Drugs for Type 2 Diabetes

(edited for NEPHO use)

Abbreviations: BID - twice daily; CVD - cardiovascular disease; MOA - mechanism of action; PO - by mouth; SC - subcutaneously; TID - three times daily.

Class/Expected A1C Reduction[c]	Specific Agents	Initial Dose[a] (Approx cost for 30-day supply[b])	Advantages [a,1-3]	Disadvantages[a,1-3]
Alpha-glucosidase inhibitor 0.5% to 1%[3] MOA: Slows intestinal carbohydrate digestion/absorption.	Acarbose (*Precose*, others) Miglitol (*Glyset*)	**Acarbose** INITIAL: 25 mg PO TID ($45) **Miglitol** INITIAL: 25 mg PO TID ($145)	Lack of hypoglycemia when used as monotherapy Weight neutral Reduces postprandial glucose values Not absorbed Likely reduces CVD events (acarbose) Beneficial in the treatment of prediabetes (acarbose)[9]	Modest effect on A1C Flatulence Diarrhea Need for frequent dosing
Amylin analog 0.5% to 1%[5] MOA: Slows gastric emptying, increases the feeling of fullness, reduces postprandial glucagon secretion.	Pramlintide (*Symlin*)	**Pramlintide** INITIAL: 60 mcg SC prior to major meals (≥250 kcal or containing ≥30 g carbohydrate) ($590)	Lack of hypoglycemia when used as monotherapy Weight loss Reduces postprandial glucose values Increases feeling of fullness after meal	Modest effect on A1C Nausea Vomiting Hypoglycemia if insulin dose is not reduced Need for frequent dosing Injectable
Biguanide 1% to 1.5%[3] MOA: Inhibits hepatic glycogenolysis and gluconeogenesis. Enhances insulin sensitivity in muscle and fat.	Metformin (*Glucophage*, *Glucophage XR*) Available in combination with alogliptin, glimepiride, glipizide, glyburide, linagliptin, pioglitazone, rosiglitazone, saxagliptin, sitagliptin, repaglinide, and canagliflozin. See specific agents.	**Metformin** INITIAL 500 mg PO BID or 850 mg PO once daily (less than $20/month)	Lack of hypoglycemia Weight neutral Likely reduces CVD events Beneficial in the treatment of prediabetes[10]	Diarrhea Abdominal cramping B12 deficiency Lactic acidosis (rare) in patients with cardiovascular, renal, or hepatic dysfunction
Dipeptidyl peptidase-4 (DPP-4) inhibitor ("gliptins") or incretin enhancer 0.5% to 1%[3] (However, some experts feel that the actual range is lower [e.g., ≤0.7%].) MOA: Inhibits degradation of endogenous incretins resulting in increased insulin secretion in response to elevated blood glucose, decreased glucagon secretion, slowed gastric emptying, and increased satiety.	Alogliptin (*Nesina*) With metformin (*Kazano*) With pioglitazone (*Oseni*) Linagliptin (*Tradjenta*) With metformin (*Jentadueto*) With empagliflozin (*Glyxambi*) Saxagliptin (*Onglyza*) With metformin (*Kombiglyze XR*) Sitagliptin (*Januvia*) With metformin (*Janumet*, *Janumet XR*)	**Alogliptin** INITIAL 25 mg PO once daily ($310) **Linagliptin** INITIAL: 5 mg PO once daily ($330) **Saxagliptin** INITIAL: 2.5 or 5 mg PO once daily ($325) **Sitagliptin** INITIAL: 100 mg PO once daily ($330)	No hypoglycemia when used as monotherapy Weight neutral Generally well tolerated	Dosage modification with renal impairment needed (sitagliptin, saxagliptin, alogliptin) CYP3A4 interactions (saxagliptin, linagliptin) May be associated with pancreatitis[6] May worsen heart failure (saxagliptin)[7,13] May cause severe joint pain[12]

Class/Expected A1C Reduction[c]	Specific Agents	Initial Dose[a] (Approx cost for 30-day supply[b])	Advantages [a,1-3]	Disadvantages[a,1-3]
Glucagon-like, peptide-1 (GLP-1) agonist or incretin mimetic 1% to 1.5%[3] MOA: Stimulation of GLP-1 receptors results in increased insulin secretion in response to elevated blood glucose, decreased glucagon secretion, slowed gastric emptying, and increased satiety. (GLP-1 is an incretin hormone.) For more information, see our *PL Chart*, *Comparison of GLP-1 Agonists*.	Albiglutide (*Tanzeum*) Dulaglutide (*Trulicity*) Exenatide (*Byetta*) Exenatide extended-release (*Bydureon*) Liraglutide (*Victoza*)	**Albiglutide** INTIAL 30 mg SC once weekly ($325) **Dulaglutide** INITIAL 0.75 mg SC once weekly ($490) **Exenatide** INITIAL: 5 mcg SC BID ($480) **Exenatide extended-release** INITIAL: 2 mg SC once weekly ($475) **Liraglutide** INITIAL: 0.6 mg SC once daily x 1 week, then increase to 1.2 mg SC once daily ($430)	Lack of hypoglycemia when used as monotherapy Weight loss Reduces postprandial glucose values In patients who need more than one or two antidiabetes agents, combination injectable therapies of basal insulin and a GLP-1 agonist is an efficient, emerging strategy.	Headache Nausea (often transient) Diarrhea Dosage modification with renal dysfunction needed (albiglutide, dulaglutide) Avoid in severe renal impairment (exenatide) May be associated with pancreatitis[6] Associated with thyroid cell cancer in rodents May be associated with renal insufficiency[8] Injectable
Insulin 1.5% to 3.5%[5]	Various.	See our *PL Charts*, *Initiation and Adjustment of Insulin Regimens for Type 2 Diabetes* and *Comparison of Insulins and Injectable Diabetes Meds*.	Effective in all patients Reduced microvascular complications Consider starting insulin, in combination with metformin therapy with or without other noninsulin therapies when the blood glucose is >300 mg/dL to 350 mg/dL and/or the A1C ≥10%. Insulin may be more effective than other therapies when hyperglycemia is severe, especially if the patient is symptomatic or has any catabolic features (e.g., weight loss, ketosis).	Hypoglycemia Weight gain Injectable
Meglitinide 0.5% to 1%[3] MOA: Stimulates pancreatic insulin secretion.	Nateglinide (*Starlix*) Repaglinide (*Prandin*, others) With metformin (*PrandiMet*)	**Nateglinide** INITIAL: 60 to 120 mg PO TID with meals ($105) **Repaglinide** INITIAL: 0.5 mg PO TID w/ meals if A1C <8%;1 - 2 mg TID w/ meals if A1C ≥8% ($50)	Reduces postprandial glucose values Can be used in place of sulfonylureas in patients with irregular meal schedules or in those who develop late hypoglycemia with a sulfonylurea	Hypoglycemia if taken without food or if severe renal impairment Weight gain Frequent dosing Discontinue when more complex insulin regimens (e.g., basal plus prandial insulins) are started[3]
Sodium-glucose co-transporter 2 (SGLT2) inhibitor or "flozins" 0.5% to 1%[1] MOA: Blocks glucose	Canagliflozin (*Invokana*) With metformin (*Invokamet*) Dapagliflozin (*Farxiga*) Empagliflozin (*Jardiance*)	**Canagliflozin** INITIAL: 100 mg PO once daily ($340) **Dapagliflozin** INITIAL: 5 mg PO once	Lack of hypoglycemia Weight loss May reduce blood pressure	Genital fungal infections (male and female) Urinary tract infection Increased urination Hypotension Increase LDL Do not use if eGFR <45 mL/min/1.73m^2

Class/Expected A1C Reduction[c]	Specific Agents	Initial Dose[a] (Approx cost for 30-day supply[b])	Advantages [a,1-3]	Disadvantages[a,1-3]
reabsorption in kidney, increases glucosuria.	With linagliptin (*Glyxambi*) With metformin (*Synjardy*)	daily ($340) **Empagliflozin** INITIAL 10 mg PO once daily ($340)		(canagliflozin, empagliflozin) or <60 mL/min/1.73m^2 (dapagliflozin) Fractures (rare, in susceptible patients)[4] Decrease in BMD (canagliflozin).[11] May be associated with increased risk of bladder cancer (dapagliflozin) Possible association with ketoacidosis[14]
Sulfonylurea-second generation 1% to 1.5%[3] MOA: Stimulates pancreatic insulin secretion.	Glyburide (*Diabeta*, *Glynase*, *Micronase*, others) With metformin (*Glucovance*) Glipizide (*Glucotrol*, *Glucotrol XL*, others) With metformin (*Metaglip*) Glimepiride (*Amaryl*, others) With metformin (*Amaryl M*) With pioglitazone (*Duetact*) With rosiglitazone (*Avandaryl*)	**Glyburide (avoid due to hypoglycemia)** INITIAL: 2.5 mg PO once daily (less than $10/month) **Glipizide** INITIAL: 5 mg PO once daily (less than $10/month) **Glimepiride** INITIAL: 1 mg PO once daily (less than $10/month)	Initially, good efficacy Inexpensive	Hypoglycemia, especially with renal dysfunction (less with glimepiride versus glyburide)[5] Weight gain (glyburide more than glipizide, glimepiride) Reduced efficacy over time For the elderly and those with hepatic or renal dysfunction, start with low doses and titrate up Discontinue when more complex insulin regimens (e.g., basal plus prandial insulins) are started[1]
Thiazolidinedione (TZD) 1% to 1.5%[3] MOA: Increases insulin sensitivity in muscle and fat.	Pioglitazone (*Actos*) With metformin (*Actoplus Met* or *Actoplus Met XR*) With glimepiride (*Duetact*) With alogliptin (*Oseni*) Rosiglitazone (*Avandia*) With metformin (*Avandamet*) With glimepiride (*Avandaryl*)	**Pioglitazone** INITIAL: 15 mg PO once daily (less than $20) **Rosiglitazone** INITIAL: 4 mg PO once daily ($115)	Lack of hypoglycemia when used as monotherapy Improves HDL cholesterol Reduced triglycerides (pioglitazone) May reduce CVD (pioglitazone)	Weight gain Volume retention, congestive heart failure Increased fracture risk Increases LDL (rosiglitazone) May possibly increase the risk of bladder cancer (pioglitazone)
Others – bile acid sequestrant 0.5% to 1%[3] MOA: May reduce hepatic glucose production, may increase incretin levels, and decreases GI glucose absorption.	Colesevelam (*Welchol*)	**Colesevelam** INITIAL: 3.75 g PO per day (taken as six tablets once daily, or three tablets BID, with meals) ($470)	No hypoglycemia Weight neutral Safe in CVD Lowers LDL cholesterol	Constipation Nausea, bloating Increased triglycerides Drug interactions

a. **Information based on most current U.S. product information unless otherwise noted**: *Precose* (March 2015), *Glyset* (February 2015), *Symlin* (March 2015), *Glucophage* (March 2015), *Onglyza* (May 2013), *Januvia* (March 2015), *Tradjenta* (May 2014), *Byetta* (February 2015), *Bydureon* (March 2015), *Victoza* (March 2015), *Starlix* (January 2013), *Prandin* (March 2012), *Diabeta* (October 2013), *Glucotrol* (February 2011), *Amaryl* (February 2012), *Actos* (August 2012), *Avandia* (May 2012), *Welchol* (January 2014), *Cycloset* (March 2011), *Diabinese* (October 2013), tolazamide (Mylan; December 2009), tolbutamide (Mylan; February 2009), *Invokana* (March 2015), *Nesina* (June 2013), *Farxiga* (March 2015), *Jardiance* (August 2014), *Tanzeum* (March 2015), *Invokamet* (March 2015), *Trulicity* (March 2015).

b. Approximate prices based on WAC for 30-day supply (of generic product if available, generic prices may vary considerably). If WAC not available (chlorpropamide, tolazamide, tolbutamide), AWP for 30-day supply used.

c. A1C reductions are estimates using monotherapy.

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