

Understanding the Diabetes Medicine Maze

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Background

HbA1c is a test used to measure long-term blood sugar control in people with [diabetes](#). Normal HbA1c levels are usually less than 6 percent in people without diabetes; people with diabetes usually have higher HbA1c results.

Studies have shown that the higher the HbA1c, the greater the chance for developing long-term problems related to diabetes. This includes such problems as [heart disease](#), [diabetic retinopathy](#), [diabetic neuropathy](#), and diabetic nephropathy. By getting blood sugar levels under control, it may be possible to decrease the chances for developing these [diabetes complications](#).

How the medications work

In people with diabetes, blood glucose levels are too high. These high levels occur because glucose remains in the blood rather than entering cells, where it belongs.

People with type 1 diabetes don't make insulin. For them, insulin therapy is the only way to keep blood glucose levels down.

People with type 2 diabetes tend to have two problems: they don't make quite enough insulin and the cells of their bodies don't take in glucose as easily as they should.

Oral [diabetes medications](#) help control blood sugar levels in people whose bodies still produce some insulin (the majority of people with [type 2 diabetes](#)) along with making specific [dietary changes](#) and getting regular [exercise](#). Several of these diabetes pills are often used in combination to achieve optimal blood sugar control.

Remember that people with type 2 diabetes tend to have two problems that lead to increased sugar (glucose) in the bloodstream: They don't make enough insulin to move glucose into cells where it belongs and the body's cells become "resistant" to insulin, meaning they don't take in glucose as well as they should.

In time, people with type 2 diabetes develop what's called "beta-cell failure." This means that the cells in the pancreas that make insulin no longer are able to release insulin in response to high [blood sugar levels](#). Therefore, these people often require insulin injections, either in combination with their diabetes pills, or just insulin alone to manage their diabetes.

8 Main Categories of Medications:

All of these classes of drugs manage type 2 diabetes: sulfonylureas, biguanides, thiazolidinediones, alpha-glucosidase inhibitors, meglitinides and DPP-4 inhibitors. They work in different ways to help diabetes patients but they all help to maintain good blood glucose control.

Sulfonylureas:

Sulfonylureas stimulate the beta cells of the pancreas to release more insulin. These medications are the oldest of the oral diabetes drugs, and until 1995 they were the only drugs available for managing type 2 diabetes. Sulfonylureas stimulate the pancreas to release more insulin into the blood stream. Hypoglycemia can be a side effect of these drugs. Many of these drugs are only effective for a few years and then may stop working. They are inexpensive. If you're allergic to sulfa, you can't take a sulfonylurea.

There are several "generations" of this classification of medicines. Second and third generations are more widely prescribed today.

First generation: Orinase, Tolinase and Diabinese

Second generation: Glucotrol (glipizide), Glucotrol XL (extended-release glipizide), Micronase or Diabeta (glyburide)

Third generation: Amaryl (glimepiride)

Side effects of first- and second-generation sulfonylureas include:

- Hypoglycemia (low blood sugar)
- Upset stomach
- Skin rash or itching
- Weight gain
- Low sodium level

Biguanides:

These drugs work by affecting the production of glucose that comes from digestion. They don't cause hypoglycemia and even help with weight loss and lower cholesterol numbers. They are the most commonly prescribed drugs for type 2 diabetes. Glucophage (metformin) and Glucophage XR (metformin extended release) are the most well known of these drugs.

Biguanides lower blood glucose levels primarily by decreasing the amount of glucose produced by the liver. It can also decrease the amount of sugar absorbed into the body (from the diet) and can make **insulin** receptors in muscle tissue more sensitive, helping the body respond better to its own insulin. These diabetes pills improve insulin's ability to move sugar into cells especially into the muscle cells. All of these effects cause a decrease in blood sugar levels.

It is usually taken two times a day. A side effect of metformin may be diarrhea, but this is improved when the drug is taken with food.

Biguanides should not be used in people who have kidney damage or **heart failure** because of the risk of precipitating a severe build up of acid (called lactic acidosis) in these patients. Biguanides can decrease the HbA1c 1%-2%.

Because the medication does not increase the amount of insulin produced by the body, it is less likely to cause dangerously low blood sugar (hypoglycemia), as many other diabetes medications can do.

Side effects for biguanide medications include:

- Upset stomach (**nausea**, diarrhea)
- Metallic taste in mouth

It can be taken with a sulfonylurea.

Alpha-Glucosidase Inhibitors:

Glyset (miglitol) and Precose (acarbose) are the two most prescribed alpha-glucosidase inhibitors (aka "starch blockers"). These drugs help the body to lower blood glucose levels by blocking the breakdown of starches, such as bread, potatoes, and pasta in the intestine. They also slow the breakdown of some sugars, such as table sugar. Their action slows the rise in blood glucose levels after a meal. They should be taken with the first bite of a meal. They are often prescribed in conjunction with other diabetes medications. These drugs may cause diarrhea or gas.

Side effects for alpha-glucosidase inhibitors include:

- Stomach upset (gas, diarrhea, nausea, cramps) -- may not be a good choice if you have a history of stomach or bowel trouble

Thiazolidinediones :

Rosiglitazone (Avandia) and pioglitazone (ACTOS) are in a group of drugs called thiazolidinediones. These diabetes pills improve insulin's effectiveness (improving insulin resistance) in muscle and in fat tissue. They lower the amount of sugar released by the liver and make fat cells more sensitive to the effects of insulin. A decrease in the HbA1c of 1%-2% can be seen with this class of oral diabetes medications. These drugs may take a few weeks before they have an effect in lowering blood sugar. They should be used with caution in people with heart failure. Your doctor will do periodic blood testing of your liver function when using this diabetes medicine. These drugs work by sensitizing muscle and fat cells to accept insulin more readily. Actos (pioglitazone) and Avandia (rosiglitazone) are the only two thiazolidinediones marketed today. **As of May 21, 2007, the Food and Drug Administration has issued a safety alert regarding the possibility of heart attacks or other fatal cardiovascular events when taking Avandia.**

The first drug in this group, troglitazone (Rezulin), was removed from the market because it caused serious liver problems in a small number of people. So far rosiglitazone and pioglitazone have not shown the same problems, but users are still monitored closely for liver problems as a precaution. Both drugs appear to increase the risk for heart failure in some individuals. Both drugs are effective at reducing A1C and generally have few side effects.

Side effects for thiazolidinediones are rare but may include:

- Elevated liver enzymes
- Liver failure
- Respiratory infection
- Headache
- Fluid retention

Meglitinides:

The brand names for these drugs are Prandin (repaglinide) and Starlix (nateglinide). This class of drugs is similar to the alpha-glucosidase inhibitors in that they are taken before each meal. But these drugs stimulate the beta cells of the pancreas to produce more insulin in relationship to how much glucose is in the blood. High sugars make this class of diabetes medicines release insulin. They are said to be glucose dependent. These stimulate insulin production when there is glucose present in the blood. If blood sugar is low, the drug does not work as well. This is unlike the sulfonylureas that cause an increase in insulin release, regardless of glucose levels, and can lead to [hypoglycemia](#). They can be used in combination with some other oral medications for increased effectiveness.

Because sulfonylureas and meglitinides stimulate the release of insulin, it is possible to have hypoglycemia (low blood glucose levels).

Side effects of meglitinides include:

- Hypoglycemia (low blood sugar)
- Stomach upset

DPP-4 Inhibitors:

Januvia (sitagliptin phosphate) and Onglyza (saxagliptin) are in a class of drugs called DPP-4 inhibitors. These lower blood sugar levels by blocking an enzyme known as dipeptidyl peptidase IV or DPP-4. DPP-4 inhibitors help improve A1C without causing hypoglycemia. They work by preventing the breakdown of a naturally occurring compound in the body, GLP-1. GLP-1 reduces blood glucose levels in the body, but is broken down very quickly so it does not work well when injected as a drug itself. By interfering in the process that breaks down GLP-1, DPP-4 inhibitors allow it to remain active in the body longer, lowering blood glucose levels only when they are elevated. It is this increase in incretin hormones that is responsible for the beneficial actions of Januvia and Onglyza, including increasing insulin production in response to meals and decreasing the amount of glucose (sugar) that the liver produces. DPP-4 inhibitors do not tend to cause weight gain and tend to have a neutral or positive effect on cholesterol levels. They do not need to be taken with a meal, unlike some other classes of oral diabetes medications. Because incretin hormones are more active in response to higher blood sugar levels (and are less active in response to low blood sugar), the risk of dangerously low blood sugar (hypoglycemia) is low with this drug class.

Incretin Mimetics:

These mimic the action of incretin hormones which help the body make more insulin. They also slow the rate of digestion so that glucose enters the blood more slowly. People on incretin mimetics feel full longer, which reduces food intake, which helps some people lose weight while on the medication.

Exenatide (brand name **Byetta**) is in a new class of drugs for the treatment of type 2 diabetes called incretin mimetics. Incretins are gut-derived peptides that are normally secreted in response to meals. Exenatide has been approved for use by people with type 2 diabetes who have not achieved their target A1C levels using metformin, a sulfonylurea, or a combination of metformin and a sulfonylurea. Exenatide is a synthetic version of exendin-4, a naturally-occurring hormone that was first isolated from the saliva of the lizard known as a Gila monster. Exenatide works to lower blood glucose levels primarily by increasing insulin secretion. Because it only has this effect in the presence of elevated blood glucose levels, it does not tend to increase the risk of hypoglycemia on its own, although hypoglycemia can occur if taken in conjunction with a sulfonylurea.

Byetta (exenatide) is an injectable medication. It is not an insulin and it does not take the place of insulin. It is used for type 2 diabetes only. Byetta comes in a pre-filled injector pen. The dose is 5 mcg, to start, twice a day within 60 minutes of your morning and evening meals.

The primary side effect is nausea, which tends to improve over time.

Antihyperglycemic Synthetic Analogs:

These are medications that are created as synthetic versions of human substances, in this case a human hormone called amylin, which is used by the pancreas to lower blood glucose levels.

Symlin (pramlintide acetate): Symlin is an injectable medication which is used with insulin for tighter blood glucose control. Symlin can increase the risk of severe hypoglycemia, therefore patients who are put on Symlin are selected carefully and monitored closely by their healthcare providers.

Pramlintide injections taken with meals have been shown to modestly improve A1C levels without causing increased hypoglycemia or weight gain and even promoting modest weight loss. The primary side effect is nausea, which tends to improve over time and as an individual patient determines his or her optimal dose.

Because of differences in chemistry, pramlintide cannot be combined in the same vial or syringe with insulin and must be injected separately. Pramlintide has been approved for people with type 1 diabetes who are not achieving their goal A1C levels and for people with type 2 diabetes who are using insulin and are not achieving their A1C goals.

Oral Medications That May Prevent Diabetes or Heart Attack:

Recent studies show that some oral medications may help prevent diabetes and/or its complications. Metformin and Precose seem to reduce a person's risk of developing type 2 diabetes, particularly when combined with an appropriate diet and regular exercise. Research is ongoing to fully explore all the additional benefits of diabetes medications. Actos has been shown to reduce the risk of heart attack, stroke, and premature death in those with type 2 diabetes. Researchers continue to look into the preventative benefits of other medications.

Oral combination therapy

Because the drugs listed above act in different ways to lower blood glucose levels, they may be used together. For example, a biguanide and a sulfonylurea may be used together. Many combinations can be used. Though taking more than one drug can be more costly and can increase the risk of side effects, combining oral medications can improve blood glucose control when taking only a single pill does not have the desired effects. Switching from one single pill to another is not as effective as adding another type of diabetes medicine.

There are several combination diabetes pills that combine two medications into one tablet. One example of this is Glucovance, which combines glyburide (a sulfonylurea) and metformin. Others include Metaglip, which combines glipizide (a sulfonylurea) and metformin, and Avandamet which utilizes both metformin and rosiglitazone (Avandia) in one pill.

Your doctor may prescribe a combination of 2 or even 3 types of medicine to help control your blood sugar levels. Some combinations are available together in one pill. Some of these include a combination of a thiazolidinedione and a biguanide (Avandamet and ACTOplus Met) or a sulfonylurea and a biguanide (Glucovance and Metaglip).

Diabetes pills don't work for everyone. Although most people find that their blood glucose levels go down when they begin taking pills, their blood glucose levels may not go near the normal range.

Also, if you plan to become pregnant, you will need to control your diabetes with diet and exercise or with insulin. It is not safe for pregnant women to take oral diabetes medications.

There is no "best" pill or treatment for type 2 diabetes. You may need to try more than one type of pill, combination of pills, or pills plus insulin.

What about insulin?

Although it is a common practice to try pills before insulin, you may start on insulin based on several factors.

These factors include:

- how long you have had diabetes
- how high your blood glucose level is
- what other medicines you take
- your overall health

Because diabetes pills seem to help the body use insulin better, some people take them along with insulin shots. The idea behind this "combination" therapy is to try to help insulin work better.

The New, and the Tried and True

By [Debra Manzella, R.N.](#), About.com

Medication Reference Chart For Type 2 Diabetes

MEDICATIONS FOR TYPE 2 DIABETES				
Classification	Medication	Route	The way it works	Time and Dose
Sulfonylureas	Glimepiride (Amaryl) Glipizide (Glucotrol) Glipizide ER (Glucotrol XL) Glyburide	Oral	Increases insulin production	1 or 2 times a day
Biguanides	Glucophage (aka Metformin) Glucophage XR	Oral	Lowers glucose from digestion	2-3 times a day, XR once a day
Alpha-Glucosidase Inhibitors	Glyset and Precose	Oral	Slows digestion, slows glucose production	Take before each meal
Thiazolidinediones	Actos and Avandia	Oral	Lowers glucose production	Once daily with or without food
Meglitinides	Prandin and Starlix	Oral	Increases insulin production	5-30 minutes before meals
DPP-4 Inhibitors	Januvia	Oral	Lowers glucose by blocking an enzyme	100 mg. once a day
Incretin Mimetics	Byetta	Injectable	Helps the pancreas make insulin, slows digestion	10 mcg. Inject within an hour of AM and PM meals
Anti-hyperglycemic	Symlin	Injectable	Controls postprandial blood glucose	15 mcg. Inject before major meals



Debra Manzella, R.N.

Type 2 Diabetes Guide

Nutritional Supplements:

Multivitamin

Chromium and Cinnamon are debatable

Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes.

1. *R A Anderson, N Cheng, N A Bryden, M M Polansky, N Cheng, J Chi and J Feng*

Abstract

Chromium is an essential nutrient involved in normal carbohydrate and lipid metabolism. The chromium requirement is postulated to increase with increased glucose intolerance and diabetes. Individuals being treated for type 2 diabetes (180 men and women) were divided randomly into three groups and supplemented with: 1) placebo, 2) 1.92 micromol (100 microg) Cr as chromium picolinate two times per day, or 3) 9.6 micromol (500 microg) Cr two times per day. These data demonstrate that supplemental chromium had significant beneficial effects on HbA1c, glucose, insulin, and cholesterol variables in subjects with type 2 diabetes. The beneficial effects of chromium in individuals with diabetes were observed at levels higher than the upper limit of the Estimated Safe and Adequate Daily Dietary Intake.

Chromium supplements: chromium, diabetes, and weight loss

Chromium and cholesterol. It's too early to recommend chromium supplements for cholesterol. But there may be an exception to that rule when it comes to low HDL (good) cholesterol. The best ways to boost HDL levels are lifestyle changes such as exercise and diet. But if those don't help, chromium may be worth a try. Some clinical trials have reported a benefit. Chromium and heart disease. A new study reports a link between chromium levels and heart attack risk: the lower the levels, the higher the risk. The association of low chromium and heart attacks was unrelated to diabetes or diet. Chromium and diabetes. Since chromium influences insulin action and glucose metabolism, diabetes is a logical candidate for chromium replacement therapy. However, studies have yielded conflicting results. The American Diabetes

Association states that "at present, benefit from chromium supplements has not been conclusively demonstrated." It's an invitation for more scientific study. Is chromium right for you? When it comes to dietary chromium, the answer is yes; whole grains, nuts, broccoli, and green beans, which contain the mineral, are all healthful foods. But before you opt for supplements, talk with your doctor.

Effect of Cinnamon on Glucose Control and Lipid Parameters

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Abstract

Cinnamon contains biologically active substances that have demonstrated insulin-mimetic properties. In vitro ([1,2](#)) and in vivo ([3,4](#)) studies have shown that cinnamon enhances glucose uptake by activating insulin receptor kinase activity, autophosphorylation of the insulin receptor, and glycogen synthase activity. Other recent studies have demonstrated the ability of cinnamon to reduce lipid levels in fructose-fed rats, potentially via inhibiting hepatic 3-hydroxy-3-methylglutaryl CoA reductase activity ([5,6](#)).

Several clinical trials ([7-11](#)) have investigated the impact of cinnamon on glucose and plasma lipid concentrations in patients with diabetes but yielded conflicting results and had modest sample sizes. Therefore, we performed a meta-analysis of randomized controlled trials of cinnamon to better characterize its impact on glucose and plasma lipids.

OBJECTIVE—To perform a meta-analysis of randomized controlled trials of cinnamon to better characterize its impact on glucose and plasma lipids.

RESULTS—Five prospective randomized controlled trials ($n = 282$) were identified. Upon meta-analysis, the use of cinnamon did not significantly alter A1C, FBG, or lipid parameters. Subgroup and sensitivity analyses did not significantly change the results.

CONCLUSIONS—Cinnamon does not appear to improve A1C, FBG, or lipid parameters in patients with type 1 or type 2 diabetes.

Other Meds:

Aspirin, Cholesterol medication, blood pressure medications

The cost of care

Costs vary widely among the different medications. Even the same medication can vary in price from store to store. Call around to find the best price for the one you take.

Generic versions of some sulfonylureas are available. These cost less than brand-name products and in general are reliable. There is now a generic Metformin (brand name Glucophage).

- References:
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