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Drugs for Type 2 Diabetes

Updated December 2024

--Information in chart may differ from product labeling. For place in therapy, see our resource, *Stepwise Treatment of Type 2 Diabetes*.--

Dosing/Cost [a]	A1C Reduction [b]	Weight Gain/Neutral/ Loss	Hypoglycemia Risk	Comments
Alpha-glucosidase inhibitors: acarbose and miglitol (US)				
Initial 25 mg once daily to TID **Max** 300 mg (acarbose: 150 mg if <60 kg), divided TID.[2] US: acarbose ~$50, miglitol ~$280; Canada ~$30 (acarbose)	0.7% to 0.8% (acarbose),[1] ~0.3% to 0.8% (miglitol monotherapy)[3]	Neutral[1]	No[4]	• MOA: slows intestinal carbohydrate digestion/absorption to reduce postprandial glucose; taken with meals.[2] • GI side effects (e.g., abdominal pain, flatulence, diarrhea).[1,2]
Dipeptidyl peptidase-4 (DPP-4) inhibitors: **Alogliptin** (*Nesina*; with metformin [*Kazano*]; with pioglitazone [*Oseni* (US)]; authorized generics [US]). **Linagliptin** (*Tradjenta* [US]; *Trajenta* [Canada]; with metformin [*Jentadueto*, *Jentadueto XR* (US)]; with empagliflozin [*Glyxambi* (US)]; with metformin and empagliflozin [*Trijardy* XR (US)]). **Saxagliptin** (*Onglyza* [Canada], generics; with metformin [*Konboglyze* (Canada), generics (US)]; with dapagliflozin [*Qtern* (US)]). **Sitagliptin** (*Januvia*, *Zituvio* [US]; with metformin [*Janumet*, *Janumet XR*, *Zituvimet* (US), *Zituvimet XR* (US), generics (Canada)]; with ertugliflozin [*Steglujan* (US)]).				
Alogliptin 25 mg once daily.[2] US: ~$200; Canada: ~$40 (*Kazano* 25/1700 mg) **Linagliptin** 5 mg once daily.[2] US: ~$530; Canada: ~$80 **Saxagliptin** 2.5 to 5 mg once daily.[2] US: ~$250; Canada: ~$50 **Sitagliptin** 100 mg once daily.[2] US: $80; Canada: ~$90	0.5% to 0.7%[1]	Neutral[8]	No[4]	• MOA: increases insulin secretion in response to elevated blood glucose, decreases glucagon secretion, and slows gastric emptying.[1] Reduces postprandial glucose.[9] • Risk of new or worsening heart failure (saxagliptin and alogliptin).[8] Rare cases of severe joint pain, pancreatitis, and bullous pemphigoid.[1,4] • Have not been effective in youth.[5,6] • CYP3A4 interactions (linagliptin, saxagliptin).[2] • Dosage modification with kidney impairment needed (see footnote c).[2]
GLP-1 agonists: see our chart, *Comparison of GLP-1 and GIP/GLP-1 Receptor Agonists*.				
Insulin: See our chart, *Comparison of Insulins* (*US*)(*Canada*) for available products and cost.				
Initial: consider basal insulin 0.1 to 0.2 units/kg for adults or 0.25 to 0.5 mg/kg basal insulin for youth.[4,6] No maximum dose.[1]	0.9% to 1.2% or more[1]	+ 1 to 3.5 kg or more[1]	Yes[4]	• MOA: promotes uptake of glucose into muscle and fat tissues; inhibits glucose production.[2]
Meglitinide: nateglinide (US) and repaglinide				
Nateglinide 180 to 360 mg, divided TID with meals.[2] US: ~$180 **Repaglinide**: **Initial** 1 to 2 mg with meals (0.5 mg if A1C <8%).[2] **Max** 16 mg, divided four times daily.[2] US: ~$50; Canada: ~$60	0.7% to 1.1%[1]	+ 1.4 to 3.3 kg[1]	Yes (but less than with sulfonylureas)[7,8]	• MOA: stimulates pancreatic insulin secretion.[2] • Taken within 30 min before a meal; skip dose if skipping meal.[2] • Reduces postprandial glucose more than sulfonylureas.[7] • Safer than sulfonylureas in kidney impairment.[1]

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Metformin (*Fortamet* [US], *Glucophage* [Canada], *Glumetza*, generics). Available as an oral solution (US). Available in combination with DPP-4 inhibitors, SGLT2 inhibitors, and sulfonylureas (see below).				
Immediate release: **Initial** 850 mg once daily (adults only) or 500 mg BID. **Max** 2,000 to 2,550 mg,* divided BID to TID.[2] US: ~$15; Canada: <$5). *max dose 2,000 mg for 10 to 17 years of age.[2] **Extended release**: **Initial** 500 mg once daily. **Max** 2,000 mg, once daily or divided BID.[2] US ~$60; Canada ~$90	1% (as monotherapy)[1]	Weight neutral to modest weight loss.[4] Ameliorates insulin weight gain.[7]	No[4]	• MOA: inhibits glucose production and absorption; increases insulin sensitivity in muscle and fat.[2] • Mitigate GI effects (e.g., diarrhea, nausea) with slow titration of an extended-release product, with food.[2,4] • Potential for lactic acidosis. Can be started in patients with an eGFR >45 mL/min/1.73m^2 (Canada: ≥30 mL/min/1.73m^2)[1,4] Hold for eGFR <30 mL/min/1.73m^2, or illness or procedure posing risk of intravascular volume depletion or kidney injury.[4] • Test vitamin B12 level periodically.[4] • First-line oral agent for youth (with insulin, if appropriate [see below]).[5,6]
Pioglitazone (*Actos* [US], generics; with metformin [*ACTOplus Met*, generics (US)]; with glimepiride [*Duetact*, generics (US)], with alogliptin [*Oseni*, generics])				
Initial 15 to 30 mg once daily.[2] **Max** 45 mg once daily.[2] US: <$10; Canada: ~$30 **Pediatrics**: Consider a max dose of 30 mg/day; 45 mg dose has limited additional benefit with more side effects.[6]	·0.7% to 0.9%[1]	+ 2 to 2.5 kg or more.[1]	No[4]	• MOA: increases insulin sensitivity in liver, muscle, and fat.[2] • Reduces triglycerides.[8] • Glycemic control is better sustained over diabetes course than metformin or sulfonylureas.[9] • Serious adverse effects: edema, heart failure (avoid in patients with symptomatic heart failure), fractures.[1,8] • Do not use in bladder cancer, and use caution in patients with a history of bladder cancer.[2] Counsel patients to report hematuria or increased or painful urination.[2]

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Sodium-glucose co-transporter 2 (SGLT2) inhibitors: **Bexagliflozin** (*Brenzavvy* [US]). **Canagliflozin** (*Invokana*; with metformin [*Invokamet*, *Invokamet XR* (US)]). **Dapagliflozin** (*Farxiga* [US], *Forxiga* [Canada], generics; with metformin [*Xigduo XR*, generics]; with saxagliptin [*Qtern* (US)]). **Empagliflozin** (*Jardiance*; with linagliptin [*Glyxambi* (US)]; with metformin [*Synjardy*, *Synjardy XR* (US)], with linagliptin and metformin [*Trijardy XR* (US)]). **Ertugliflozin** (*Steglatro* [US]; with metformin [*Segluromet* (US)]; with sitagliptin [*Steglujan* (US)]).				
Bexagliflozin 20 mg once daily.[2] (US: ~$50 [from Cost Plus][11]) **Canagliflozin**:* **Initial**: 100 mg once daily. **Max** 300 mg once daily.[2] US: ~$600; Canada: ~$100 **Dapagliflozin**: **Initial** 5 mg once daily. **Max** 10 mg once daily.[2] US: ~$380; Canada: ~$20 **Empagliflozin**:* **Initial** 10 mg once daily. **Max** 25 mg once daily.[2] US: ~$630; Canada: ~$90 **Ertugliflozin**: **Initial** 5 mg once daily. **Max** 15 mg once daily.[2] US: ~$360 *dosing for ages ≥10 years	0.5% to 0.7% (adults);[1] 0.2% (pediatrics)[7]	-- Weight loss (2 to 3 kg in adults, 0.79 kg in pediatrics).[1,10]	No[4]	• MOA: blocks glucose and sodium reabsorption in the kidney; increases urinary excretion of glucose, sodium, and uric acid; and decreases plasma volume.[2] • Serious adverse effects: genital yeast infections (male/female), UTI, ketoacidosis (rare), volume depletion, acute pancreatitis (rare),[2,14] fracture risk (conflicting evidence),[15] Fournier's gangrene (rare; in men and women).[2,12-15] • See our chart, *Perioperative Management of Diabetes*, and FAQ, *Hyperglycemia in the Hospital* for information on prevention and management of SGLT2 inhibitor-associated euglycemic ketoacidosis. • For information on use in kidney impairment, see footnote d.
Sulfonylurea-second generation: Gliclazide (generics [Canada]; *Diamicron-MR,* generics [Canada]). **Glimepiride** (*Amaryl* [US], generics; with pioglitazone [*Duetact*, generics (US)]). **Glipizide** (generics (US); *Glucotrol XL*, generics (US); with metformin [generics (US)]). **Glyburide** (*DiaBeta* [US], generics; *Glynase*, generics [US]; with metformin [generics (US)])				
Gliclazide (standard): **Initial** 80 mg BID. **Max** 160 mg BID.[16] Canada: ~$10 **Gliclazide** (modified release): **Initial** 30 mg once daily. **Max** 120 mg once daily.[17] Canada: <$5 **Glimepiride**: **Initial** 1 to 2 mg once daily (1 mg in kidney impairment). **Max** 8 mg once daily.[2] US: <$10; Canada: $70 **Glipizide IR**: **Initial** 5 mg once daily. **Max** 20 mg BID.[2] US: <$10 **Glipizide XL**: **Initial** 5 mg once daily. **Max** 20 mg once daily.[2] US: ~$15 **Glyburide** (standard): **Initial** 2.5 to 5 mg once daily. **Max** 10 mg BID.[2] US: ~$15; Canada: <$10 **Glyburide** (micronized): **Initial** 1 to 3 mg once daily. **Max** 12 mg (once daily or in divided BID.[2] US: ~$35	0.6% to 1.2%[1]	+ 1.2 to 3.2 kg[1] Less weight gain with glipizide and glimepiride versus glyburide.[19]	Yes, especially with glyburide and/or in kidney impairment.[1] Hypoglycemic risk with glipizide or gliclazide < glimepiride < glyburide.[9,18]	• MOA:stimulates pancreatic insulin secretion.[1] • Efficacy is relatively short-lived.[1] • Avoid sulfonylureas in the elderly, in patients with hypoglycemia risk, and in patients who are overweight or obese.[8,18] • Not preferred in youth due to weight gain and hypoglycemia (requires self-monitoring of blood glucose), and potential for accelerated loss of beta-cell function.[6] • Avoid glyburide in kidney impairment.[1,4]

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Footnotes

a. Dosing is for adults unless otherwise specified. Pricing (for generic when available) is based on wholesale acquisition cost (WAC) of max dose unless otherwise specified. US medication pricing by Elsevier, accessed December 2024. Canadian price is wholesale.

b. Expected reduction as a metformin add-on, unless otherwise noted.

c. Max dose of DPP-4 inhibitors in kidney impairment:

- **Alogliptin**: CrCl 30 to 59 mL/min, 12.5 mg once daily. CrCl <30 mL/min. (including hemodialysis), 6.25 mg once daily.[2]
- **Saxagliptin**: eGFR <45 mL/min/1.73m^2 (including hemodialysis), 2.5 mg once daily. Give dose after hemodialysis.[2]
- **Sitagliptin**: eGFR 30 to 44 mL/min/1.73m^2, 50 mg once daily. eGFR <30 mL/min/1.73m^2 (including hemodialysis), 25 mg once daily.[2]

d. Use of SGLT2 antagonists in kidney impairment:

- **Bexagliflozin**: not recommended if eGFR <30 mL/min/1.73m^2.[2]
- **Canagliflozin**: do not initiate if eGFR <20 mL/min/1.73m^2.[2] Reduce dose to 100 mg/day in patients with eGFR <60 mL/min/1.73m2.2 Limited efficacy for glycemic control if eGFR <30 mL/min/1.73m^2, but can continue for CV or kidney indications until dialysis is needed.[2]
- **Dapagliflozin**: do not initiate if eGFR <25 m:/min/1.73m^2.[2] Limited efficacy for glycemic control if eGFR <45 mL/min/1.73m2, but can continue for CV or kidney indications until dialysis is needed.[2]
- **Empagliflozin**: do not initiate if eGFR <20 mL/min/1.73m^2.[2] Reduce dose to 10 mg/day in patients with eGFR <30 mL/min/1.73m^2 (US).[2] Limited efficacy for glycemic control if eGFR <30 mL/min/1.73m^2, but can continue for CV or kidney indications until dialysis is needed.[2]
- **Ertugliflozin**: limited efficacy for glycemic control if eGFR <45 mL/min/1.73m^2, but can continue for CV or kidney indications until dialysis is needed.[4]

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