Interim Guidance: Pharmacological treatment of type 2 diabetes in adults

**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

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

**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)
- 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

- 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/1.73m²:
  - Stop metformin if the eGFR is below 30 ml/minute/1.73m².
  - 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/1.73m².

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.

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.

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.