

Table 21.1 Medications Used to Treat Diabetes

Medication	Indications	Dosing	Side effects affecting rehab	Other side effects or considerations
Biguanides: Increases sensitivity of insulin by decreasing hepatic gluconeogenesis (primary effect) and increasing peripheral insulin sensitivity (secondary effect).				
Metformin (Glucophage) immediate- and extended-release formulations and in combination products with other antidiabetic drugs	Decreases A1C by 1%-2% and decreases FPG (fasting plasma glucose) by 60-80 mg/dl.	Immediate release: 500 or 850 mg/day by mouth with dinner; increase dose every 2 wk until euglycemia is maintained. Normal effective daily dose is 500-2500 mg/day given in two divided doses. Take with food.	Cog: 0 S: 0 A: 0 Motor: 0 D: ++ Com: 0 F: 0	Used as monotherapy or with sulfonylurea, thiazolidinedione, or insulin. Decreases levels of vitamin B ₁₂ ; provide B-12 supplementation. Avoid in patients with creatinine >1.5 due to increased risk of lactic acidosis. Advantages: When used as monotherapy Glucophage rarely causes hypoglycemia; it does not increase insulin levels. Glucophage improves cardiovascular health by lowering lipid levels and by not causing weight gain; most effective in patients who are overweight or who have dyslipidemia or high fasting plasma glucose. Disadvantages: Side effects of nausea, vomiting, diarrhea, and metallic taste; take with food to minimize adverse gastrointestinal side effects.
Second-generation sulfonylureas: Secretagogues; increase production of insulin by the beta cells in the pancreas in patients with residual beta-cell function.				
Glipizide (Glucotrol, Glucotrol XL)	Achieves A1C decreases of 1%-2%.	5 mg/day by mouth. Maximum dose of 40 mg/day. Doses >20 mg are given in divided doses twice/day. Maximum dose of Glucotrol XL (long acting) is 20 mg once/day by mouth.	Cog: + S: 0 A: 0 Motor: + D: 0 Com: 0 F: +	Advantages: Inexpensive. More effective in newly diagnosed patients (diagnosed within the previous 5 yrs), who are close to ideal body weight, and who have fasting plasma glucose levels of <200 mg/dl. Disadvantages: Weight gain, allergy, photosensitivity, beta-cell burnout with decreased efficacy, hypoglycemia.
Glyburide (Diabeta, Glycron, Glynase, Micronase)	Achieves A1C decreased of 1%-2%.	Start at 5 mg/day by mouth in untreated, symptomatic patients; maximum dose of 20 mg/day. Glynase (micronized formulation): Start at 3 mg/day by mouth; maximum dose of 12 mg/day.	Cog: + S: 0 A: 0 Motor: + D: 0 Com: 0 F: +	May increase cardiovascular risk by increased weight gain and increased lipid levels. Start at 2.5 mg/day by mouth for elderly patients and patients with hepatic or renal disease.
Third-generation sulfonylureas: Secretagogues; increase production of insulin by the beta cells in the pancreas in patients with residual beta-cell function.				
Glimepiride (Amaryl)	Achieves A1C decreases of 1%-2%.	Usual starting dose is 1-2 mg by mouth/day with breakfast; usual maintenance dose is 1-4 mg by mouth/day. Maximum dose of 8	Cog: + S: 0 A: 0 Motor: + D: 0 Com: 0	Advantages: Inexpensive. More effective in newly diagnosed patients who are close to their ideal body weight and with fasting plasma glucose levels of <200 mg/dl. Disadvantages: Weight gain, allergy,

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		mg by mouth/day.	F: +	photosensitivity, beta-cell burnout with decreased efficacy, hypoglycemia. May increase cardiovascular risk by increased weight gain, increased lipid levels.
Meglitinides: Short-acting insulin secretagogues; act on the adenosine triphosphate-dependent potassium channels in pancreatic beta cells, allowing calcium channels to open and increasing insulin release.				
Repaglinide (Prandin)	Reduces PPG increases in glucose levels. Take only before meals, needs glucose to work (food dependent). Stimulates pancreatic insulin secretion within 20 min of oral administration.	0.5-4 mg by mouth before meals; may dose 2-4 times/day before meals. Maximum dose of 16 mg/day in divided doses with meals.	Cog: 0 S: 0 A: 0 Motor: 0 D: 0 Com: 0 F: 0	Low risk of hypoglycemia; minimizes hyperglycemia after meals. Short-acting insulin secretagogue; action depends on functional beta cells in pancreatic islets. Stimulates pancreatic insulin secretion within 20 min of oral administration.
Nateglinide (Starlix)	Reduces PPG increases in glucose levels. Take only before meals, needs glucose to work (food dependent). Stimulates pancreatic insulin secretion within 20 min of oral administration.	120 mg by mouth 3 times/day before meals; may decrease to 60 mg by mouth 3 times/day before meals.	Cog: 0 S: 0 A: 0 Motor: 0 D: 0 Com: 0 F: 0	Low risk of hypoglycemia; minimizes hyperglycemia after meals. Short-acting insulin secretagogue; action depends on functional beta cells in pancreatic islets. Stimulates pancreatic insulin secretion within 20 min of oral administration.
Insulins: Exogenous replacement of natural hormone insulin used to prevent and treat hyperglycemia in type 1 and type 2 diabetics.				
Glargine (Lantus)	Long acting insulin used in the treatment and prevention of hyperglycemia. Decreases A1C 1-2%.	Usually dosed once/day (twice/day in brittle diabetics). Onset is 1 h, peak is 1 h, and duration is 24 h.	Cog: + S: 0 A: + Motor: + D: + Com: + F: +	Used with short-acting insulin given with meals. Longer effects than detemir (Levemir) allows once/day dosing in more patients. Side effects: Weight gain, hypoglycemia. Loses effectiveness over time. Patients with type 2 diabetes need relatively large doses. Rotate site of injection to prevent lipodystrophy.
Detemir (Levemir)	Long acting insulin used in the treatment and prevention of hyperglycemia. Decreases A1C 1-2%.	Usually dosed once/day (twice/day in brittle diabetics). Onset is 1 h, peak is 1 h, and duration is 24 h.	Cog: + S: 0 A: + Motor: + D: + Com: + F: +	Used with short-acting insulin; administered with meals. May need to be dosed twice/day. Side effects: Weight gain, hypoglycemia. Loses effectiveness over time. Patients with type 2 diabetes need

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				relatively large doses. Rotate site of injection to prevent lipodystrophy.
NPH insulin (Humulin N, Novolin N)	Intermediate acting insulin used in the treatment and prevention of hyperglycemia. Decreases A1C 1-2%.	Usually dosed twice/day before breakfast and before dinner. Onset is 2-4 h, peak is 4-10 h, and duration is 10-16 h.	Cog: + S: 0 A: + Motor: + D: + Com: + F: +	May be used with short-acting insulin; administered with meals. Side effects: Weight gain, hypoglycemia. Loses effectiveness over time. Patients with type 2 diabetes need relatively large doses. Rotate site of injection to prevent lipodystrophy.
Regular insulin (Novolin R, Humulin R)	Short acting insulin used in the treatment and prevention of hyperglycemia. Decreases A1C 1-2%. Can be given as IV infusion.	30-60 min before meals or as continuous infusion in the critically ill patient. Onset is 2-4 hrs, peak is 2-3 hrs, and duration is 3-6 hrs.	Cog: + S: 0 A: + Motor: + D: + Com: + F: +	Multiple daily injections: Before meals 3 times/day, along with basal insulin at bedtime. Side effects: Weight gain, hypoglycemia. Loses effectiveness over time. Patients with type 2 diabetes need relatively large doses. Rotate site of injection to prevent lipodystrophy.
Glulisine (Apidra) Lispro (Humalog) Aspart (NovoLog)	Rapid acting insulin used in the treatment and prevention of hyperglycemia. Decreases A1C 1-2%.	Dosed immediately before or immediately after meals. Onset is <15 min, peak is 1-2 h, and duration is 3-4 h.	Cog: + S: 0 A: + Motor: + D: + Com: + F: +	Commonly given with meals; may be administered immediately after meal. Side effects: Weight gain, hypoglycemia. Loses effectiveness after time. Patients with type 2 diabetes need relatively large doses. Rotate site of injection to prevent lipodystrophy.
Thiazolidinediones: Act as insulin sensitizers; reduce glucose production in the liver and increase glucose utilization in skeletal muscle. Onset of action is 12-16 wk; may preserve beta function and slow progression of diabetes.				
Rosiglitazone (Avandia)	Decreases A1C by 0.6%-1.9%; decreases FPG by 50-80 mg/dl.	4-8 mg/day by mouth or divided twice/day. As of September 23, 2010, available only via a restricted-access program by the Food and Drug Administration.	Cog: 0 S: 0 A: 0 Motor: + D: + Com: 0 F: +	These agents are used as monotherapy or with sulfonylurea, metformin, meglitinide, DPP-4 inhibitors, exenatide, or insulin. Side effects: Liver failure (rare), plasma volume expansion, edematous weight gain increasing the risk of congestive heart failure exacerbations.
Pioglitazone (Actos)	Decreases A1C by 0.6%-1.9%; decreases FPG by 50-80 mg/dl.	15-30 mg by mouth/day; may titrate dose upward increase to maximum dose of 45 mg/day to maintain euglycemia. Maximal effect may not be achieved for up to 12 wks.	Cog: 0 S: 0 A: 0 Motor: + D: + Com: 0 F: +	Osteoporosis; increased rates of upper and distal lower limb fracture in both men and women. Do not use while pregnant or breastfeeding or in children. Actos may be associated with increased risk of bladder cancer. Avandia available under FDA REMS due to cardiovascular risks.
Alpha-glycosidase inhibitors: Inhibit carbohydrate digestion in the gastrointestinal tract, delaying postmeal glucose spikes.				
Acarbose (Precose)	Decreases A1C by 0.5%-1%; decreases	Start at 25 mg by mouth 3 times/day before meals with first	Cog: 0 S: 0 A: 0	Used as monotherapy or with sulfonylurea, thiazolidinedione, metformin, or insulin therapy.

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	FPG by 40-50 mg/dl.	bite of food; titrate dose upwards if needed every 4-8 wk based on 1 h PPG glucose levels and tolerance. Maximum dose of 100 mg by mouth 3 times/day.	Motor: 0 D: ++ Com: 0 F: 0	Useful in treatment of patients with significant PPG blood glucose, obese patients, or those with a high risk of hypoglycemia. Advantages: Does not cause hypoglycemia when used as monotherapy. Side effects: GI upset, take with food to minimize gastrointestinal upset. Elevated liver enzyme levels. Dose should be increased slowly. Dose is taken with the first bite of a meal of at least 300 cal. If the patient does not eat, the medicine should not be taken.
Miglitol (Glyset)	Decreases A1C by 0.5%-1%; decreases FPG by 40-50 mg/dl.	Start at 25 mg by mouth 3 times/day before meals with first bite of food; increase to 50 mg 3 times/day after 4-8 wks; may increase as needed. Maximum dose of 100 mg by mouth 3 times/day.	Cog: 0 S: 0 A: 0 Motor: 0 D: ++ Com: 0 F: 0	
Dipeptidyl peptidase-4 (DPP-4) inhibitors: Prevent degradation of GIP and GLP-1, increasing their effects and slowing insulin response to meals; improve insulin secretion and inhibit glucagon production.				
Sitagliptin (Januvia)	Decreases A1C by 0.5%-0.8%; decreases FPG by 15-30 mg/dl; decreases PPG glucose by 35-50 mg/dl.	100 mg by mouth once daily. For patients with creatinine clearance >30 to <50 ml/min: Dose is 50 mg by mouth/day. For patients with creatinine clearance <30 ml/min: Dose is 25 mg by mouth/day. Reduce dose when used in combination with insulin or secretagogues.	Cog: + S: 0 A: 0 Motor: 0 D: + Com: 0 F: +	Advantages: Generally well tolerated; possible hypoglycemia when used in combination with insulin or secretagogues, but does not cause hypoglycemia when used alone. Modest antihyperglycemic effects useful in the elderly. Reduce dosage for renal impairment or concurrent use of other medications that inhibit liver metabolism via the 3A4/5 pathway. May increase risk of acute pancreatitis.
Saxagliptin (Onglyza)	Decreases A1C by 0.5%-0.8%; decreases FPG by 15-30 mg/dl; decreases PPG glucose by 35-50 mg/dl.	2.5-5 mg by mouth/day. For patients with creatinine clearance <50 ml/min: Dose is 2.5 mg by mouth/day. For patients taking concurrent strong CYP450 3A4/5 inhibitors: Dose is 2.5 mg by mouth/day.	Cog: + S: 0 A: 0 Motor: 0 D: + Com: 0 F: +	
Glucagon like peptide (GLP)-1 agonists: Incretin analogs that enhance glucose-dependent insulin secretion, suppress glucagon, delay gastric emptying, and promote satiety and weight loss.				
Exenatide (Byetta) 5 mcg and 10 mcg fixed-dose prefilled pens	Decreases A1C by 1%-2%; decreases FPG by 25-60 mg/dl; decreases PPG glucose by	5 µg SC injection twice/day within 1 h of morning and evening meals; based on response, may increase	Cog: 0 S: 0 A: 0 Motor: 0 D: ++	Advantages: Improved glucose levels with reduced risk of hypoglycemia; modest improvements in blood pressure and lipids. Promote satiety and weight loss.

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	35-50 mg/dl.	to 10 µg SC twice/day after 1 mo. Peak action is 2-3 h; effects for up to 10 h.	Com: 0 F: +	Side effects: Transient nausea and vomiting. Initial dose of 0.6 mg/day is intended to reduce gastrointestinal symptoms during initial titration and does not result in adequate glycemic control.
Liraglutide (Victoza) 6 mg/ml prefilled cartridge pen	Decreases A1C by 1%-2%; decreases FPG by 25-60 mg/dl; decreases PPG glucose by 35-50 mg/dl.	Start at 0.6 mg SC/day for 1 wk and then increase to 1.2 mg/day; if glycemic control is not achieved, may increase dose. Maximum dose of 1.8 mg/day. Administer SC in the abdomen, thigh, or upper arm. Administer once/day at any time of day, independently of meals. Peak levels at 9-12 h post dose; half-life is 13 h.	Cog: + S: 0 A: 0 Motor: 0 D: ++ Com: 0 F: +	Drug interactions: Delayed gastric emptying and decreased acid secretion may affect absorption of other medications. During initiation, reduce dose of concomitantly administered insulin secretagogues (i.e., sulfonylureas, meglitinides) to reduce risk of hypoglycemia. May increase risk of acute pancreatitis. FDA approved REMS in place due to possible link to thyroid-C cell cancer; prescriber to determine whether benefits outweigh risk.
Amylin derivative: Synthetic analog of human amylin, a naturally occurring hormone made in pancreatic beta cells; used in patients who have not achieved desired glucose control despite optimal insulin therapy.				
Pramlintide acetate (Symlin) 60 prefilled pen injector for lower doses of 15-60 mcg and 120 prefilled pen injector for doses of 60-120 mcg	Helps reduce PPG and reduces fluctuation of glucose levels during the day; improves long-term glucose control.	Type 2 diabetics: Start at 60 µg SC before meals; titrate to maintenance dose of 120 µg. Type 1 diabetics: Start at 15 µg SC before meals; titrate in 15 µg increments to 30-60 µg.	Cog: 0 S: 0 A: 0 Motor: 0 D: + Com: 0 F: 0	Indicated to treat type 1 or type 2 diabetes in combination with insulin. Advantages: Improves long-term control (A1C) compared with insulin alone. Reduces spikes in PPG, glucagon secretion, and regulates food intake by centrally mediated appetite modulation. Reduces needed dose of insulin and promotes weight loss. May need to adjust dose of insulin to maintain euglycemia. Side effects: Nausea. Slows gastric emptying, which can affect absorption of other medications.

Cog = cognition; S = sedation; A = agitation or mania; Motor = discoordination; D = dysphagia; Com = communication; F = falls; FPG = fasting plasma glucose; PPG = postprandial glucose; A1C = glycosylated hemoglobin; GIP = glucose-dependent insulinotropic polypeptide; GLP-1 = glucagon like peptide-1; SC = subcutaneous; DPP-4 = dipeptidyl peptidase-4; FDA = U.S. Food and Drug Administration; REMS = risk and evaluation mitigation strategy.

The likelihood rating scale for encountering the side effects is as follows: 0 = Almost no probability of encountering side effects. + = Little likelihood of encountering side effects. +/+ = Low probability of encountering side effects; however, probability increases with increased dosage. ++ = Medium likelihood of encountering side effects. +++ = High likelihood of encountering side effects, particularly with high doses. ++++ = Highest likelihood of encountering side effects; best to avoid in at-risk patients.