

# Diabetes Medications:

## Biguanides:

*Metformin* is the only medication currently available within this class of drugs, and it is generally the first choice of medications for use in treatment of Type 2 diabetes. Most individuals who are newly diagnosed will begin use of Metformin immediately.

Metformin improves the body's ability to respond to insulin by decreasing insulin resistance. It works primarily in the liver to control blood glucose by 1) preventing the liver from releasing excess sugar; 2) helping the body respond better to the insulin the pancreas already makes; and 3) decreasing the amount of sugar that is absorbed in the intestines.

Metformin reduces A1C by up to 1.5 percentage points. In contrast to most other antidiabetic drugs, Metformin often leads to modest weight reduction or weight stabilization. Metformin has also been found to lower blood cholesterol levels.

Other brand names for Metformin: Glucophage®, Glucophage XR®, Glumetza®, Riomet®, and Fortamet®

**Side Effects:** The most common side effects of Metformin are gastrointestinal. These may include a metallic taste in the mouth, mild anorexia, nausea, abdominal discomfort, and soft bowel movements or diarrhea. The symptoms are often mild and transient, and can be minimized by slow introduction of the medication, with gradual increase in dosage as needed. Side effects may be reduced by taking Metformin directly after a meal, and by use of an extended release formula. Avoiding the use of "sugar free" foods that contain artificial sweeteners or sugar alcohols may also be helpful. Metformin should be used with caution in patients who have impaired liver function, liver disease, heart failure, history of lactic acidosis, or alcohol abuse.

## Sulfonylureas:

*Sulfonylureas* are the oldest class of oral blood glucose lowering medications. They work by stimulating the pancreas to increase insulin production, and can lower blood glucose levels by approximately 20 percent. Their effectiveness, however, often decreases over time because the pancreas becomes overworked and worn out when there is ongoing insulin resistance.

**First Generation Sulfonylureas:** Acetohexamide, Chlorpropamide (Diabinese®), and Tolbutamide (Orinase®)

**Second Generation Sulfonylureas:** Glipizide (Glucotrol, or Glucotrol® XL); Gliclazide (Diamicron R, or Diamicron MR®); Glyburide (Glibenclamide®, Diabeta®, Micronase®, and Glynase® PresTab); and Glimepiride (Amaryl®)

**Sulfonylurea Combination Drugs:** ACTOplus met™ (Actos™ plus Metromin); Avandamet™ (Avandia® plus Metromin); Avandaryl™ (Avandia™ plus Amaryl®); Metablip™ (Glipizide™ plus Metformin); and Glucovance™ (Glyburide plus Metformin)

**Side Effects:** Although sulfonylurea drugs have similar effects on blood glucose, they differ in the ways they are taken, the side effects they may cause, and in the way they interact with other drugs. The major adverse effect of sulfonylureas is low blood sugar or hypoglycemia. Hypoglycemia induced by some of the older long-acting sulfonylureas may be severe and prolonged in the absence of appropriate therapy. Shorter acting sulfonylureas, such as Glipizide and Gliclazide are less likely to cause hypoglycemia than the older, First generation medications. Sulfonylureas should be used with caution in patients with increasing age, alcohol abuse, poor nutrition, serious liver or renal problems, and should not be used by patients who are allergic to sulfa drugs.

## Meglitinides:

Meglitinides stimulate the pancreas to release more insulin right at the start of a meal. They are short-acting glucose lowering medications that have similar action to that of Sulfonylureas, with a similar or slightly decreased efficiency in decreasing blood glucose. They can generally be used in people who have allergy to sulfa or sulfonylurea medications. Meglitinides have a short action time and are often taken before meals to stimulate “first phase” insulin production in response to meals. If a meal is skipped, they should not be taken.

Meglitinides include: Nateglinide (Starlix®), and Repaglinide (Prandin®)

**Side Effects:** May cause hypoglycemia. Should be used with caution in people with liver disease.

## Insulin:

In the past, insulin was not used in people with Type 2 diabetes until their blood glucose levels were unable to be controlled with use of oral medications and lifestyle change. There is increasing evidence, however, that use of insulin at earlier stages may improve insulin sensitivity and help preserve the ability of the pancreas to continue making insulin. Insulin injections can therefore be used as a first-line treatment for some individuals with Type 2 diabetes, and discontinued once the body is able to maintain normal blood glucose levels through use of diet, exercise, and other oral hypoglycemic medications.

## GLP-1 Agonists:

*Glucagon-like peptide-1 (GLP-1)* is a naturally occurring hormone that is produced in the intestines of healthy individuals during digestion of food. GLP-1 stimulates the pancreatic beta cells to produce insulin in response to food intake, and decreases liver output of glucose following a meal. The hormone slows gastric (stomach) emptying which improves satiety (feeling of fullness). It decreases blood glucose excursions (highs and lows) by decreasing the spike in blood glucose following meals. And, it helps the pancreas respond to rising levels of blood glucose with increased insulin production.

**GLP-1 Agonists include:** Exenatide (Byetta®) and Liraglutide (Victoza®) GLP-1

*GLP-1* agonists may help preserve pancreatic function, and their use has been associated with weight loss.

**Side Effects:** May cause nausea, vomiting, diarrhea, dizziness, headache, feeling jittery, dyspepsia, or decreased appetite. Some people experience a sensation of bloating or fullness that feels like nausea, which may be due to eating more than the stomach can hold. Use of GLP-1 Agonists may delay the absorption of oral medications that are taken concurrently.

## **DPP-IV Inhibitors:**

This class of medications slows the activity of an enzyme called anpeptidase IV (DPP-IV) which breaks down incretin hormones such as GLP-1 and GIP. This in turn prolongs the activity of GLP-1 and GIP. In healthy individuals, GLP-1 and GIP hormones are released by the intestine throughout the day, and levels increase in response to a meal. This improves after meal blood glucose levels by slowing gastric (stomach) emptying, increasing insulin production, and decreasing production of glucose in the liver. People with diabetes have limited production of GLP-1 and GIP incretin hormones, which are rapidly deactivated by DPP-IV enzymes. Use of DPP-IV inhibitors therefore allows the incretin hormones to remain active for a longer period of time.

*DPP-IV inhibitors* include: Sitagliptin (Januvia™); Sitagliptin in combination with Metformin (Janumet™); and Saxagliptin (Onglyza™)

**Side Effects:** May cause runny nose, sore throat, or headache

## **Amylin/Symlin:**

*Amylin* is a naturally occurring hormone that is co-secreted with insulin by the pancreatic beta cells. It is secreted in response to food intake and the blood glucose that follows a meal. Beta cell dysfunction in diabetes results in a reduced secretion of amylin as well as insulin. *Symlin* is an amylin like agent with effects similar to those of amylin. Symlin slows gastric (stomach) emptying, reduces the rate at which glucose enters the bloodstream, decreases after meal glucose output from the liver by suppressing glucagon secretion, and decreases food intake by enhancing satiety (feeling of fullness). Use of Symlin can potentially lead to weight loss. Daily blood glucose fluctuations are reduced with use of Symlin which tends to improve quality of life as well as overall blood glucose control.

**Side Effects:** Can cause nausea, loss of appetite (anorexia), vomiting and headache. The incidence and severity of nausea generally decreases over time when Symlin is started at a low dose and slowly increased. Severe low blood glucose (hypoglycemia) can occur when insulin dosages are not adjusted (generally requiring a 50% reduction in mealtime insulin), and is more common in type 1 diabetes. Symlin should not be used in case of hypersensitivity to Symlin, confirmed diagnosis of gastroparesis, or hypoglycemia unawareness. Use of Symlin may delay the absorption of oral medications that are taken concurrently.

## TZDs or Thiazolidinediones:

This class of medications works on the muscle cells to make them more sensitive to insulin. They reduce insulin resistance and improve the ability of insulin to enter the body's cells. TZDs may lower A1C by 0.5 to 1.4 percentage points, and are generally used in combination with other glucose lowering medications. It may take up to 12 weeks to see the full benefit of their use.

*Thiazolidinediones* include: Pioglitazone (Actos™) and Rosiglitazone (Avandia®)

Thiazolidinedione combination drugs include: ACTOplus met™ (Actos™ plus Metformin), Avandamet™ (Avandia® plus Metformin), Avandaryl™ (Avandia® plus Amaryl®)

*Side Effects:* Caution is advised in use of these medications for individuals with liver and heart disease. Blood tests for liver function are required. TZDs may also cause fluid build up (edema) which often appears in the lower legs. Weight gain or shortness of breath should be reported to health care provider immediately.

## Alpha-glucosidase Inhibitors:

These medications work in the small intestine by blocking or slowing the digestion of carbohydrate starches and sugars, which helps decrease the peak in blood glucose levels following a meal. They have an additive blood glucose lowering effect for individuals who also use sulfonylurea, Metformin, or insulin therapy. They are less potent than other glucose lowering medications, with an expected A1C reduction of 0.5 to 0.8 percentage points.

*Alpha glucosidase inhibitors* include: Acarbose (Precose®) and Miglitol (Glyset®)

*Side Effects:* The main side effects are flatulence and diarrhea, which often limits their acceptance.