Appendix 1 Pharmacological agents for glycaemia control

Pharmacological agent	Mode of action	Remark
Insulin Rapid-acting analogues Short-acting (Human Regular) Intermediate-acting (Human NPH) Basal insulin analogues	Activates insulin receptors to reduce hepatic glucose production and increase glucose breakdown	Conventional treatment for type 1 or 2. Has the highest efficacy for controlling glycaemia but could cause hypoglycemia and weight gain
Biguanides Metformin	Activates AMP activated protein kinase and protein kinase A (PKA) to suppress glucose production in liver	Highly effective in maintaining blood glucose level, low risk of causing hypoglycemia and the first line of pharmacological treatment for both type 1 and type 2 diabetes; could cause lactic acidosis
Sulfonylurea Example of commonly used: Glipizide, Gliclazide, Glibenclamide and Glimepiride	Closes K-ATP channels on plasma membranes of β-cell to increase insulin secretion	Highly effective combination with metformin, considered if response to metformin is poor. Used to achieve controlled blood glucose but continuous use could result in weight gain and inexpensive regarding cost
Thiazolidinediones Pioglitazone	Activates nuclear transcription factor PPAR-γ to enhance insulin sensitivity	Highly effective combination with metformin, considered if response to metformin is poor. Used to achieve controlled blood glucose but associated with cardiovascular risk
Dipeptidyl peptidase 4 (DPP-4) inhibitor Sitagliptin, vildagliptin, Saxagliptin and linagliptin	Increase insulin secretion and reduce glucagon secretion	Intermediate effectiveness with neutral effect on weight gain. Has low risk of causing hypoglycemia but relatively expensive
Injectable Glucagon-like peptide-1 agonists Exenatide and Liraglutide	Bind to a membrane GLP receptor causing insulin release from the pancreatic beta cells	They have a lower risk of causing hypoglycemia, but main concern over the safety profile due to proliferative effects in the pancreas. Advantage of weight loss probably due to its side effects of nausea due to gastric motility reduction and relatively expensive
Sodium–Glucose Co-transporter 2 Inhibitor (SGLT2) Canagliflozin and Dapagliflozin	Blocks glucose reabsorption by the kidney, increasing excretion via urine	Intermediate effectiveness with possibility of causing weight loss. Has low risk of causing hypoglycemia but relatively expensive. Common side effect is urinary tract infection.
Meglitinides Rrepaglinide and Nateglinide	Rapid-acting insulin secreting agents by blocking potassium ATP channels on plasma membranes of β-cell	Can cause bone fractures and oedema in addition to remarks on sulfonylurea

α-glucosidase inhibitors Acarbose and Migitol	Slows digestion of carbohydrate in the intestine	Intermediate efficacy on glycaemia
Injectable Amylin analogues Pramlintide	Activates amylin receptors to increase glucose breakdown and reduce hepatic glucose production.	Intermediate effectiveness on glycaemia, could cause weight loss due to slowing gastric emptying rate
Colesevelam	Reduce glucose production in the liver by binding bile acids in the liver	Modest effectiveness on glycaemia but can cause constipation and increase TG concentrations
Bromocriptine	Activates dopaminergic receptors causing hypothalamic stimulated metabolism and increases insulin sensitivity	Intermediate effectiveness, reduces risk of CVD, but causes dizziness and nausea

Adapted from ADA standards 2016 (6)