

Type 2 Diabetes Mellitus (T2DM) Adult Treatment Pathway

Target Blood Pressure 140/80mmHg (130/80 if complication present)

Target HbA_{1c} (48-53mmol/mol) 6.5-7.0% or agreed target

Target Total Cholesterol <5mmol/L and LDL<3mmol/L

HbA_{1c} ≥6.5% after 3-6months, initiate drug therapy:

Healthy diet, weight control and physical activity

Monotherapy

Efficacy [§]
Hypoglycaemia risk
Weight
Side effects
Costs (£)

Metformin	
Efficacy [§]	High
Hypoglycaemia risk	Low
Weight	Neutral / Loss
Side effects	Nausea and diarrhoea
Costs (£)	Low
If metformin not tolerated, consider metformin modified release (MR)	



HbA_{1c} ≥7.5% after ~3months, proceed to:

Choose any ONE of the oral treatment options below to ADD to metformin

Dual therapy

Efficacy [§]
Hypoglycaemia risk
Weight
Side effects
Costs (£)

Dipeptidyl peptidase-4 inhibitors (DPP4-i) "ending gliptin"
Intermediate Low Neutral Rare Medium
Safe: low risk of hypo suggested dual combination with metformin

Sodium-glucose-cotransporter-2 inhibitors (SGLT2-i) "ending flozin"
Intermediate Low Loss: ~2kg Genital thrush Medium
Safe: low risk of hypo suggested dual combination with metformin

Sulfonylurea (SU)
High Moderate Gain: ~1.5-2kg Hypoglycaemia Low
Potent but consider risk of hypo + weight gain

Thiazolidinediones (TZD)
High Low Gain: ~4-5kg Oedema, Heart failure, Fractures Low
Potent but consider risk of weight gain + other side effects

Injectable treatment to add to metformin

Glucagon-like-peptide-1 receptor agonist (GLP-1)
High Low Loss: ~1-3kg Nausea (initially) High
Potent: please discuss with Community Diabetes Nursing Service (CDNS)

Insulin (basal)
Highest High Gain: ~4-5kg Hypoglycaemia Variable
Potent: please discuss with CDNS



HbA_{1c} ≥7.5% after ~3months, proceed to:

Suggested oral triple combination based on safety

Triple therapy

Metformin
SGLT2-i "ending flozin"
DPP4-i "ending gliptin"
Safest: low risk of hypo + weight neutral/loss
Contact Community Diabetes Nursing Service if HbA _{1c} not achieved after ~3 months of triple therapy.

[§]Efficacy is an estimated improvement in HbA_{1c}:
 Highest Efficacy = >2% drop
 High Efficacy = 1-2% drop
 Intermediate efficacy = upto 1% drop

Antidiabetics					Prevention of Cardiovascular disease*
Therapeutic class	Drug [‡]	Physiological action	Costs*	Additional Information	Antihypertensives [‡] Target Blood Pressure 140/80mmHg (130/80 if complication present)
Biguanides	Metformin Metformin MR	<ul style="list-style-type: none"> ↓ gluconeogenesis ↑ peripheral glucose utilisation 	Low	Most of these drugs should not be used if patient has significant renal and/or liver disease, for more details consult British National Formulary (BNF) or Summary of Product Characteristics (SPC).	<div style="display: flex; justify-content: space-around;"> <div style="border: 1px solid black; padding: 5px; width: 45%;">Patients aged <55years</div> <div style="border: 1px solid black; padding: 5px; width: 45%;">Patients aged >55years or black of African or Caribbean family origin</div> </div> <div style="display: flex; justify-content: space-around; margin-top: 10px;"> <div style="border: 1px solid black; padding: 5px; width: 45%; text-align: center;"> Step 1 Angiotensin-converting enzyme inhibitor (ACEi), if not tolerated angiotensin II receptor blocker (ARB-II) </div> <div style="border: 1px solid black; padding: 5px; width: 45%; text-align: center;"> Step 1 Calcium-channel blocker (CCB) </div> </div> <div style="text-align: center; margin-top: 10px;"> Step 2: ACEi / ARB-II + CCB </div> <div style="text-align: center; margin-top: 10px;"> Step 3: ACEi / ARB-II + CCB + Thiazide-like diuretic </div> <div style="text-align: center; margin-top: 10px;"> Step 4: Resistant hypertension Add Alpha-blocker or Beta-blocker or Spironolactone </div>
Sulfonylurea (SU)	Gliclazide Glipizide	<ul style="list-style-type: none"> Augments insulin secretion Effective but needs some residual pancreatic β-cell activity 	Low		
Thiazolidinediones (TZD)	Pioglitazone	<ul style="list-style-type: none"> ↓ peripheral insulin resistance ↓ blood glucose concentration 	Low		
Dipeptidyl peptidase-4 inhibitors (DPP4-i)	Saxagliptin Vildagliptin Linagliptin Sitagliptin Alogliptin	<ul style="list-style-type: none"> ↑ insulin secretion (<i>glucose-dependent</i>) 	Medium		
Sodium-glucose-cotransporter-2 inhibitors (SGLT2-i)	Dapagliflozin Canagliflozin Empagliflozin	<ul style="list-style-type: none"> Blocks renal glucose reabsorption ↑ glucosuria 	Medium		
Glucagon-like-peptide-1 receptor agonist (GLP-1)	Exenatide Exenatide MR Liraglutide Lixisenatide Dulaglutide	<ul style="list-style-type: none"> ↑ insulin secretion (<i>glucose-dependant</i>) 	High		
					Lipid Management[‡] Target Total Cholesterol <5mmol/L and LDL<3mmol/L <i>(the lower the better)</i>
					Primary prevention – Atorvastatin; if 10-year CVD risk ≥10% (QRISK2). Secondary prevention – Atorvastatin

[‡]Refer to SPC (<http://www.medicines.org.uk/emc/default.aspx>) or BNF (<http://www.medicinescomplete.com/mc/index.htm>) for all dosage, cautions, contraindications, interactions and adverse effects for each drug.

*Refer to NICE pathways, treatment steps for hypertension. December 2015 and NICE guidance, cardiovascular disease: risk assessment and reduction, including lipid modification. July 2014 for full details.

^{*}Cost criteria per month at the usual dose:

Low - ≤£10; Medium – ≤£40; High - >£50

References:

1. British National Formulary (BNF) 69 accessed from: www.medicinescomplete.com
2. Management of Hyperglycemia in Type 2 Diabetes, 2015: A Patient-Centered Approach. Update to a Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2015; 38:140–149 | DOI: 10.2337/dc14-2441
3. NICE guidance. Blood glucose lowering therapy for type 2 diabetes. July 2014
4. NICE guidance. Type 2 diabetes in adults: management NG 28. December 2015
5. NICE guidance. Type 2 diabetes: newer agents. May 2009
6. NICE pathways. Treatment steps for hypertension. December 2015.
7. NICE guidance. Cardiovascular disease: risk assessment and reduction, including lipid modification. July 2014.