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General Treatment Strategies
Diabetes Mellitus

Type of Diabetes	Basic Treatment Strategy
Type 1 DM	Medical nutrition therapy (MNT) + physical exercise + continuous glucose monitoring (CGM; is preferred): ▪ Insulin ▪ The preferred method of delivery is via automated insulin delivery (AID) + continuous subcutaneous insulin infusion (CSII) device ▪ +/- pramlintide
Type 2 DM	Medical nutrition therapy (MNT) + physical exercise (for all patients) + consider antidiabetic treatment options that also factor in the presence of other comorbidities (e.g., CVD, heart failure, CKD, obesity): ▪ Monotherapy or a combination of non-insulin-based therapy ▪ Addition of insulin (usually a basal or long-acting insulin) to existing non-insulin-based therapy ▪ Insulin-based therapy (combination short and long/basal acting agents) ▪ Treatment of other metabolic complications (e.g., hypothyroidism)

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Antidiabetic Medications
Categorized as Secretagogues

Drug Category	Main Effect	Drugs
Secretagogues = Increase insulin secretion		
Meglitinides	Stimulate insulin release from the pancreatic beta-cells (Note: Shorter half-life of ~1 hr compared to sulfonylureas)	Nateglinide Repaglinide
Sulfonylureas	Stimulate insulin release from the pancreatic beta-cells; +/- reduces hepatic glucose output (Note: 2nd Generation have longer half-lives of ~10 hours)	
1st Generation **(Historical Reference Only)**	Longer half-life / duration of action	Chlorpropamide (DSC) Tolazamide (DSC) Tolbutamide (DSC)
2nd Generation	Shorter duration of action compared to 1st generation agents	Glimepiride Glipizide Glyburide

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Antidiabetic Medications

Categorized as Non-Secretagogues

Drug Category	Primary Effects	Drugs
Non-Secretagogues or Augment Pancreatic Insulin		
Alpha-Glucosidase Inhibitor	Delays the breakdown of complex carbs & absorption of glucose → post-prandial effects on glucose.	Acarbose Miglitol
Amylinomimetic	Reduces postprandial glucose increases.	Pramlintide
Biguanides	Reduces hepatic glucose production (reduce fasting glucose levels)	Metformin
DPP-4 Inhibitors	Prevents the metabolism of incretins that regulate insulin synthesis, glucagon release, & hepatic glucose output.	Alogliptin, linagliptin, saxagliptin, sitagliptin
GIP/GLP-1 Agonist	The additional GIP activity + GLP-1 agonist effect provides synergy to augment glucose-dependent actions, more effective weight loss, and sustained reductions in A1C	Tirzepatide
GLP-1 Agonists	Augments glucose-dependent insulin secretion and weight loss that favors sustained reductions in A1C.	Dulaglutide, exenatide, liraglutide, lixisenatide (with insulin glargine), semaglutide
SGLT2 Inhibitors	Prevents reabsorption of glucose by the kidney, thereby increasing renal elimination of glucose from the body.	Bexagliflozin, canagliflozin, dapagliflozin, empagliflozin, ertugliflozin
TZD	Regulates genes involved in glucose homeostasis and lipid metabolism and improves the cell's response to insulin.	Pioglitazone, rosiglitazone (DSC)

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Antidiabetic Medications

Considerations with Other Comorbidities

MEDICAL CONDITION	CONSIDER	CAUTION (or) AVOID
Overweight or Obese	• Metformin • GIP/GLP-1 Receptor Agonist • GLP-1 Receptor Agonists • DPP-4 Inhibitors • SGLT2 Inhibitors	• Sulfonylurea (SU) • Meglitinides • Insulin
Dyslipidemia	• Metformin	• +/- TZD
Renal Impairment or CKD	• GLP-1 Receptor Agonists • SGLT2 Inhibitors (+/-)	• Metformin (especially in AKI) • DPP-4 Inhibitors (+/-) • SGLT2 inhibitors (+/-) • Alpha-Glucoside Inhibitors (AGIs)
Heart Failure	• SGLT2 Inhibitors > GLP-1 Receptor Agonists	• TZD (avoid) • +/- Metformin (if hospitalized) • DPP-4 Inhibitors (+/-; alogliptin & saxagliptin)
CAD or ASCVD	• GLP-1 Receptor Agonists • SGLT2 Inhibitors	• TZD (avoid)
Gastroparesis		• GLP-1 Receptor Agonists • Pramlintide
IBD, IBS, +/- Partial Bowel Obstruction		• Alpha-Glucoside Inhibitors (AGIs)
Risk of Euglycemic DKA		• SGLT2 Inhibitors
Pancreatitis		• DPP-4 Inhibitors • GLP-1 & GIP-1 Receptor Agonists
Osteoporosis/Fractures		• TZD and +/- SGLT2 Inhibitors
Thyroid C-Cell Tumors/MTC/MEN 2)		• GLP-1 & GIP-1 Receptor Agonists

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