Appendix D: PRESCRIBING ALGORITHM FOR THE TREATMENT OF TYPE 2 DIABETES IN ADULTS

1st LINE **In ADDITION to lifestyle measures**	**SET GLYCAEMIC TARGET: HbA1c <7% (53 mmol/mol) OR INDIVIDUALISED AS AGREED**			
	USUAL APPROACH		**ALTERNATIVE APPROACH: if osmotic symptoms or intolerant of metformin**	
	METFORMIN	IF OSMOTIC SYMPTOMS (POLYURIA, POLYDIPSIA) CONSIDER **SULPHONYLUREA** FIRST. ONCE OSMOTIC SYMPTOMS RESOLVED, ADD OR REPLACE **METFORMIN**.	**SULPHONYLUREA**	IF SEVERE OSMOTIC SYMPTOMS WITH WEIGHT LOSS OR POSSIBILITY OF TYPE 1 DIABETES **(URGENT-PHONE SECONDARY CARE IMMEDIATELY, BTUH AMBULATORY CARE)** ↓ **BASAL INSULIN***
EFFICACY	MODERATE		HIGH	
CV BENEFIT	YES		NO	
HYPOGLYCAEMIA RISK	LOW		HIGH	
WEIGHT	NEUTRAL/REDUCTION		GAIN	
MAIN ADVERSE EVENTS	GASTROINTESTINAL		HYPOGLYCAEMIA	
IN CKD STAGE 3A	MAXIMUM 2 g DAILY		CAREFUL MONITORING [1]	
2nd LINE **In ADDITION to lifestyle measures**	**IF NOT REACHING TARGET AFTER 3–6 MONTHS [2], REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE**			
	ADD ONE OF (CHOICE DEPENDENT ON INDIVIDUAL PATIENT CIRCUMSTANCES, ADD ONE AT A TIME):			
	SULPHONYLUREA *OR*	**DPP-4 INHIBITOR* *OR***	**SGLT2 INHIBITOR* *OR***	**PIOGLITAZONE (specialist)***
EFFICACY	HIGH	LOW/MODERATE	MODERATE	MODERATE
CV BENEFIT	NO	NO	YES (EMPAGLIFLOZIN AND CANAGLIFLOZIN)	PROBABLE (BUT FLUID RETENTION)
HYPOGLYCAEMIA RISK	HIGH	LOW	LOW	LOW
WEIGHT	GAIN	NEUTRAL	LOSS	GAIN
MAIN ADVERSE EVENTS	HYPOGLYCAEMIA	FEW	GENITAL MYCOTIC INFECTIONS	OEDEMA/FRACTURES [5]
IN CKD STAGE 3A	CAREFUL MONITORING [1]	REDUCE DOSE [3]	DO NOT INITIATE [4]	DOSE UNCHANGED
3rd LINE **In ADDITION to lifestyle measures**	**IF NOT REACHING TARGET AFTER 3–6 MONTHS, REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE [6]**			
	ADD *EITHER* AN ADDITIONAL ORAL AGENT FROM A DIFFERENT CLASS			
	SULPHONYLUREA *OR*	**DPP-4 INHIBITOR* *OR***	**SGLT2 INHIBITOR* *OR***	**PIOGLITAZONE* (specialist)**
	OR AN INJECTABLE AGENT			
	GLP-1 AGONIST*: *If BMI is ≥35kg/m² in people of European descent (adjust for ethnic groups) and there are specific psychological or medical problems associated with high body weight, or BMI<35kg/m² and insulin is unacceptable because of occupational implications or weight loss would benefit other co-morbidities*		**BASAL INSULIN*:** *If BMI <30kg/m²*	
EFFICACY	HIGH	• stop DPP-4 inhibitor • consider reducing sulphonylurea • continue metformin • can continue pioglitazone • can continue SGLT2 inhibitor • aim for reduction of at least 11 mmol/mol (1.0%) in HbA1c and a 3% weight loss at 6 months (or individualised target)	HIGH	• inject before bed • use NPH (isophane) insulin - or longer-acting analogues if previous history of hypoglycaemia, or if hypoglycaemia on NPH (isophane) insulin • can continue metformin, pioglitazone, DPP-4 inhibitor or SGLT2 inhibitor • can reduce or stop sulphonylurea
CV BENEFIT	YES (SEMAGLUTIDE/LIRAGLUTIDE)		NO	
HYPOGLYCAEMIA RISK	LOW		HIGHEST	
WEIGHT	LOSS		GAIN	
MAIN ADVERSE EVENTS	GASTROINTESTINAL		HYPOGLYCAEMIA	
IN CKD STAGE 3A	DOSE UNCHANGED [7]		DOSE UNCHANGED [8]	
4th LINE **In ADDITION to lifestyle measures**	**IF NOT REACHING TARGET AFTER 3–6 MONTHS, REVIEW ADHERENCE: THEN GUIDED BY PATIENT PROFILE ADD ADDITIONAL AGENT(S) FROM 3rd LINE OPTIONS (NEED SPECIALIST INPUT)**			

NOTES:
***Continue medication at each stage if EITHER individualised target achieved OR HbA1c falls more than 0.5% (5.5 mmol/mol) in 3–6 months. DISCONTINUE IF EVIDENCE OF INEFFECTIVENESS.**
Algorithm does not apply in severe renal or hepatic insufficiency. 1. Consider dose reduction. 2. Do not delay if first line options not tolerated / inappropriate. 3. See BNF: no dose reduction required for linagliptin. 4. See BNF: specific agents can be continued at reduced dose. 5. Pioglitazone is contraindicated in people with (or with a history of) heart failure or bladder cancer. 6. Do not combine dapagliflozin with pioglitazone. 7. Caution with exenatide when eGFR<50 ml/min/1.73 m^2. 8. Adjust according to response.

DRUG CLASS	FORMULARY CHOICE	ADDITIONAL INFORMATION
BIGUANIDES	METFORMIN	• Start low dose, with gradual dose escalation, best taken with/after a meal/evening meal. • GI side effects often improve after a few days of continued therapy, or with a small dose reduction. • Modified release: reserved for those who suffer with persistent GI side effects only after gradual titration with standard release metformin (prescribe as brand name **Sukkarto SR**).
SULPHONYLUREAS	GLICLAZIDE *(1st line)* *(consider glimepiride if compliance issues)*	• Holders of group 2 licenses (bus and lorry drivers) taking sulphonylureas must be able to provide evidence of checking blood glucose at least twice per day and at times relevant to driving. • Holders of group 1 licenses (car drivers and motorcyclists) taking sulphonylureas need not notify the DVLA provided they have experienced no more than one episode of severe hypoglycaemia in the last 12 months and, if needed, check blood glucose at times relevant to driving and are under regular review.
DPP-4 INHIBITORS	ALOGLIPTIN	• Recommended dose of alogliptin is 25mg once daily. -Dose reduction in moderate renal impairment (eGFR 30-50ml/min): 12.5 mg once daily. -Dose reduction in severe renal impairment (eGFR < 30 ml/min): 6.25 mg once daily. • *Consider linagliptin in patients with end stage/deteriorating renal function only.*
SGLT2 INHIBITORS	EMPAGLIFLOZIN or DAPAGLIFLOZIN	• In individuals with type 2 diabetes and established cardiovascular disease, SGLT2 inhibitors with proven cardiovascular benefit (currently empagliflozin and canagliflozin) should be considered *AFTER* and in addition to metformin. • Risk of diabetic ketoacidosis (DKA) and lower limb amputation. DKA may present atypically, with relatively normal glucose levels. MHRA guidance advises testing for raised ketone levels in people with symptoms of DKA, even if plasma glucose levels are near normal. • Small risk of developing a genital yeast or fungal infection (most commonly thrush in women) due to more glucose being excreted in the urine. • Continue canagliflozin if requested by secondary care (may be recommended for renoprotective effect in specific cases)
THIAZOLIDINEDIONES	PIOGLITAZONE	• For specialist use only, to be considered in insulin resistant patients, or as an alternative to injectable therapy • Contraindicated in people with (or with a history of) heart failure or bladder cancer. • The risk of fracture/osteoporosis should be considered during long-term use of pioglitazone. • Be aware of possibility of macular oedema if patients report disturbances in visual acuity
GLP-1 AGONIST	SEMAGLUTIDE (LIRAGLUTIDE-up to 1.2mg once daily, for specialist endocrine use in specific cases)	• For individuals with type 2 diabetes and established cardiovascular disease, GLP-1 receptor agonists with proven cardiovascular benefit should be considered *AFTER* and in addition to metformin. • When a GLP-1 receptor agonist is added to a sulphonylurea, a reduction in sulphonylurea dose should be considered. • People taking GLP-1 receptor agonists may hold a regular (Group 1) driving licence without restriction, but must notify the DVLA if they hold a Group 2 licence.
MEGLITINIDES	REPAGLINIDE	• Specialist recommendation. Licensed as monotherapy or in combination with metformin.
COMBINATION PRODUCTS ARE NOT ROUTINELY RECOMMENDED AND NOT SUPPORTED FOR PRESCRIBING		

Title	Prescribing algorithm for the treatment of type 2 diabetes in adults
Reference	SIGN 154: Pharmacological management of glycaemic control in people with type 2 diabetes, November 2017, https://www.sign.ac.uk/assets/sign154.pdf
Version	1
Author	Medicines Management Team
Approved by	Basildon & Brentwood CCG: Prescribing Subgroup, Patient Quality and Safety Committee, Board Thurrock CCG: Medicines Management and Safety Group, Patient Quality and Safety Committee, Transformation & Sustainability Committee, Board South Essex Medicines Management Committee
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