Know Your Diabetes Medication

Type 2 Diabetes is a complex and challenging condition. Managing it often requires a multifaceted approach, combining lifestyle changes with medication. Typically, Metformin is the first medication prescribed when you're diagnosed with T2D. Unfortunately, many patients don't reach their glycemic targets with Metformin alone, and additional medication is needed.

With various medication classes available, each with its own history and benefits, it's important to understand your options to make informed decisions. Because different drugs act in different ways to lower glucose levels, they can be used together to help you achieve your goals. For instance, Metformin and <u>BRENZAVVY</u> (an SGLT-2 inhibitor) may be used together to maintain optimal glucose levels. Many other combinations are also possible.

In this article, we will explore the most used medications for T2D, discussing how they work, their costs, efficacy, and potential side effects. This information will help you prepare for discussions with your doctor about your treatment plan.

See a quick comparison of the most commonly used T2D medications on the next page.

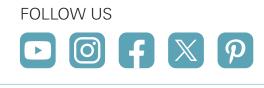
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Commonly Used T2D Medications

DRUG CLASS	MEDICATIONS	HOW IT WORKS	A1C REDUCTION	RETAIL PRICE
Biguanides	Metformin	 First-line treatment option. Primarily works by reducing glucose production in the liver. 	1–2%	\$4–\$15
Sulfonylureas	GlipizideGlyburideGlimepiride	 Stimulate the pancreas to release more insulin 	1–2%	\$6-\$24
DPP-4 Inhibitors	JANUVIAZITUVIOKOMBOLYZETRADJENTA	 By blocking the action of DPP- 4, these medications increase levels of gut hormones (GLP-1 and GIP) to promote insulin release. 	0.5–1%	\$550–\$760
SGLT-2 Inhibitors	JARDIANCEBRENZAVVYINVOKANAFARXIGA	 Block the reabsorption of glucose in the kidneys, causing it to be excreted through urine. These medications also provide cardiovascular benefits. 	0.5–1%	\$520–\$720
GLP-1 Agonists	 OZEMPIC MOUNJARO BYETTA VICTOZA RYBELSUS 	 Supplement a gut hormone (GLP-1), which promotes insulin release and aids in weight loss. 	1–1.5%	\$900–\$1,300





Metformin:

First-Line Treatment Option with Multi-Modes of Action



Reduce glucose production in the liver



Increase insulin sensitivity in muscle cells

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Reduce glucose absorption in the intestines

Drug Class	Biguanides
Examples	Metformin is the only medication in this class
Retail Cost	\$4–\$15
A1C Reduction	1%–2% as monotherapy. Can provide additional A1C reduction when combined with other medications.

Metformin has been a mainstay in T2D management since its discovery in the 1920s. Its use expanded in the 1950s, and it gained widespread popularity in the 1990s due to its efficacy, safety profile, and affordability.

Metformin remains the first-line medication for T2D and is often prescribed as the initial therapy and may be combined with other medications as the disease progresses.

Metformin works on multiple levels to control blood sugar levels:

- Primarily reduces the amount of glucose produced by the liver
- Increases insulin sensitivity in muscle cells, which enhances glucose uptake from the bloodstream into muscles
- Reduces the absorption of glucose from the intestines

Common side effects of metformin include gastrointestinal symptoms like nausea and diarrhea. However, these usually improve over time and can often be managed with lifestyle modifications or changes in dosage.

Metformin is on our Wholesale Price List

- \$37 for 180 tablets or \$70 for 360 tablets
- Free shipping





Sulfonylureas:

Stimulate Insulin Production



Target beta cells in the pancreas to stimulate insulin release

Drug Class	Sulfonylureas
Examples	Glipizide, glyburide, glimepiride
Retail Cost	\$6-\$24
A1C Reduction	1%–2%. They may become less effective over time and can cause weight gain.

Sulfonylureas gained popularity for their ability to stimulate insulin secretion from the pancreas to lower blood sugar levels.

These medications target beta cells in the pancreas. Sulfonylureas attach to certain receptors on these cells, which causes the cells to release more insulin into the bloodstream.

Sulfonylureas were once the mainstay of T2D treatment and remain widely prescribed today, especially as second-line agents when metformin alone is insufficient. However, their popularity has waned in recent years with the emergence of newer drug classes offering additional benefits.

Common side effects of sulfonylureas include hypoglycemia (low blood sugar), weight gain, and gastrointestinal upset. They may also carry a risk of cardiovascular events, particularly in high doses or in individuals with pre-existing heart conditions.

<u>Glipizide</u>, glyburide, and glimepiride are on our <u>Wholesale</u> <u>Price List</u>

- \$37 for 180 tablets or \$70 for 360 tablets
- Free shipping





DPP-4 Inhibitors:

Increase Gut Hormone Levels to Promote Insulin Release



Increase GLP-1 and GIP levels in the intestines

Drug Class	Dipeptidyl Peptidase-4 (DPP-4) Inhibitors
Examples	JANUVIA & ZITUVIO (<u>sitagliptin</u>), KOMBOLYZE (saxagliptin), <u>TRADJENTA</u> (linagliptin)
Retail Cost	\$550-\$760
A1C Reduction	0.5%–1%. They are often used as second- line therapy to provide additional A1C reduction.

<u>DPP-4 inhibitors</u> entered the T2D treatment landscape in the early 2000s. These drugs gained attention for their novel mechanism of action: they enhance body's natural ability to lower glucose levels.

When we eat, our gut releases two hormones, GLP-1 and GIP. These hormones prompt the pancreas to release insulin, which helps lower blood sugar levels. However, the enzyme DPP-4 quickly inactivates these hormones, limiting their effectiveness. DPP-4 inhibitors block the DPP-4 enzyme, allowing GLP-1 and GIP to remain active longer and enhance insulin secretion.

DPP-4 inhibitors quickly gained popularity as second-line options. They are typically well-tolerated and have a low risk of causing hypoglycemia (low blood sugar) when used alone or in combination with metformin. DPP-4 inhibitors are a popular choice due to their favorable side effect profile.

Side effects of DPP-4 inhibitors may include upper respiratory tract infections, headache, and nasopharyngitis. While generally well-tolerated, there may be a low risk of pancreatitis or joint pain.

Get <u>generic Sitaglipin</u> (a DPP-4 inhibitor) for \$80/month with free shipping exclusively through Marley Drug.





SGLT-2 Inhibitors:

Remove Access Sugar through Urine



Block glucose reabsorption in the kidneys



Get <u>BRENZAVVY</u> (an SGLT-2 inhibitor) for \$59.95/month with free shipping exclusively through Marley Drug.

Drug Class	Sodium-Glucose Co-Transporter-2 (SGLT- 2) Inhibitors
Examples	BRENZAVVY (bexagliflozin) <u>INVOKANA</u> (canagliflozin), <u>FARXIGA</u> (dapagliflozin), JARDIANCE (empagliflozin)
Retail Cost	\$520–\$720
A1C Reduction	0.5%–1%. They also offer cardiovascular and renal benefits. Individual responses may vary.

<u>SGLT-2 inhibitors</u>, such as <u>BRENZAVVY</u>, emerged in the 2010s as a new class of T2D medications. Unlike previous drug classes that primarily focus on insulin production or sensitivity, SGLT-2 inhibitors target glucose directly.

In our bodies, glucose is continuously filtered by the kidneys and then reabsorbed back into the bloodstream. SGLT-2 proteins, located almost exclusively in the kidneys, are responsible for about 90% of this glucose reabsorption.

SGLT-2 inhibitors reduce glucose reabsorption in the kidneys, leading to more glucose being excreted in the urine.

These medications have gained popularity in recent years, particularly for their cardiovascular and renal benefits beyond glycemic control. Clinical trials have demonstrated reductions in the risk of cardiovascular events and progression of kidney disease in individuals with T2D and established cardiovascular disease or chronic kidney disease.

The most common side effects of SGLT-2 inhibitors include an increased risk of genital and urinary tract infections, such as yeast infections in women and urinary tract infections in both men and women. Patients may also experience increased urination and thirst. Additionally, a mild to moderate decrease in blood pressure, potentially causing dizziness or fainting, is another common side effect.



GLP-1 Agonists:

Mimic a Gut Hormone that Promotes Insulin Release



Supplement GLP-1 which promotes insulin secretion

Drug Class	Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists
Examples	BYETTA (exenatide), VICTOZA (liraglutide), <u>OZEMPIC & RYBELSUS</u> (semaglutide), <u>MOUNJARO</u> (tirzepatide)
Retail Cost	\$900–\$1,300
A1C Reduction	1%–1.5%. They also promote weight loss

The history of GLP-1 agonists dates back to their introduction in the early 2000s. Initially, their use was limited due to the inconvenience of daily dosing schedules and other practical considerations. However, the arrival of Ozempic in 2017 revolutionized this class of drugs with a once-weekly injection regimen.

GLP-1 agonists work by supplementing the body with a form of GLP-1 that is resistant to the enzyme DPP-4. Normally, DPP-4 quickly deactivates natural GLP-1, but the synthetic form used in these medications is not easily broken down. This resistance to DPP-4 allows GLP-1 to last longer in the gut, providing more sustained blood sugar control.

GLP-1 helps regulate blood sugar levels in several ways:

- Promotes insulin secretion
- Slows stomach emptying, which reduces the rate at which glucose enters the bloodstream
- Signals the brain that you're full

Additionally, Rybelsus, approved in 2019, is the first and only oral medication in this class, offering a convenient once-daily alternative to injections.

Common side effects may include nausea, vomiting, diarrhea, and injection-site reactions. Rare side effects may include pancreatitis and thyroid tumors.

• Get OZEMPIC for \$1,200

- Get MOUNJARO for \$1,286
- Get <u>RYBELSUS</u> for \$1,070.81



