associated with obesity, **or**
-have a BMI lower than 35 kg/m^2, **and** for whom insulin therapy would have significant occupational implications, **or** weight loss would benefit other significant obesity-related comorbidities

Metformin contraindicated or not tolerated

If HbA1c rises to 48 mmol/mol (6.5%) on lifestyle interventions:

- Consider:

-**SU (gliclazide)** or a **DPP-4i (alogliptin)**

- Agree an individual HbA1c level on a case by case basis

FIRST INTENSIFICATION
If insufficient response:

- Consider dual therapy with:

-**SU (gliclazide)** and a **DPP-4i (alogliptin)**

- Support the person to aim for their individual HbA1c level

SECOND INTENSIFICATION
If insufficient response:

- Stop alogliptin and consider:

-**SU (gliclazide)** and an **SGLT-2i (empagliflozin)*, or SU (gliclazide)** and a **GLP-1 mimetic (lixisenatide)****

- Consider insulin-based treatment
- Support the person to aim for their individual HbA1c level

- Reinforce advice about adherence to drug treatment.
- Introduce drugs in a stepwise manner.
- When starting insulin therapy, continue to offer metformin for people without contraindications or intolerance.

Reference: Type 2 diabetes in adults: management, NICE guideline NG28 (December 2015)
* and ** combination not formally recommended in NICE guideline NG28

Prescribing Information-formulary choices and additional information. Measure HbA1c levels every 3-6-monthly until HbA1c is stable on unchanging therapy. Measure HbA1c levels every 6 months once HbA1c level and blood glucose lowering therapy are stable.

Metformin

- First line: prescribe standard release as **Glucophage** tablets.
- Modified release: reserved for those who suffer with persistent GI side effects only after gradual titration with standard release metformin (prescribe as **Sukkarto SR**).
- Review the dose of metformin if the eGFR is below 45 ml/minute/1.73m^2:
    - Stop metformin if the eGFR is below 30 ml/minute/1.73m^2.
    - Prescribe metformin with caution for those at risk of a sudden deterioration in kidney function and those at risk of eGFR falling below 45ml/minute/1.73m^2.

Glitazones (thiazolidinediones): Pioglitazone (specialist recommendation)

- Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture.
- **Do not** offer or continue pioglitazone if there are any of the following:
    - heart failure or history of heart failure
    - hepatic impairment
    - diabetic ketoacidosis
    - current, or a history of, bladder cancer
    - uninvestigated macroscopic haematuria
- MHRA guidance (2011) advises that 'prescribers should review the safety and efficacy of pioglitazone in individuals after 3–6 months of treatment to ensure that only patients who are deriving benefit continue to be treated'.

Sodium glucose co-transporter 2 (SGLT-2) inhibitors

- **Empagliflozin** is the first choice formulary SGLT-2 inhibitor.
- Only continue treatment if there is a reduction of between 5 and 6 mmol/mol (≥0.5% points) in HbA1c in 6 months. **If not discontinue treatment.**
- Dose of concomitant insulin or sulfonylurea may need to be reduced.
- Check renal function before treatment and at least annually.
- Not recommended in moderate to severe renal failure (eGFR<60ml/minute).
- Common side effects: dyslipidaemia, back pain, genital infections, UTI, dysuria, polyuria.
- Serious and life-threatening cases of diabetic ketoacidosis have been reported in people taking SGLT-2 inhibitors or shortly after stopping the SGLT-2 inhibitor. MHRA guidance (2015) advises testing for raised ketones in people with symptoms of diabetic ketoacidosis, even if plasma glucose levels are near normal.

Sulfonylureas (SU)-Gliclazide

- Avoid glibenclamide-long acting and greater risk of hypoglycaemia.

DPP4 inhibitors-gliptins

- **Alogliptin (Vipidia)** is the first choice formulary DPP-4 inhibitor.
- The recommended dose of alogliptin is 25mg once daily.
    - For patients with moderate renal impairment (eGFR 30-50ml/min) dose of 12.5 mg once daily.
    - For patients with severe renal impairment (eGFR < 30 ml/min) dose of 6.25 mg once daily.
- Linagliptin is the second line DPP-4 inhibitor in patients with end stage/ deteriorating renal function only.
- Only continue treatment if there is a reduction of between 5 and 6 mmol/mol (≥0.5% points) in HbA1c in 6 months. **If not discontinue treatment.**
- When used in combination with a sulphonylurea or insulin, a lower dose of the sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia.

Glucagon-like peptide-1 (GLP-1) mimetic

- **Lixisenatide** (Lyxumia) is the first choice formulary GLP-1 mimetic.
    - Dulaglutide (Trulicity) is second line, if patient does not tolerate lixisenatide.
- Patients with no or very little response to one GLP-1 receptor agonist should not be offered another one.
- Only continue treatment if a reduction of at least 11 mmol/mol (1.0%) in HbA1c and a weight loss of at least 3% of initial body weight is achieved at 6 months. If not discontinue treatment.
- When lixisenatide or dulaglutide is added to a sulfonylurea, a reduction in the dose of the sulfonylurea may be considered to reduce the risk of hypoglycaemia.

This guidance on pharmacological treatment of type 2 diabetes in adults is interim guidance for primary care use, and will be reviewed in 2017.