Guideline Name	**Core stepped approach to medical treatment of type 2 diabetes**[1]
Date of Issue:	March 2014
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Step 1 HbA1c range >58mmol/mol

Start metformin at 500mg od, and titrate to 1g bd. Consider continuing at lower dose if GI side effects[2]**.**

Alternates
A sulphonylurea can be used if metformin is contraindicated or not tolerated.
Pioglitazone[3] **30 mg or DPP4 inhibitor**[4] **(currently Alogliptin** 25mg od**) are licensed for use as monotherapy, and can be used by patients who cannot take both metformin and sulphonylurea.**

Step 2 HbA1c >58mmol/mol after Step 1

Add sulphonylurea – usually gliclazide 80mg od, and titrate to max 160mg bd if required. Where hypoglycaemia is a risk or there is concern about weight gain, do not use a gliclazide.
Pioglitazone or DPP4 inhibitor can be added as a second drug to either metformin or sulphonylurea.

For BMI>25 an SGLT2[5] **is NICE-approved for addition to metformin and/or sulphonylurea.**

Step 3 HbA1c still >58mmol/mol [6]

HbA1c 59-85 mmol/mol Add 3rd oral or isophane insulin
HbA1c ≥85 mmol/mol add isophane insulin[7] **at night, or twice daily**[8]**If BMI ≥35 consider Lixisenatide 10mcg increasing to 20mcg**[9]**, and review oral therapies (e.g. stop SU or DPP4 inhibitor).**
OR in patients with strong reason to avoid insulin (e.g. vocational driving licence) add 3rd oral

Date taken to APC:	5th March 2014	**Date Ratified by MMC on Behalf of the Board:**	27th March 2014
Amendment Date	5th June 2015	**Date ratified by GP MOC**	15th June 2015

References

[1] Adapted from NICE guidelines
[2] Consider **MR Metformin** if metformin is poorly tolerated
[3] **Pioglitazone**
Tablet with proven cardiovascular safety, but usually some weight gain.
Renal impairment: OK.
Side effects: weight gain, fluid retention.
Contraindications: heart failure, bladder cancer, haematuria, risk of osteoporosis.
[4] **DPP-4 inhibitors (alogliptin, sitagliptin, vildagliptin, saxagliptin, linagliptin)**
Tablet with no weight gain and few side effects, but long-term benefit not proven.
Renal impairment: OK, but reduced dose (see DPP4 guideline for detail).
[5] **$SGLT_2$ inhibitors (empagliflozin, dapagliflozin, canagliflozin)**

	*empagliflozin	dapagliflozin	*canagliflozin
Monotherapy	✓	✓	✓
Dual therapy	✓	✓	✓
Triple therapy	✓	✓	✓
Administration: orally once daily	✓	✓	✓
Max decrease in HbA1c when used as monotherapy	-0.66 to -0.78	-0.89	-0.77 to -1.03
Decrease in body wt. (monotherapy)	-2.2 to -2.48kg	-3.16kg	-2.8 to -3.9kg
Cost per annum	£476	£476	£476 to £608.21

*can be used at lower dose when eGFR drops < 60 ml/min/1.73m^2 at reduced dose. Empagliflozin and canagliflozin should be stopped when eGFR is <45ml/min/1.73m^2 and dapagliflozin stopped when < 60 ml/min/1.73m^2
[6] Average HbA1c reduction is about 11 mmol/mol with newer drugs, but may be individual variation, and some patients do show a greater response.
[7] When HbA1c is very high, you will usually not achieve good control by adding one of these drugs. Insulin is preferred for patients with very poor control.
[8] **Insulin should be the usual option after metformin and sulphonylurea.**
The newer drugs are aggressively marketed, but insulin remains a valuable therapy for type 2 diabetes and we have a huge amount of experience with it.
Insulin is “cleaner” and should be used in significant renal or hepatic impairment.
Insulin choice Insuman Basal, or Insuman Comb 15,25 or 50
[9] **GLP-1 analogues (Lixisenatide exenatide, liraglutide)**.
Injection giving some weight loss, but long-term benefit not proven.
NICE: only if BMI>35, unless psychological or occupational reasons to avoid insulin.
Weight reduction – average 2-4kg, though significant individual variation.
Renal impairment: OK if eGFR >30
Side effects: nausea, bloating. Contraindications: risk of pancreatitis, bowel surgery.
Consider changing to Liraglutide if nauseous or sub-optimal response, or Bydureon if once weekly injection required.