# Drugs for Type 2 Diabetes

(last modified December 2023)

The table below summarizes the agents available for the treatment of type 2 diabetes, including expected A1c reduction when added to metformin, cost, adverse effects, and other pertinent information (e.g., place in therapy, pediatric use, cardiorenal benefit). For additional details on cardiovascular benefits associated with drugs for type 2 diabetes, see our chart, *Diabetes Medications: Cardiovascular and Kidney Impact.*

| **Expected A1c Reduction[b]/MOA** | **Maximum Daily Dose[2,24,42] (Cost/30 Days)[a]** | **Notable Adverse Effects** | **Comments** |
|---|---|---|---|
| **Alpha-glucosidase inhibitors**: acarbose and miglitol (US) | | | |
| 0.7% to 0.8% (acarbose, when added to metformin)[1]<br>~0.3% to 0.8% (miglitol, as monotherapy)[3]<br>MOA: slows intestinal carbohydrate digestion/absorption.[2] | **Acarbose**<br>300 mg, divided TID<br>(US: ~$50)(Canada: $30.84)<br><br>**Miglitol**<br>300 mg, divided TID<br>(US: ~$280) | • GI (e.g., abdominal pain, flatulence, diarrhea).[1,2]<br>• Relatively low risk of hypoglycemia.[1] | • Weight neutral.[1]<br>• Taken at the start of each main meal.[2]<br>• Reduces postprandial glucose.[6]<br>• Beneficial in the treatment of prediabetes (acarbose).[5,7] |
| **Amylin analog**: pramlintide (US)(*Symlin*) | | | |
| 0.3% to 0.4% (when added to insulin with or without metformin and/or a sulfonylurea)[4,40]<br><br>MOA: slows gastric emptying, causes satiety, and reduces postprandial glucagon secretion.[2] | **Pramlintide**<br>120 mcg/dose (usually 360 mcg/day; divided, prior to major meals)<br>(~$2,390) | • GI (e.g., nausea, vomiting).[2]<br>• Hypoglycemia can occur if used with insulin. Reduce mealtime insulin dose to reduce risk.[2] | • Weight loss (~1 kg).[4]<br>• Injectable.[2]<br>• Taken immediately before each main meal.[2]<br>• Reduces postprandial glucose.[8] |

| **Expected A1c Reduction[b]/MOA** | **Maximum Daily Dose[2,24,42] (Cost/30 Days)[a]** | **Notable Adverse Effects** | **Comments** |
|---|---|---|---|
| **Biguanide**: metformin (*Fortamet* (US), *Glucophage* (Canada), *Glumetza*, generics). Available in combination with alogliptin, canagliflozin, dapagliflozin, empagliflozin, ertugliflozin (US), glipizide (US), glyburide (US), linagliptin, pioglitazone (US), saxagliptin, and sitagliptin. See specific agents. | | | |
| 1% (as monotherapy)[1]<br><br>MOA: inhibits glucose production and absorption; increases insulin sensitivity in muscle and fat.[2] | **Metformin**<br>2,000 to 2,550 mg,* divided BID to TID<br>(US: <$10)(Canada: <$10)<br><br>**Metformin XR/ER**<br>2,000 mg, once daily or divided BID<br>(US: <$20)(Canada: $76.40)<br><br>*max dose 2,000 mg for 10 to 17 years of age.[2] | • GI (e.g., diarrhea, nausea, abdominal discomfort).[1,2,4] Address with slow titration, of an extended-release formulation taken with food.[4]<br>• Low risk of hypoglycemia when used as monotherapy.[4]<br>• Lactic acidosis (very rare) in patients with unstable heart failure, severe kidney impairment, or liver impairment.[4,9,11]<br>• B12 deficiency. Consider periodic testing.[4,27] | • First-line with diet and exercise for **glucose control** (but not for cardiorenal risk-reduction), for prediabetes (adults), and for youth ≥10 years of age.[4,7,27]<br>• Available as an oral solution (US).<br>• Weight neutral to modest weight loss.[4]<br>• Ameliorates insulin weight gain.[10]<br>• May reduce CV events and mortality.<br>• Safe in patients with stable heart failure and moderate kidney impairment:[4,9]<br>  ○ Can be initiated in patients with an eGFR >45 mL/min/1.73m$^2$. (Canada: ≥30 mL/min/1.73m2)[1,12]<br>  ○ Discontinue if eGFR falls below 30 mL/min/1.73m$^2$.[12] |
| **Dipeptidyl peptidase-4 (DPP-4) inhibitor ("gliptins") or incretin enhancer**:<br>• alogliptin (*Nesina*; with metformin [*Kazano*]; with pioglitazone [*Oseni* (US)]; authorized generics [US])<br>• linagliptin (*Tradjenta* [US]; *Trajenta* [Canada]; with metformin [*Jentadueto*, *Jentadueto XR* (US)]; with empagliflozin [*Glyxambi* (US)]; with metformin and empagliflozin [*Trijardy XR* (US)])<br>• saxagliptin (*Onglyza*, generics [Canada]; with metformin [*Konbiglyze* (Canada), *Kombiglyze XR* (US)]; with dapagliflozin [*Qtern* (US)])<br>• sitagliptin (*Januvia*; with metformin [*Janumet*, *Janumet XR*]; with ertugliflozin [*Steglujan* (US)]) | | | |
| 0.5% to 0.7%[1]<br><br>MOA: increases insulin secretion in response to elevated blood glucose, decreases glucagon secretion, and slows gastric emptying.[1] | **Alogliptin** 25 mg once daily<br>(US: $195)(Canada: $71.28)<br><br>**Linagliptin** 5 mg once daily<br>(US: $525.08)(Canada: $77.06)<br><br>**Saxagliptin** 5 mg once daily<br>(US: $485.08)(Canada: $49.23)<br><br>**Sitagliptin** 100 mg once daily<br>(US: $547.20)(Canada: $90.30) | • Generally well tolerated.[14]<br>• Low risk of hypoglycemia when used as monotherapy.[4]<br>• Weight neutral.[7]<br>• Rare cases of pancreatitis.[1]<br>• New or worsening heart failure (saxagliptin and alogliptin).[7]<br>• Rare cases of severe joint pain.[1] | • Not first-line. Alternative for glycemic control in patients with hypoglycemia risk or overweight/obesity.[7] Reduces postprandial glucose.[13]<br>• Have not been effective in youth.[27,43]<br>• Discontinue when more complex insulin regimens (e.g., basal plus prandial insulins) are started.[4]<br>• Dosage modification with kidney impairment needed (alogliptin, saxagliptin, sitagliptin).[2]<br>• CYP3A4 interactions (linagliptin, saxagliptin).[2] |

| **Expected A1c Reduction[b]/MOA** | **Maximum Daily Dose[2,24,42] (Cost/30 Days)[a]** | **Notable Adverse Effects** | **Comments** |
|---|---|---|---|
| **Glucagon-like, peptide-1 (GLP-1) agonist or incretin mimetic**:<br>• dulaglutide (*Trulicity*)<br>• exenatide (*Byetta* [US]) and exenatide extended release (*Bydureon BCise* [US])<br>• liraglutide (*Victoza;* with insulin degludec [*Xultophy*])<br>• lixisenatide (*Adlyxin* [US]; *Adlyxine* [Canada]; with insulin glargine [*Soliqua*])<br>• semaglutide (*Ozempic*, *Rybelsus*) | | | |
| Dulaglutide 1.8%[33]<br><br>Exenatide 0.96%[32]<br><br>Exenatide extended release 1.5% adults;[34] 0.36% pediatrics[35]<br><br>Liraglutide ~1.6% adults;[32] 0.5% pediatrics[36]<br><br>Lixisenatide ~1%[32]<br><br>Semaglutide 2.3% (metformin +/- sulfonylureas)[38]<br><br>Semaglutide, oral (plus metformin or SGLT2 inhibitor) 1.2%[32]<br><br>MOA: increases insulin secretion in response to elevated blood glucose, decreases glucagon secretion, slows gastric emptying.[1] | **Dulaglutide** 4.5 mg once weekly (US; $930.88)(Canada: $233.68 [1.5 mg once weekly])<br><br>**Exenatide** 10 mcg twice daily (US: $825.19)<br><br>**Exenatide extended release** 2 mg once weekly (US: $803.35)<br><br>**Liraglutide** 1.8 mg once daily (US: ~$1,117)(Canada: $325.05)<br><br>**Lixisenatide** 20 mcg once daily (US: NA)(Canada: $131.87)<br><br>**Semaglutide** 2 mg once weekly (US: $935.77)(Canada: $227.74 [1 mg once weekly])<br><br>**Semaglutide, oral** 14 mg once daily (US: $935.77)(Canada: $233.38) | • GI (e.g., diarrhea, nausea, vomiting).[10]<br>• Low risk of hypoglycemia when used as monotherapy.[4]<br>• Unclear association with acute pancreatitis.[15]<br>• Low risk of gallbladder disease.[16]<br>• May lead to retinopathy complications.[1]<br>• Linked to pancreatic and medullary thyroid cancer in rats.[10] | • First-line for CV disease or high CV risk (dulaglutide, liraglutide, semaglutide [injection]).[7]<br>• Add-on to metformin and/or insulin in youth ≥10 years of age (liraglutide, once-weekly exenatide).[35,44]<br>• In adults who need "higher glycemic efficacy," generally start with a GLP-1 agonist, then add basal insulin.[4]<br>• Weight loss (up to 14 pounds [6.4 kg] with semaglutide injection).[38]<br>• All are injectable, but an oral formulation of semaglutide is available.<br>• Avoid if eGFR <45 mL/min/1.73m$^2$ (extended-release exenatide), <30 mL/min/1.73m$^2$ (immediate-release exenatide), or <15 mL/min/1.73m$^2$ (lixisenatide).[2]<br>• Reduces postprandial glucose.[13]<br>• CV benefit (dulaglutide, liraglutide, semaglutide [injection]).<br>• Kidney benefit (except exenatide [unknown]). |

| Expected A1c Reduction[b]/MOA | Maximum Daily Dose[2,24,42] (Cost/30 Days)[a] | Notable Adverse Effects | Comments |
|---|---|---|---|
| **Glucagon-like, peptide-1 (GLP-1) agonist and glucose-dependent insulinotropic polypeptide (GIP) agonist (a "twincretin"):**<br>• tirzepatide (*Mounjaro*) | | | |
| 2.3%[31]<br><br>MOA: increases insulin sensitivity, increases insulin secretion in response to elevated glucose, decreases glucagon secretion, slows gastric emptying.[31,37] | **Tirzepatide** 15 mg once weekly (US: $1,023.04)(Canada: $330) | • GI (e.g., diarrhea, nausea, vomiting).[31,37]<br>• Low risk of hypoglycemia when used as monotherapy.[4]<br>• Pancreatitis rarely reported in clinical trials (23 events per 10,000 years of exposure [~twice the placebo rate]).[31,37]<br>• Low risk of gallbladder disease in clinical trials (0.6% vs 0% placebo).[31,37]<br>• Linked to medullary thyroid cancer in rats.[31,37] | • More weight loss than GLP-1 agonists (up to 25 pounds [11.2 kg] with maximum dose in patients with type 2 diabetes).[31,37]<br>• More A1c reduction than most GLP-1 agonists.<br>• No CV or kidney outcomes data yet.<br>• Monitor for retinopathy progression.[31,37]<br>• May delay oral contraceptive absorption.[31,37] Advise switching to a non-oral contraceptive or adding a barrier contraceptive for four weeks after initiation or a dosage increase.[31,37] |
| **Insulin**: See our chart, Comparison of Insulins (US)(Canada) for available products. | | | |
| 0.9% to 1.2% or more[1]<br><br>MOA: promotes uptake of glucose into muscle and fat tissues; inhibits glucose production.[2] | No maximum dose.[1]<br>See our chart, *Comparison of Insulins* (US)(Canada), for cost info. | • Hypoglycemia.[4] Educate patient to prevent, recognize, and manage.[1]<br>• Highest risk of weight gain (1 to 3.5 kg or more).[1] | • Adults: consider initial therapy with insulin if blood glucose is ≥300 mg/dL (≥16.7 mmol/L) and/or A1c is >10%.[4]<br>• Pediatrics: initial treatment of choice if A1c ≥8.5%, or ketoacidosis is present. See **footnote d**. |
| **Meglitinide**: nateglinide (US) and repaglinide (*GlucoNorm* [Canada], generics) | | | |
| 0.7% to 1.1%[1]<br><br>MOA: stimulates pancreatic insulin secretion.[2] | **Nateglinide**<br>360 mg, divided TID<br>(US: ~$67)<br><br>**Repaglinide**<br>16 mg, divided four times daily<br>(~$75)(Canada: $63.24) | • Hypoglycemia.[7] Educate patient to prevent, recognize, and manage.[1]<br>• Weight gain: 1.4 to 3.3 kg.[1] | • Reduces postprandial glucose more than sulfonylureas.[10]<br>• Safer than sulfonylureas in kidney impairment.[1]<br>• Taken before each meal; hold dose if skipping meal.[2,13]<br>• Less hypoglycemia than sulfonylurea.[7] |

| Expected A1c Reduction[b]/MOA | Maximum Daily Dose[2,24,42] (Cost/30 Days)[a] | Notable Adverse Effects | Comments |
|---|---|---|---|
| **Sodium-glucose co-transporter 2 (SGLT2) inhibitors**:<br>• bexagliflozin (*Brenzavvy* [US])<br>• canagliflozin (*Invokana*; with metformin [*Invokamet*, *Invokamet XR*])<br>• dapagliflozin (*Farxiga* [US]; *Forxiga*, generics [Canada]; with metformin [*Xigduo XR*, generics (Canada)]; with saxagliptin [*Qtern* (US)])<br>• empagliflozin (*Jardiance*; with linagliptin [*Glyxambi* (US)]; with metformin [*Synjardy, Synjardy XR* (US)], with linagliptin and metformin [*Trijardy XR* (US)])<br>• ertugliflozin (*Steglatro* [US]; with metformin [*Segluromet* (US)]; with sitagliptin [*Steglujan* (US)]) | | | |
| 0.5% to 0.7% (adults);[1] 0.2% (pediatrics)[43]<br><br>MOA: blocks glucose and sodium reabsorption in the kidney, increases urinary excretion of glucose, sodium, and uric acid, and decrease in plasma volume.[2] | **Bexagliflozin** 20 mg once daily (US: $47.85 [from Cost Plus][45])<br><br>**Canagliflozin** 300 mg once daily (US: $598.56)(Canada: $93.67)<br><br>**Dapagliflozin** 10 mg once daily (US: $565.29)(Canada: $22.11)<br><br>**Empagliflozin** 25 mg once daily (US: $593.30)(Canada: $89.65)<br><br>**Ertugliflozin** 15 mg once daily (US: $340.80) | • Low risk of hypoglycemia when used as monotherapy.[4]<br>• Genital fungal (yeast) infections (male/female).[17]<br>• UTI (may be severe).[18]<br>• Ketoacidosis (rare).[18]<br>• Increased urination may lead to volume depletion, hypotension, syncope, falls, and acute kidney injury that may require dialysis.[2]<br>• Hyperkalemia (canagliflozin) in kidney impairment, especially with high baseline potassium or use with medications that reduce potassium excretion.[2]<br>• Rare reports of acute pancreatitis.[21]<br>• Fracture risk (canagliflozin, dapagliflozin; conflicting evidence).[7,41]<br>• Fournier's gangrene (rare; in men and women). Onset: days to years.[17]<br>• Amputation risk (canagliflozin; conflicting evidence).[7,41] Consider amputation risk factors (ulcer or amputation history; reduced sensation). Emphasize foot care and monitor for foot/leg pain, tenderness, or sores.[1,19] | • First-line for patients with CV disease, high CV risk, heart failure, or CKD.[7]<br>  ○ CV benefit (canagliflozin, dapagliflozin [heart failure], empagliflozin, ertugliflozin heart failure], sotagliflozin).<br>  ○ Kidney benefit (canagliflozin, dapagliflozin, empagliflozin).<br>• Add-on to metformin or insulin for patients ≥10 years of age (empagliflozin).[43]<br>• Weight loss (2 to 3 kg in adults, 0.79 kg in pediatrics).[1,43]<br>• For information on use in kidney impairment, see **footnote c**. |

| **Expected A1c Reduction[b]/MOA** | **Maximum Daily Dose[2,24,42] (Cost/30 Days)[a]** | **Notable Adverse Effects** | **Comments** |
|---|---|---|---|
| **Sulfonylurea-second generation**<br>• gliclazide (*Diamicron* [brand discontinued], generics [Canada]; *Diamicron-MR,* generics [Canada])<br>• glimepiride (*Amaryl* [US], generics; with pioglitazone [*Duetact*, generics (US)]),<br>• glipizide (*Glucotrol* [brand discontinued], generics (US); *Glucotrol XL*, generics (US); with metformin [generics (US)])<br>• glyburide (*DiaBeta* [US], generics; *Glynase*, generics [US]; with metformin [generics (US)]) | | | |
| 0.6% to 1.2%[1]<br><br>MOA: stimulates pancreatic insulin secretion.[1] | **Gliclazide** (standard) 320 mg (daily doses ≥160 mg should be divided BID)(Canada: $12.06)<br><br>**Gliclazide** (modified release) 120 mg once daily (Canada: <$10)<br><br>**Glimepiride** 8 mg once daily (US: ~$15)(Canada: $67.96)<br><br>**Glipizide IR** 40 mg (daily doses >30 mg should be divided BID) (US: <$10)<br><br>**Glipizide XL** 20 mg once daily (US: ~$25)<br><br>**Glyburide** (standard) 20 mg (daily doses >10 mg can be divided BID) (US: ~$25)(Canada: <$10)<br><br>**Glyburide** (micronized) 12 mg (once daily or in divided doses) (US: ~$20) | • Hypoglycemia, especially with glyburide and/or in kidney impairment.[1] Educate patient to prevent, recognize, and manage.[1]<br>o Hypoglycemic risk with glipizide or gliclazide < glimepiride < glyburide.[13,22]<br>• Weight gain: 1.2 to 3.2 kg.[1]<br>o Less weight gain with glipizide and glimepiride versus glyburide.[23] | • Sulfonylureas lack cardiovascular benefit.[22]<br>• Efficacy is relatively short-lived.[1]<br>• Consider for glycemic control in patients for whom cost is a barrier to treatment.[7]<br>• Discontinue when more complex insulin regimens (e.g., basal plus prandial insulins) are started.[4]<br>• Avoid sulfonylureas in the elderly, in patients with hypoglycemia risk, and in patients who are overweight or obese.[7,22]<br>• 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.[27]<br>• Avoid glyburide in kidney impairment.[1,4]<br>• Start low and titrate. Periodically consider need for dose reduction as the patient ages and circumstances change (e.g., reduced oral intake, kidney impairment).[25] |

| Expected A1c Reduction[b]/MOA | Maximum Daily Dose[2,24,42] (Cost/30 Days)[a] | Notable Adverse Effects | Comments |
|---|---|---|---|
| **Thiazolidinedione (TZD)**: pioglitazone (*Actos* [US], generics; with metformin [*ACTOplus Met*, generics (US)]; with glimepiride [*Duetact*, generics (US)], with alogliptin [*Oseni*, authorized generics]) | | | |
| 0.7% to 0.9%[1]<br>MOA: increases insulin sensitivity in liver, muscle, and fat.[2] | **Pioglitazone** 45 mg once daily (US: ~$10)(Canada: $31.72) | • Low risk of hypoglycemia when used as monotherapy.[4]<br>• Edema.[1]<br>• Weight gain: 2 to 2.5 kg or more.[1]<br>• Heart failure.[1] Avoid in patients with symptomatic heart failure.[7]<br>• Increased fracture risk.[1]<br>• Do not use in active 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] | • Reduces risk of recurrent stroke.[7]<br>• Beneficial in the treatment of prediabetes.[7]<br>• Lowers triglycerides.[7]<br>• Glycemic control is better sustained over diabetes course than metformin or sulfonylureas.[13]<br>• Not preferred in youth due to weight gain (especially with insulin). Could consider if metformin is not tolerated and cardiac function is normal, given that youth have tend to have severe insulin resistance. Consider a max dose of 30 mg/day (45 mg dose has limited additional benefit with more side effects).[27] |
| **Others – bile acid sequestrant**: colesevelam (*Welchol*, generics [US]) | | | |
| 0.5%[28]<br>MOA: may reduce liver glucose production, increase GLP-1 levels, and decrease glucose absorption.[28,29] | **Colesevelam**<br>3.75 gm, given once daily or divided BID<br>(US: ~$350 [powder for suspension]; ~$120 [tablets]) | • Low incidence of mild to moderate hypoglycemia.[28]<br>• GI (e.g., constipation, nausea, dyspepsia).[28]<br>• May increase triglycerides.[28] | • Diabetes is not a Health Canada-approved indication.[26]<br>• Weight neutral.[7]<br>• Lowers LDL cholesterol.[28]<br>• May decrease absorption of other meds.[2] |
| **Others – dopamine agonist**: bromocriptine (*Cycloset* [US]) | | | |
| 0.5% (when added to metformin and a sulfonylurea)[30]<br>MOA: increases insulin sensitivity.[30] | **Bromocriptine** 4.8 mg once daily (~$999.58) | • Infrequent hypoglycemia.[2,30]<br>• Nausea, rhinitis, headache.[30]<br>• Orthostasis (may include nausea and sweating as well as dizziness).[30] | • Weight neutral.[7]<br>• Avoid with strong CYP3A4 inhibitors.[30]<br>• May worsen psychosis.[30]<br>• Take within 2 hours of awakening, with food.[2] |

a. Unless otherwise specified, pricing (for generic when available) is based on wholesale acquisition cost (WAC). US medication pricing by Elsevier, accessed July 2023. Canadian price is wholesale.

b. As a metformin add-on, unless otherwise noted.
c. Use of SGLT2 antagonists in kidney impairment:
    - **Bexagliflozin**: not recommended if eGFR <30 mL/min/1.73m$^2$.[46]
    - **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/1.73m$^2$.[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/1.73m2.[2] 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.[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] (Canada: empagliflozin contraindicated for glycemic control if eGFR <20 mL/min/1.73m$^2$.[39]).
    - **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.[2]
d. **Insulin** use in **pediatrics**: Start basal insulin at 0.25 to 0.5 units/kg. Attempt transition to metformin over two to six weeks (once labs have stabilized), by decreasing insulin each time metformin in increased.[27] Offer continuous glucose monitoring to youth receiving multiple daily injections or continuous subcutaneous insulin infusion.[20]

**Abbreviations**: BID = two times daily; BMD = bone mineral density; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; LDL = low-density lipoprotein; MOA = mechanism of action; TID = three times daily; UTI = urinary tract infection.

*Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.*

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