ACHIEVING CONTROL IN TYPE 2 DIABETES

Review diet, exercise and adherence to medication before making dose adjustments or prescribing additional therapy, and discontinue new agents if no evidence of effectiveness (ie <5.5mmol/mol improvement in HbA1c) at 3-6 months
HbA1c target individualised eg ≤53mmol/mol on single agent, ≤58mmol/mol on two or more agents

Patient factors	**<**25kg/m^2 **OR** Osmotic symptoms. If weight loss check ketones ?T1DM	≥25kg/m^2			
Diet and exercise	1 month (Treat immediately if symptomatic)	3 months If appropriate, consider advising patients that remission of type 2 diabetes can be achieved with weight loss of 10-15kg			
First-line oral monotherapy	SULFONYLUREA (SU)	METFORMIN (MET) (SUs, SGLT2 inhibitors ("flozins"), DPP4 inhibitors ("gliptins") or PIO can all be used as alternate first line therapies in metformin intolerance)			
Second-line oral therapy (dual therapy)	SU + MET	MET + ONE of the following:			
		DPP-4 inhibitors ("gliptins") Consider if weight gain and/or hypos are a concern.*	SU Consider if BMI <27kg/m^2 but can be used at any BMI	PIOGLITAZONE (PIO) Consider if hypos are a concern.* See PIO prescribing algorithm. Avoid in heart failure.	SGLT2 inhibitors** ("flozins") Consider if weight gain and/or hypos are a concern and/or high CV risk* or heart failure. Do not initiate for glucose lowering alone if eGFR<60.
Third-line oral therapy (triple therapy)	Not appropriate – require INS initiation	MET + TWO of the following: Or consider injectable therapy eg insulin if BMI <30kg/m^2, GIP/GLP1 therapy if BMI >30kg/m^2 and high CV risk**			
		DPP-4 inhibitors ("gliptins") Consider if weight gain and/or hypos are a concern.*	SU Consider if BMI <27kg/m^2 but can be used at any BMI	PIO Consider if hypos are a concern.* See PIO prescribing algorithm. Avoid in heart failure.	SGLT2 inhibitors** ("flozins") Choose if weight gain and/or hypos are a concern and/or high CV risk * or heart failure. Do not initiate for glucose lowering alone if eGFR<60.
GIP/GLP-1 therapy (Alternative third line)	Not appropriate	Alternative third line therapy if high CV risk** or obesity GIP/GLP1 can be used with insulin, metformin and/or SGLT2 inhibitor • stop DPP-4 and consider reduction of SU/insulin dose on initiation • Injectable GLP-1 preferred (if available) given proven CV benefit			
Insulin therapies		Usually start with basal insulin at bed • Use NPH/isophane insulin eg Humulin I • Analogue insulin eg Insulin glargine, can be considered if high risk of hypoglycaemia or once daily administration by district nurse • Can continue metformin and/or SGLT2 inhibitor • Caution if on PIO (risk of fluid retention) • Consider reducing or stopping SU			
	* Falls in the elderly, driving, occupation, alcohol consumption. **Favour SGLT2 inhibitors/GLP1 receptor agonists in individuals with cardiovascular and renal disease.				

SU; sulfonylurea, MET; metformin, PIO; pioglitazone, SGLT2; sodium-glucose co-transporter 2 inhibitor, DPP-4; Dipeptidylpeptidase-4 inhibitor, GLP-1 – Glucagon-like peptide-1 agonist, INS; insulin, SMBG – self-monitoring of blood glucose.

	Sulfonylureas		Biguanide	Thiazolidine-dione	DPP4 inhibitors	
Medication	**Gliclazide**	**Glipizide**	**Metformin (std prep)**	**Pioglitazone**	**Alogliptin**	**Linagliptin**
Initiation dose	40 to 80mg before breakfast	2·5 to 5mg before breakfast	500mg with breakfast for 1 week then 500mg twice daily	15mg once daily if elderly or on insulin 30mg once daily for all other patients	25mg once daily	5mg once daily
Dose titration increment	40 to 80mg	2·5 to 5mg	500mg to 1 gram	15mg	NA	NA
Titration interval	3 monthly (if using SMBG <3 monthly)	3 monthly (if using SMBG <3 monthly)	3 monthly	Elderly or on insulin – 3 months if no ADRs Other patients - 6 months	NA	NA
Maximum dose	160mg twice daily before meals	20mg daily as divided doses with meals	1 gram twice daily	45mg daily	25mg daily	5mg daily
Treatment failure critiera[#]	<5·5mmol/mol reduction in HbA1c in 6 months	<5·5mmol/mol reduction in HbA1c in 6 months	<5·5mmol/mol reduction in HbA1c in 6 months	<5·5mmol/mol reduction in HbA1c in 6 months	<5·5mmol/mol reduction in HbA1c in 6 months	<5·5mmol/mol reduction in HbA1c in 6 months
Renal impairment	<50mL/min initially 20 to 40mg daily, monitor closely and use with caution	<50mL/min initially 2·5mg daily, monitor closely and use with caution	Avoid if <30mL/min Caution if 30 to 45mL/min	Dose as in normal renal function	≥30 -<50mL/min 12.5mg once daily<30mL/min - 6.25mg once daily	Dose as in normal renal function
Hepatic impairment	Reduce dose	Reduce dose	Withdraw if tissue hypoxia likely	Avoid	Avoid in severe hepatic impairment	Dose as in normal hepatic function
Notes	• weight gain • SMBG at higher doses	• weight gain • SMBG at higher doses	• low risk of hypo • Stop during any dehydrating illness or if acutely unwell • Consider modified release preparation in those with GI side effects	• avoid in any degree of LV dysfunction • weight gain • takes 4 to 5 months to alter HbA1c • small increased risk of bladder Ca • consider fracture risk	• weight neutral • low risk of hypo • avoid in moderate to severe heart failure • avoid if history of pancreatitis	• weight neutral • low risk of hypo • avoid if history of pancreatitis

[#]Unless at individualised target. If treatment failure criteria not met on maximum tolerated dose consider withdrawal of medication, substitution or addition of another medication.

	SGLT2 inhibitors (see additional guidance on prescribing for renal/cardiac disease)			GLP1 receptor agonists (subcut)				GLP1 agonist (Oral)
Medication	**Dapa-gliflozin**	**Cana-gliflozin**	**Empa-gliflozin**	**Lira-glutide (daily)**	**Sema-glutide (weekly)**	**Dula-glutide (weekly)**	**Exena-tide (weekly)**	**Sema-glutide (daily)**
Initiation dose	10mg once daily (5mg if severe hepatic impairment)	100mg once daily	10mg once daily Not recommended if >85 years	600 micrograms once daily	0.25mg once weekly (prescribe single prefilled 0.25mg pen)	1.5mg once weekly (0.75mg weekly if monotherapy)	2mg once weekly	3mg once daily (taken on empty stomach 30mins before eating/drinking /other meds)
Dose titration increment	NA	To 300mg daily	Can be increased to 25mg once daily	600 micrograms once daily	Increase to 0.5mg after 4 weeks (using 0.5mg pen)	1.5mg	NA	To 7mg, then 14mg
Titration interval	NA	If no side effects at 3-6 months	If no side-effects at 3-6 months	Increase from 0.6mg at 1 week	4 weeks	6months if required	NA	4 weeks
Maximum dose	10mg daily	300mg (reduce to 100mg/day if eGFR falls <60ml/min)	25mg daily (reduce to 10mg if eGFR falls <60ml/min)	Usually 1·2mg once daily, exceptionally 1·8mg/day	1mg once weekly	4·5mg once weekly.	2mg once weekly	14 mg daily
Treatment failure criteria[#]	<5·5mmol/mol reduction in HbA1c in 6 months, unless using for renoprotection or heart failure	<5·5mmol/mol reduction in HbA1c in 6 months, unless using for renoprotection or heart failure	<5·5mmol/mol reduction in HbA1c in 6 months, unless using for CV benefit or heart failure	<11mmol/mol reduction in HbA1c ± <3% weight loss in 6 months	<11mmol/mol reduction in HbA1c ± <3% weight loss in 6 months	<11mmol/mol reduction in HbA1c ± <3% weight loss in 6 months	<11mmol/mol reduction in HbA1c ± <3% weight loss in 6 months	<11mmol/mol reduction in HbA1c ± <3% weight loss in 6 months
Renal impairment	Can continue if eGFR <45ml/min for renoprotection or heart failure	Can continue if eGFR <45 ml/min for renoprotection if proteinuria	Can continue if eGFR <45ml/min for CV benefits or heart failure	Avoid if eGFR <30ml/min	Avoid if eGFR <15ml/min	Avoid if eGFR <15ml/min	Avoid if eGFR <30ml/min.	Avoid if eGFR <15ml/min
Hepatic impairment	5mg daily, increase according to response	Avoid in severe hepatic impairment	Avoid in severe hepatic impairment	Avoid in severe hepatic impairment	Avoid in severe hepatic impairment	No dosage adjustment required.	Dose as in normal hepatic function	Avoid in severe hepatic impairment
Notes	• promotes weight loss • low risk of hypo • risk of DKA • discontinue if acutely unwell or dehydrating illness	• promotes weight loss • low risk of hypo • risk of DKA • discontinue if acutely unwell or dehydrating illness • avoid if high risk feet	• promotes weight loss • low risk of hypo • risk of DKA • discontinue if acutely unwell or dehydrating illness	• promotes weight loss • diabetes <10yrs • avoid if history of pancreatitis	• promotes weight loss • diabetes <10yrs • avoid if history of pancreatitis • caution if diabetic retinopathy	• promotes weight loss • diabetes <10yrs • avoid if history of pancreatitis • Needle pre-attached	• promotes weight loss • diabetes <10yrs • avoid if history of pancreatitis	• must be taken on empty stomach with water, 30mins before eating, drinking or taking other medications

[#]Unless at individualised target. If treatment failure criteria not met on maximum tolerated dose consider withdrawal of medication, substitution or addition of another medication.

	GIP/GLP receptor agonist (subcut)	
Medication	**Tirzepatide**	
Initiation dose	2.5mg once weekly	
Dose titration increment	2.5mg	
Titration interval	Monthly, continue at lowest effective dose	
Maximum dose	15mg once weekly	
Treatment failure criteria[#]	Weight loss <5% and/or HbA1c reduction <5mmol/mol at 6months	
Renal impairment	No dose adjustment required	
Hepatic impairment	Use with caution in severe hepatic impairment	
Notes	• promotes weight loss • low risk of hypo (reduce/stop sulfonylurea) • avoid if history of pancreatitis • caution if diabetic retinopathy • may reduce effectiveness of oral contraceptive pill	
	[#]Unless at individualised target. If treatment failure criteria not met on maximum tolerated dose consider withdrawal of medication, substitution or addition of another medication.	