Drug Rx Type 2 Diabetes

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Metformin

eGFR	Metformin
60-120	1g bid
30-60	1g od
15-30	500mg od
< 15	✕

DPP-4 inhibitors

Vildagliptan (Galvus) 50-100mg PO od

Prevents breakdown of endogenous GLP-1 and GIP → modest glucose-dependent **insulin increase** and glucagon suppression

Needs β - cell function
Check c-peptide

Modest efficacy; possible pancreatitis; severe joint pain; avoid saxagliptin in heart failure and use caution with alogliptin; do not combine with a GLP-1 receptor agonist or tirzepatide

Good for >75yo and eGFR < 30
Monitor LFTs

SGLT2 inhibitors

Useful in
CVD / CHF
Renal disease
ACR ++
BMI +

Empagliflozin (Jardiance) 10-25mg PO od

Blocks proximal **renal** sodium–glucose cotransporter-2 → urinary glucose and sodium loss

Low hypoglycaemia risk, modest weight/BP reduction; **major heart-failure** and **kidney protection**; selected agents reduce cardiovascular events

Genital fungal infection, **volume depletion**; rare euglycaemic **ketoacidosis**; withhold during fasting, major surgery or severe illness; glucose-lowering efficacy declines at low eGFR, although cardiorenal benefit may remain

Don't use in pregnancy, < 18, eGFR < 30 , recurrent UTI, renal calculi

Sulphonylureas

Needs β - cell function
Check c-peptide

Gliclizide 40-160mg od

Closes pancreatic β-cell ATP-sensitive potassium channels → **insulin release** independent of glucose

Hypoglycaemia and **weight gain**; caution in older adults, irregular food intake and kidney/liver impairment; avoid long-acting glyburide/glibenclamide where hypoglycaemia risk is high

GLP-1 agonists

Needs β - cell function
Check c-peptide

Dulaglutide (Trulicity) 0.75–1.5 mg weekly, up to 4.5 mg

Glucose-dependent insulin secretion, reduced glucagon, delayed gastric emptying and increased satiety

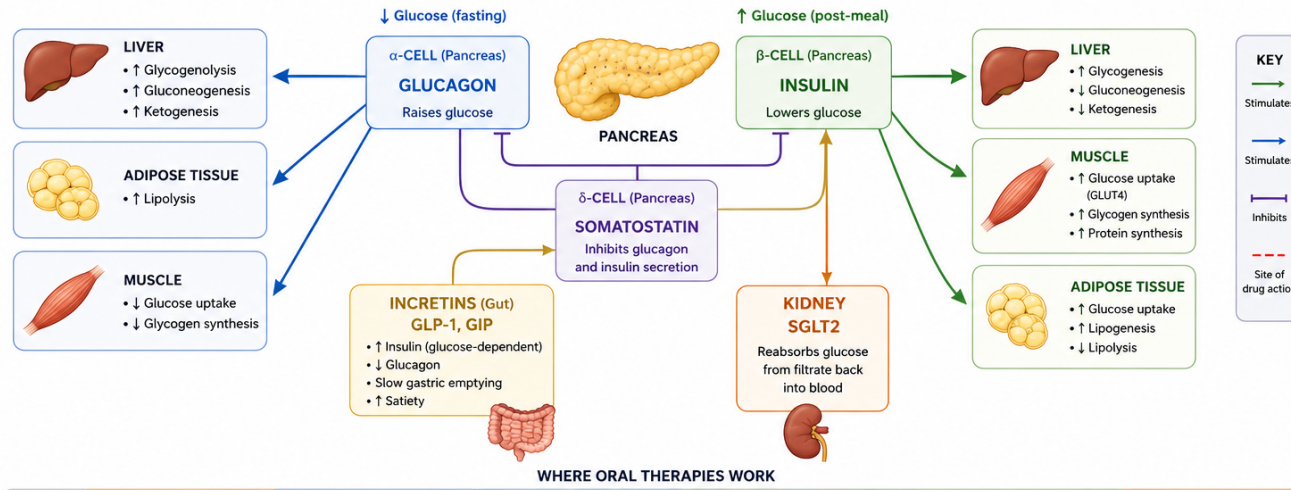
High glucose efficacy; substantial weight loss; selected agents reduce cardiovascular events and may provide kidney benefit

Nausea, vomiting, gallbladder disease; avoid in pregnancy; generally avoid with severe gastroparesis; contraindicated for agents carrying the warning in patients with personal/family history of medullary thyroid carcinoma or MEN2

β - cell failure / low c-peptide

Insulins

HORMONES INVOLVED IN GLUCOSE REGULATION AND SITES OF ACTION OF ORAL DIABETES THERAPIES



WHERE ORAL THERAPIES WORK

	METFORMIN (Biguanide)	SULFONYLUREAS (e.g. gliclazide, glipizide)	MEGLITINIDES (e.g. repaglinide)	DPP-4 INHIBITORS (e.g. sitagliptin, linagliptin)	α-GLUCOSIDASE INHIBITORS (e.g. acarbose)	SGLT2 INHIBITORS (e.g. dapagliflozin, empagliflozin)
Site/Target	LIVER (↓ hepatic glucose production)	PANCREAS (β-cell) (Increases insulin secretion)	PANCREAS (β-cell) (Increases insulin secretion)	INCRETIN PATHWAY (Inhibits DPP-4 enzyme)	INTESTINE (Brush border enzymes)	KIDNEY (Proximal tubule) SGLT2 transporter
Mechanism	↓ Gluconeogenesis ↑ Insulin sensitivity	Closes K_{ATP} channels → ↑ Insulin release (Glucose-independent)	Closes K_{ATP} channels → ↑ Insulin release (Short-acting)	↑ Endogenous GLP-1 & GIP → ↑ Insulin (glucose-dependent) → ↓ Glucagon	Delays carbohydrate breakdown & absorption → ↓ Post-prandial glucose	↓ Glucose reabsorption → ↑ Urinary glucose excretion
Key Points	First-line therapy Weight neutral / loss	Risk of hypoglycaemia Weight gain	Take with meals Lower hypoglycaemia risk than sulfonylureas	Weight neutral Low hypoglycaemia risk	GI side effects Weight neutral	Weight loss ↓ BP, CV & renal benefit Genital mycotic infections

Note: All therapies require adequate lifestyle measures. Choice of therapy is individualised based on patient factors, comorbidities, risk of hypoglycaemia, weight goals and cost. This diagram reflects major hormonal pathways and sites of action of oral agents in type 2 diabetes.