A GLIMPSE AT OPTIMAL T2D MANAGEMENT: ENHANCING OUTCOMES WITH GLP-1 RAS

GLP-1 Profile Resource Library

APPROVED GLP-1 RA AGENTS	MOA	FREQUENCY / APPROVED DOSING	MODE OF ADMINISTRATION	GLYCEMIC EFFECTS / EXTRA-GLYCEMIC EFFECTS	GENERAL ADVERSE EFFECTS / SPECIFIC CONTRAINDICATIONS	INDICATION FOR USE
DULAGLUTIDE	• Activates the GLP-1 receptor in pancreatic beta cells, increases intracellular cyclic AMP (cAMP) in beta cells leading to glucose-dependent insulin release • Decreases glucagon secretion and slows gastric emptying.	Once weekly Adults: 0.75 mg, increased to 1.5 mg, if needed	SQ Injection	High A1C lowering efficacy • FDA-approved for cardiovascular disease benefit • Significant reduction in cardiovascular outcomes, including in patients with HF • Weight loss • Benefit on renal end points in cardiovascular outcomes trials (CVOTs), driven by albuminuria outcomes	Gastrointestinal (GI) side effects (Nausea, vomiting, diarrhea, abdominal pain, decreased appetite, dyspepsia), fatigue. Risk of thyroid C-cell tumors, pancreatitis, acute kidney injury (AKI)	Irrespective of baseline HbA1C or individual HbA1C targets, a GLP-1RA with a proven CVD benefit is recommended for patients in whom atherosclerotic CVD (ASCVD) predominates. If patients are not at goal with metformin, or if metformin is contraindicated, GLP1-RAs can be used throughout the type 2 diabetes (T2D) treatment pathway, including in patients with: a need to minimize hypoglycemia; minimize weight gain or promote weight loss; high risk or established ASCVD, chronic kidney disease, or heart failure (agents with proven CVD or renal benefit preferably).
EXENATIDE EXTENDED RELEASE (XR)	• Enhances glucose-dependent insulin secretion by the pancreatic beta-cell • Suppresses inappropriately elevated glucagon secretion, and slows gastric emptying	Once weekly Adults: 2 mg	SQ Injection	Intermediate A1C lowering efficacy	GI side effects including constipation Risk of thyroid C-cell tumors, acute pancreatitis, AKI, injection site reaction Contraindications: End-stage renal disease or CRCl < 30 mL/min	

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EXENATIDE	• Enhances glucose-dependent insulin secretion by the pancreatic beta-cell • Suppresses inappropriately elevated glucagon secretion, and slows gastric emptying	Twice daily Adults: 5 µg per dose; increase to 10 µg after 1 month based on clinical response	SQ Injection	Low A1C lowering efficacy	Nausea, vomiting, dyspepsia Risk of acute pancreatitis, renal impairment Contraindications: End-stage renal disease or CRCl < 30 mL/min	
SEMAGLUTIDE (SQ)	• Selectively binds to and activates the GLP-1 receptor • Multiple actions on glucose • Binds to albumin increases half-life, resulting into decreased clearance and protection from metabolic degradation • Additionally, it is stabilized against degradation by the DPP-4 enzymes • Stimulates insulin secretion and lowers glucagon secretion • Minor delay in gastric emptying in the early postprandial phase	Once weekly Adults: 0.25 mg, increasing to 0.5 mg after 4 weeks. If required, increase to 1 mg after a further 4 weeks	SQ Injection	Highest A1C lowering efficacy • Highest reduction in HbA1C • Weight loss • FDA-approved for cardiovascular disease benefit • Significant reduction in death due to cardiovascular events (SUSTAIN and PIONEER trials) • Benefit on renal end points in CVOTs, driven by albuminuria outcomes	GI side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia Risk of thyroid C-cell tumors, pancreatitis, diabetic retinopathy, AKI	
SEMAGLUTIDE (PO)		Once Daily Adults: 3 mg for 30 days, then 7 mg, escalated to 14 mg after a further 30 days, if required	By mouth	High A1C lowering efficacy	GI side effects (nausea, vomiting, diarrhea, esophageal reflux) Risk of thyroid C-cell tumors, pancreatitis, diabetic retinopathy, AKI	

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LIRAGLUTIDE	• Activates the GLP-1 receptor in pancreatic beta cells increases intracellular cAMP leading to insulin release in the presence of elevated glucose • Decreases glucagon secretion in a glucose-dependent manner • Blood glucose lowering also involves a delay in gastric emptying	Once Daily Adults: 0.6 mg for 1 week, then 1.2 mg; if required, increase dose to 1.8 mg after a further week Children >10 years: 0.6 mg for ~1 week; only increase the dose to 1.2 mg or 1.8 mg if required	SQ Injection	High A1C lowering efficacy • FDA approved to reduce the risk of major adverse cardiovascular events (MACE), including heart attack, stroke, and cardiovascular death, in adults with T2D and established CVD. • Cardiovascular benefits in high-risk patients (LEADER-6 trial) • Weight loss • Benefit on renal end points in CVOTs, driven by albuminuria outcomes	GI side effects (nausea, vomiting, diarrhea, esophageal reflux), injection site reactions, elevated heart rate, hypoglycemia, nasopharyngitis Risk of thyroid C-cell tumors, pancreatitis, renal impairment, hypersensitivity reactions, acute gallbladder disease (cholelithiasis or cholecystitis)	
LIXISENATIDE	• Increases glucose-dependent insulin release, decreases glucagon secretion, and slows gastric emptying	Once Daily Adults: 10 µg for 14 days, then 20 µg from day 15	SQ Injection	Low A1C lowering efficacy	GI side effects, dizziness Hypersensitivity reactions, pancreatitis, AKI	

References

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