Appendix 6a

FURTHER GUIDANCE ON HYPOGLYCAEMIC AGENTS

This appendix provides detailed guidance on the formulary choices for oral and non-insulin injectable hypoglycaemic agents. The drug classes are colour coded, with the place in therapy of each drug within that group highlighted. Please refer to the FV diabetes management programme guidelines for the place in therapy for each class.

DRUG	CLASS	PLACE IN THERAPY	DOSE	DOSE CHANGES	CAUTIONS/CONTRAINDICATIONS
METFORMIN	BIGUANIDE	1ST LINE AGENT CAN BE COMBINED WITH ALL ORAL AND INJECTABLE HYPOGLYCAEMIC AGENTS	INITIALLY 500MG DAILY INCREASING TO 2 GRAMS DAILY	STOP IF eGFR <30	• TAKE WITH FOOD • CHANGE TO MR IF GI INTOLERANT • AVOID IN KETOACIDOSIS • CHECK VITAMIN B12 ANNUALLY IF METFORMIN USE ≥ 10 YEARS • INFORM PATIENT OF MEDICINE SICK DAY RULES (GIVE CARD)
GLICLAZIDE	SULPHONYLUREA (SU)	1ST LINE SU USE IF BMI<25 OR SYMPTOMATIC OR METFORMIN INTOLERANT	INITIALLY 40-80MG DAILY INCEASING TO A MAXIMUM OF 320MG DAILY (NOTE: 80MG STANDARD TABLET= 30MG M/R TABLET)	DOSE SHOULD BE REVIEWED IF ANOTHER ORAL HYPOGLYCAEMIC AGENT ADDED AVOID IN SEVERE RENAL OR HEPATIC IMPAIRMENT	• HYPOGLYCAEMIA • WEIGHT GAIN • AVOID IN PREGNACY AND BREASTFEEDING • REVIEW DOSE IN ELDERLY PATIENTS (>75 YEARS)
GLIMEPIRIDE	SULPHONYLUREA	2ND LINE SU ALTERNATIVE TO GLICLAZIDE IF COMPLIANCE PROBLEMS (LESS EXPENSIVE OPTION THAN GLICLAZIDE M/R)	INITIALLY 1MG DAILY INCEASING TO A MAXIMUM OF 6MG DAILY WITH BREAKFAST		
PIOGLITAZONE	THIAZOLIDINEDIONE (TZD)	DUAL OR TRIPLE THERAPY WITH METFORMIN/SU	15-45MG DAILY	AVOID IN HEPATIC IMPAIRMENT DIP URINE BEFORE INITIATING TREATMENT AND IF MICROSCOPIC HAEMATURIA PRESENT DO NOT PRESCRIBE CAN BE USED WITH INSULIN UNDER SPECIALIST SUPERVISION	• AVOID IN HEART FAILURE • AVOID IN ACTIVE OR HISTORY OF BLADDER CANCER • AVOID IN UNINVESTIGATED MACROSCOPIC HAEMATURIA • AVOID IN ELDERLY • AVOID IF HIGH FRACTURE RISK • MONITOR LFTs BEFORE AND DURING TREATMENT • AVOID IN PREGNANCY AND BREASTFEEDING • REFER TO OPHTHALMOLOGY IF DISTURBANCES IN VISUAL ACUITY

ALOGLIPTIN	DIPEPTIDYLPEPTIDASE – 4 (DPP4) INHIBITORS/ GLIPTINS	1ST LINE DPP4 INHIBITOR DUAL THERAPY WITH METFORMIN OR SU OR PIOGLITAZONE OR INSULIN. TRIPLE THERAPY WITH METFORMIN + SU OR PIOGLITAZONE OR INSULIN (SEE CONSENSUS STATEMENT BELOW TABLE**)	25MG ONCE DAILY	eGFR 30-50: 12.5MG eGFR <30: 6.25MG DOSES OF SU AND/OR INSULIN MAY REQUIRE TO BE REDUCED IF USED CONCOMITANTLY STOP IF STARTING GLP-1 RECEPTOR AGONIST AVOID IN SEVERE HEPATIC IMPAIRMENT	• CAUTION IN MODERATE / SEVERE HEART FAILURE • AVOID IF HISTORY OF ACUTE PANCREATITIS • AVOID IN PREGNANCY AND BREASTFEEDING • AVOID IN KETOACIDOSIS
LINAGLIPTIN	DIPEPTIDYLPEPTIDASE – 4 (DPP4) INHIBITORS/GLIPTINS	2ND LINE DPP4 INHIBITOR 1ST LINE DPP4 INHIBITOR FOR PATIENTS WITH RENAL IMPAIRMENT DUAL THERAPY WITH EITHER METFORMIN OR INSULIN TRIPLE THERAPY WITH METFORMIN + SU OR PIOGLITAZONE OR EMPAGLIFLOZIN OR INSULIN	5MG ONCE DAILY	DOSES OF SU AND/OR INSULIN MAY REQUIRE TO BE REDUCED IF USED CONCOMITANTLY STOP IF STARTING GLP-1 RECEPTOR AGONIST CAUTION IN SEVERE HEPATIC IMPAIRMENT	• AVOID IF HISTORY OF ACUTE PANCREATITIS • AVOID IN PREGNANCY AND BREASTFEEDING • AVOID IN KETOACIDOSIS • STOP IF BULLOUS PEMPHIGOID SUSPECTED

EMPAGLIFLOZIN	SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT- 2) INHIBITORS	1ST LINE SGLT-2 INHIBITOR DUAL THERAPY TRIPLE THERAPY INSULIN ADD ON DO NOT START IN PATIENT WITH HbA1C > 80 MMOL/MOL AND/OR BMI < 30	10MG -25MG ONCE DAILY	NO INTIATION IF eGFR <60 CAN CONTINUE IF eGFR < 60 WHEN ON TREATMENT BUT ADJUST DOSE TO OR MAINTAIN AT 10MG IF eGFR <45 STOP DOSES OF SU OR INSULIN MAY REQUIRE TO BE REDUCED IF USED CONCOMITANTLY AVOID IN SEVERE HEPATIC IMPAIRMENT	• AVOID IN PREGNANCY AND BREASTFEEDING • AVOID IN PATIENTS >85 YEARS • CAUTION WITH LOOP DIURETICS • CORRECT HYPOVOLAEMIA BEFORE INITIATION • AVOID IF KETOACIDOSIS • CAUTION IF RECURRENT UTI / GENITAL INFECTION • STOP IF FOURNIER'S GANGRENE SUSPECTED • REINFORCE THE IMPORTANCE OF GOOD FOOTCARE • STOP IF DEVELOP ANY FOOT COMPLICATIONS AND CONSIDER ALTERNATIVE CLASS • INFORM PATIENT OF MEDICINE SICK DAY RULES (GIVE CARD)
DAPAGLIFLOZIN	SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT- 2) INHIBITORS	2ND LINE SGLT2 INHIBITOR IN PATIENTS INTOLERANT OF EMPAGLIFLOZIN MONO THERAPY DUAL THERAPY TRIPLE THERAPY INSULIN ADD ON DO NOT START IN PATIENT WITH HbA1C > 80 MMOL/MOL AND/OR BMI < 30 NOT APPROVED LOCALLY FOR USE AS AN ADJUNCT TO INSULIN IN TYPE 1 DIABETES PATIENTS	10MG DAILY	NO INTIATION IF eGFR <60 CAN CONTINUE IF eGFR < 60 WHEN ON TREATMENT IF eGFR <45 STOP. DOSES OF SU OR INSULIN MAY REQUIRE TO BE REDUCED IF USED CONCOMITANTLY 5MG IN SEVERE HEPATIC IMPAIRMENT	• AVOID IN PREGNANCY (2 /3 TRIMESTER) AND BREASTFEEDING • CAUTION WITH LOOP DIURETICS • AVOID IF ON PIOGLITAZONE • CORRECT HYPOVOLAEMIA BEFORE INITIATION • AVOID IN KETOACIDOSIS • CAUTION IF RECURRENT UTI / GENITAL INFECTION • STOP IF FOURNIER'S GANGRENE SUSPECTED • REINFORCE THE IMPORTANCE OF GOOD FOOTCARE • STOP IF DEVELOP ANY FOOT COMPLICATIONS AND CONSIDER ALTERNATIVE CLASS • INFORM PATIENT OF MEDICINE SICK DAY RULES (GIVE CARD)

LIRAGLUTIDE	GLUCAGON-LIKE PEPTIDE-1 (GLP-1) RECEPTOR AGONISTS	1ST LINE GLP-1 RECEPTOR AGONIST IF PATIENT <55 YEARS WITH HbA1C >59, BMI >30 **AND** PREVIOUS CV EVENT	0.6 MG ONCE DAILY TITRATED TO A MAXIMUM 1.8MG DAILY	DOSES OF SU OR INSULIN MAY REQUIRE TO BE REDUCED IF USED CONCOMITANTLY AVOID IN END STAGE RENAL DISEASE OR IF SEVERE HEPATIC IMPAIRMENT	• AVOID IN PREGNANCY AND BREASTFEEDING • AVOID IN SEVERE GI DISEASE/ GASTROPARESIS • AVOID IN PANCREATITIS / CHOLECYSTITIS • AVOID IN SEVERE HEART FAILURE (NYHA CLASS IV) • HbA1C MUST REDUCE BY 11MMOL/MOL AT 6 MONTHS TO CONTINUE • STOP GLIPTIN ON INITIATION OF GLP-1 RECEPTOR AGONIST
		2ND LINE CHOICE IF PATIENT INTOLERANT OF SEMAGLUTIDE	MAXIMUM DOSE 1.2MG DAILY		
SEMAGLUTIDE	GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS (GLP1-RA)	1ST LINE GLP1-RA IF PATIENT >55 YEARS WITH HbA1C > 59 AND BMI > 30 IRRESPECTIVE OF CV HISTORY.	0.25MG ONCE WEEKLY TITRATED TO A MAXIMUM OF 1MG ONCE WEEKLY	DOSES OF SU OR INSULIN MAY REQUIRE TO BE REDUCED IF USED CONCOMITANTLY AVOID IN SEVERE RENAL IMPAIRMENT (eGFR <30) AVOID IN SEVERE HEPATIC IMPAIRMENT	• AVOID IN PREGNANCY AND BREASTFEEDING • AVOID IN SEVERE GI DISEASE/ GASTROPARESIS • AVOID IN PANCREATITIS / CHOLECYSTITIS • AVOID IN SEVERE HEART FAILURE (NYHA CLASS IV) • CAUTION IN PATIENTS WITH DIABETIC RETINOPATHY AND ON INSULIN • HbA1C MUST REDUCE BY 11MMOL/MOL AT 6 MONTHS TO CONTINUE • STOP GLIPTIN ON INITIATION OF GLP-1 RECEPTOR AGONIST
		1ST LINE GLP1-RA IN PATIENTS ≤55 YEARS WITH HbA1C > 59 AND BMI > 30 **WITHOUT** PREVIOUS CV EVENT			
XULTOPHY	BASAL INSULIN (DEGLUDEC 100UNITS) + GLP-1 RECEPTOR AGONIST (LIRAGLUTIDE 3.6MG/ 1ML)	ADD ON TO EXISTING ORAL HYPOGLYCAEMIC AGENTS	INITIALLY BETWEEN 10-16 DOSE STEPS ONCE DAILY MAXIMUM 50 DOSE STEPS DAILY (NOTE: ONE DOSE STEP CONTAINS 1 UNIT OF INSULIN AND 0.036MG OF LIRAGLUTIDE)	DOSE OF SU MAY REQUIRE TO BE REDUCED IF USED CONCOMITANTLY AVOID IN END STAGE RENAL DISEASE AVOID IN SEVERE HEPATIC IMPAIRMENT	• AVOID PREGNANCY AND BREASTFEEDING • AVOID IN SEVERE GI DISEASE/ GASTROPARESIS • AVOID IN PANCREATITIS / CHOLECYSTITIS • STOP GLIPTIN ON INITIATION OF GLP-1 AGONIST

** CONSENSUS STATEMENT RE USE OF ALOGLIPTIN IN TRIPLE THERAPY FOR ADULT PATIENTS WITH TYPE 2 DIABETES MELLITUS

Alogliptin is currently the most cost effective DPP4 inhibitor on the Forth Valley formulary for patients with T2DM.
It is currently licensed for dual and triple therapy in adults aged over 18 years (although it has not been formally studied in combination with metformin and sulphonylureas or SGLT2 inhibitors).
SMC have approved its use in dual therapy, as a submission was not made for triple therapy use.
As the agents within the DPP4 inhibitor class are believed to be similarly efficacious, Forth Valley Diabetes MCN support the use of Alogliptin as the DPP4 inhibitor of choice in dual and triple therapy in adult patients with Type 2 Diabetes Mellitus.