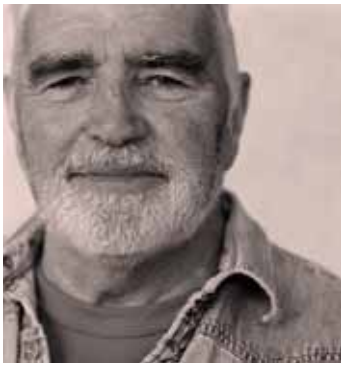
Consumer Reports Health.org

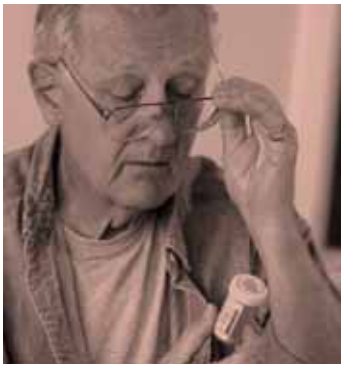
# BEST BUY DRUGS

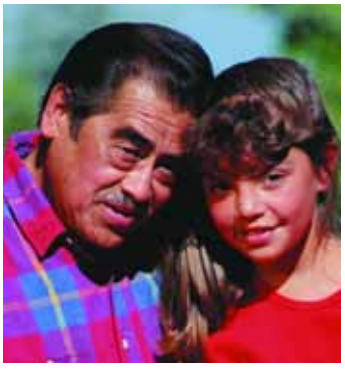


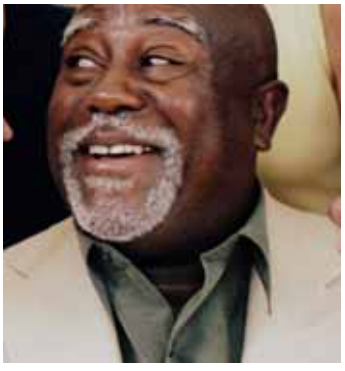
Treating Type 2 Diabetes:

## The Oral Diabetes Drugs

Comparing Effectiveness, Safety, and Price







# Our Recommendations

Six types of oral medicines (and 11 individual drugs) are now available to help the 24 million people in the U.S. with type 2 diabetes control their blood sugar when diet and lifestyle changes are not enough. Our evaluation of these medicines found the following:

- *Newer drugs are no better.* Two drugs from a class called the sulfonylureas and a drug named metformin have been around for more than a decade and work just as well as newer medicines. Indeed, several of the newer drugs are less effective than the older ones.

- *Newer drugs are no safer.* All diabetes pills have the potential to cause adverse effects, both minor and serious. The drugs' safety and side effect "profiles" may be the most important factor in your choice.

- *The newer drugs are more expensive.* The newer diabetes medicines cost many times more than the older ones.

- *Taking more than one diabetes drug is sometimes necessary.* Many people with diabetes do not get enough blood sugar control from one medicine. Two or more may be necessary. However, taking more than one diabetes drug raises the risk of adverse effects and increases costs.

Taking effectiveness, safety, adverse effects, dosing, and cost into consideration, we have chosen the following as *Consumer Reports Best Buy Drugs* if your doctor and you have decided that you need medicine to control your diabetes:

- *Metformin* – alone or with glipizide or glimepiride

- *Glipizide* and *Glipizide Sustained Release* – alone or with metformin

- *Glimepiride* – alone or with metformin

These medicines are available as low-cost generics, costing from $10 to $60 a month. If you have been diagnosed with diabetes, we recommend that you try metformin first unless your health status prevents it.

If metformin fails to bring your blood sugar into normal range, we recommend you add glipizide or glimepiride. Should either of those cause problems, Actos (pioglitazone) may be an option you and your doctor will want to consider. Be aware that Actos has been linked to a higher risk of heart failure.

*This report was updated in February 2009.*

# Welcome

This report compares the effectiveness, safety, and cost of medicines used to treat type 2 diabetes. It is part of a Consumers Union and *Consumer Reports* project to help you find safe, effective medicines that give you the most value for your health-care dollar. To learn more about the project and other drugs we've evaluated for other diseases and conditions, go to ConsumerReportsHealth.org/BestBuyDrugs.

Type 2 diabetes is one of the most serious medical conditions affecting our nation today. The number of people who have it has been rising alarmingly.

Type 2 diabetes used to be referred to as "adult onset" diabetes, but no longer. In recent years, the incidence among children and adolescents has exploded. Much of that surge is due to the dramatic increase in the last 20 years in the number of young people who are physically inactive and overweight or obese.

The statistics are sobering. An estimated 24 million people in the U.S., or about 8 percent of the population, have diabetes. That's up from 2.5 percent of the population in 1980. Despite the increase of the disease among the young, older people are still the largest age group affected: *one in five people aged 60 or over has diabetes*. And about 1.5 million people are newly diagnosed with type 2 diabetes every year.

But despite widespread attention to the diabetes epidemic, about one in three people who have diabetes – some 6 million people – have not been diagnosed and do not know they have it. And many of those who have been diagnosed are not getting adequate treatment. A quarter to a third of the people who have been diagnosed with diabetes fail to receive the medical care and medicines that research has shown to be effective.

Why is diabetes of such concern? Studies conclusively show that diabetes more than doubles the risk of developing and dying of heart disease and other problems. Indeed, the condition is as potent a predictor and risk factor for heart disease and heart attack as are cigarette smoking, high blood pressure, and uncontrolled high cholesterol. When people with diabetes go untreated for years, the damage it causes to their blood vessels almost guarantees a premature death from heart disease.

Diabetes also significantly raises the risk of a host of other problems. These include: stroke, nerve damage, kidney damage; damage to the eye as well as total blindness; liver disease, impotence, poor wound healing, and susceptibility to infections that can fester and require amputations of toes, feet, or part of a leg.

In addition, people with diabetes are very likely to have other dangerous health conditions. One recent study found that 47 percent of people with

diabetes had two other heart disease risk factors (such as smoking, high blood pressure and high cholesterol) and 18 percent had three or more.

People with uncontrolled diabetes live an average eight years less than people who do not have diabetes. At greatest risk of premature disability and death are women (of all ethnic backgrounds), African Americans, Mexican Americans, American Indians, and the indigenous people of Alaska.

Women have the same prevalence of diabetes as men, but recent studies indicate women are much more likely to die from it. Minority group members are both more prone to develop diabetes (due to genetic and environmental factors) and to become disabled or die from it (due to multiple factors, including that they are less likely to get good care).

But proper treatment can keep people with diabetes healthy. In fact, all people with diabetes who receive proper and consistent care live good quality lives, and can work and function normally.

## Type 1 and type 2 diabetes – the difference

There is widespread misunderstanding about diabetes. This section explains what the disease is and the difference between so-called type 1 and type 2.

Diabetes is a disease characterized by elevation of blood glucose (a sugar) caused by decreased production of the hormone insulin and/or increased resistance to the action of insulin by certain cells. Glucose is the body's main fuel. When you eat carbohydrates (pasta, bread, rice, grains, fruits, and vegetables), your digestive system breaks them down into glucose, which is released into the bloodstream so your body can use it for energy. Glucose also gets stored in the liver as glycogen, which can later be broken down back into glucose when the body needs fuel.

Insulin, which is produced in the pancreas, regulates both the movement of glucose into the body's cells and the breakdown in the liver of glycogen into glucose. Both actions are critical to keeping blood sugar levels within normal ranges.

About 1.5 to 2 million people in the U.S. have a form of the disease called type 1 diabetes. In this condition – usually diagnosed in childhood or the early teen years – the pancreas, over a relatively brief period of time, stops producing insulin altogether. The onset of the disease is usually abrupt, with severe symptoms that require immediate attention. Type 1 diabetes is a so-called "autoimmune" disease, which means the body attacks itself. Specifically, errant immune cells damage and destroy the part of the pancreas that produces insulin. People with type 1 diabetes must inject insulin every day.

In type 2 diabetes, the pancreas produces enough insulin, at least in the early years that a person has the disease. But for reasons that are still not

well understood, the body's cells become resistant or insensitive to it. To compensate, the pancreas pumps out increasing amounts of insulin to normalize blood glucose levels. Over time – as long as a decade – this ever-increasing production becomes unsustainable, and the pancreas' ability to produce insulin declines.

As a result, the telltale marker – and problem – of diabetes emerges: glucose levels rise in the blood because it is unable to enter the body's cells. The excess glucose is damaging to the body's tissues and leads to the symptoms of diabetes. When the glucose level gets high enough, the sugar begins to appear in the urine and causes increased urination.

Elevated blood sugar puts a strain on almost every organ and many parts of the body. Over years, it is particularly toxic to the body's blood vessels; it causes them to thicken. This leads to problems in the eyes and kidneys, the heart, the liver, and the blood circulation system. High blood sugar also damages the nerves. Proper treatment that keeps blood sugar in the normal range sharply reduces the risk of these complications.

Again, there are many theories and ideas about the causes of type 2 diabetes, and the insulin resistance that characterizes it. Studies show the disease runs in families, meaning it has a strong genetic (hereditary) component. Another cause is being overweight or obese. In some cases, this can occur due to a genetic propensity to being overweight and obese, but in most cases it is due to overeating and lack of exercise. About 55 percent of people diagnosed with diabetes in the U.S. are overweight or obese.

While recent media attention surrounding the diabetes epidemic has focused on its link to obesity, the statistic above shows that 45 percent of people with diabetes are not overweight, meaning that there are other causes of the disorder.

## Symptoms and getting tested

The symptoms of type 2 diabetes tend to develop gradually over time and include:

- Fatigue
- Frequent urination
- Increased thirst and hunger
- Blurred vision
- Numbness in your hands and legs
- Slow healing of wounds and sores

These symptoms can also be mild and/or intermittent for years. If you experience any of these – and especially if you experience two or more, for even a few days – you should see a doctor immediately.

In the early stages of the disease, symptoms may be non-existent. That's unfortunate because the damage to organs occurs even in the absence of symptoms. For this reason, it's important for people who may be at risk of diabetes to get their blood sugar levels checked regularly. Those at risk include:

- People with coronary artery disease, or vascular disease
- People who have high blood pressure
- People whose "bad" (LDL) cholesterol is elevated
- People who are overweight or obese
- Anyone with a parent or a sibling who has diabetes
- People who are Black Americans, Mexican or Latino Americans, Asian Americans, Native Americans, Pacific Islanders, or Alaskan Natives
- Women who have had diabetes during pregnancy or a baby weighing more than 9 pounds at birth

If you are in one of these groups and have never had a blood sugar check or not had one in more than a year, get it tested *as soon as possible.*

There is a disagreement in the medical community about whether all adults should have their blood sugar checked periodically. The American Diabetes Association advises that everyone aged 45 and over have a blood sugar test once every three years. But the highly-regarded U.S. Preventive Services Task Force says not enough scientific evidence exists to show that such broad screening has benefits or is worth the considerable cost.

We think the decision rests with you and your doctor and depends on an assessment of your overall health, risk factors, weight, and family history. Some doctors are inclined to check the blood sugar levels of most people over age 45 or 50, especially if they are 10 or more pounds overweight. Other doctors may be more conservative.

Blood sugar tests are inexpensive and easy, though they may have to be done a few times to yield a conclusive diagnosis. The most common one is done after an overnight fast. If your blood sugar is 126 milligrams per deciliter (mg/dl) or greater after being checked on two or three different occasions, you are considered to have diabetes. Another test assesses your blood sugar at any time (not just after an overnight fast). If this test indicates your blood sugar level is 200mg/dl or above on two or more occasions, you are considered to have diabetes.

Your doctor may also talk to you about a blood test known as "hemoglobin A1c" (pronounced hemoglobin "A," "one," "c"; usually abbreviated in print as HbA1c and often referred to by diabetes patients as "my A1c"). This is a commonly used test to evaluate blood sugar control after treatment is started. But your doctor may order this test at the time of diagnosis. There's more about this measure in the next section.

## What is pre-diabetes?

In the last decade, doctors and researchers have recognized that a large number of people in the U.S. have blood sugar levels that are above 110mg/dl (the upper limit of normal) but less than the 126mg/dl required for a diagnosis of diabetes. The most recent studies indicate that nearly 18 percent of the population – 57 million people – have blood glucose levels in this range and thus have what is called pre-diabetes. (It's also sometimes called borderline diabetes, impaired fasting glucose, or impaired glucose tolerance.)

What concerns doctors is that a growing body of research now shows that people with pre-diabetes have (a) a very high risk of developing diabetes and (b) an elevated risk of heart disease and stroke even if their glucose level never rises above 126 mg/dl.

In a recent analysis involving 10,428 people in Australia, those with pre-diabetes were found to have 2.5 times the risk of dying from heart disease over a 5-year period compared to people whose blood sugar was normal.

Such findings are leading many doctors to consider drug treatment for people with pre-diabetes. But most doctors agree, and research backs it up, that dietary and lifestyle changes can be very effective for keeping pre-diabetes under control – before any medicines need to be prescribed.

That said, this report does not specifically address treatment of pre-diabetes. If you are diagnosed with pre-diabetes we would urge you to talk with your doctor about ways to alter your diet and lifestyle, and lose weight if you need to.

Lifestyle modifications have also become a mainstay of treatment for people with full-blown diabetes. Studies consistently show that lifestyle changes alone – especially weight loss in those who are overweight or obese – can prevent the complications of diabetes. For some people, these changes can eliminate or reduce the need for drugs. The next section discusses this further.

Since many people with diabetes also have high blood pressure and/or high cholesterol, your doctor will aim to get those under control, too, using diet and lifestyle changes and medicines if necessary.

Oral diabetes medicines – pills you take by mouth – are thus just one treatment among several that doctors use to help keep people with diabetes healthy. But they are a critical part of treatment.

Today, nine classes of drugs are available to treat type 2 diabetes. That includes insulin and two other types of drugs that are given by injection. That leaves six categories of pills, which is what this report focuses on. We evaluate and compare the drugs is all six groups. We do not evaluate the injectable drugs, including the newest one, Byetta (exenatide). We also don't compare diabetes pills with treatment with insulin or combination treatments consisting of injectable drugs.

Note that even though most people prefer to avoid injections, insulin and other injectable diabetes drugs often become necessary if diet, exercise, and pills fail to keep blood sugar under control.

Like all drugs, the names of the six diabetes drug groups and the names of the individual medicines in those groups are not easy to pronounce or remember. We do our best in this report to keep things simple but unfortunately we can't avoid using these complex names.

The table below presents the groups of diabetes drugs, including those now available in combination form. The table on the next page presents the individual drugs, with their generic and brand names. We indicate whether the class has a generic available and whether an individual drug is available in generic form. Generics are much less expensive.

As you can see, the sulfonylureas and metformin are older medicines now available in generic form, while the thiazolidinediones, alpha-glucosidase inhibitors, and meglitinides are newer. Januvia (sitagliptin) was approved by the Food and Drug Administration in October 2006. It is the first in a new class of diabetes drugs.

| Type of Drug | Individual Drugs *(Brand and generic names)* | Available as a Generic? |
|---|---|---|
| Sulfonylureas | *Brands:* Amaryl, Diabeta, Glynase Prestab, Glucotrol, Glucotrol XL, Micronase<br>*Generics:* Glimepiride, Glipizide, Glyburide | Yes |
| Biguanides | *Brands:* Glucophage, Glucophage XR,<br>*Generics:* Metformin | Yes |
| Thiazolidinediones | Actos, Avandia | No |
| Alpha-glucosidase inhibitors | Precose, Glyset | No |
| Meglitinides | Prandin, Starlix | No |
| Dipeptidyl peptidase 4 inhibitors | Januvia | No |
| Combinations of sulfonylureas plus metformin | *Brands:* Glucovance, Metaglip<br>*Generics:* known by generic names of the two drugs | Yes |
| Other Combinations | Actosplus Met, Avandaryl, Avandamet, Duetact, Janumet | No |

| Generic Name | Brand Name (s) | Available as a Generic? |
|---|---|---|
| *Thiazolidinediones* | | |
| Pioglitazone | Actos | No |
| Rosiglitazone | Avandia | No |
| *Meglitinides* | | |
| Repaglinide | Prandin | No |
| Nateglinide | Starlix | No |
| *Alpha-glucosidase Inhibitors* | | |
| Acarbose | Precose | No |
| Miglitol | Glyset | No |
| *Biguanides* | | |
| Metformin | Glucophage, Glucophage XR* | Yes |
| *Sulfonylureas* | | |
| Glyburide/ glibenclamide | Diabeta, Glynase, Micronase, Prestab | Yes |
| Glipizide | Glucotrol, Glucotrol XL* | Yes |
| Glimepiride | Amaryl | Yes |
| *Dipeptidyl peptidase 4 inhibitors* | | |
| Sitagliptin | Januvia | No |

*XR=extended release, XL=long-acting

Our evaluation of diabetes drugs is based largely on a thorough, independent review of the scientific research on diabetes drugs. About 200 studies were closely examined out of thousands screened. The review was conducted in 2006-2007 by a team of physician researchers at the Johns Hopkins University Evidence-based Practice Center. This team conducted the review as part of the Effective Health Care Program sponsored by the Agency for Healthcare Research and Quality, a federal agency. The full report is available at www.effectivehealthcare.ahrq.gov/reports/final.cfm. Additional sources were used to update this review, including those used to evaluate Januvia which was not addressed in the Johns Hopkins study.

Neither the Johns Hopkins University Evidence-based Practice Center nor the Agency for Healthcare Research and Quality are in any way responsible for the advice and recommendations in this report. These entities also played no role in selecting our *Best Buy* drugs; Consumers Union is solely responsible for those.

*This report was updated in February 2009.*

# What Are the Oral Diabetes Medicines and Who Needs Them?

The six types of diabetes medicines work in different ways. But they all: (a) lower blood sugar levels; (b) help improve the body's use of glucose, (c) decrease the symptoms of high blood sugar, (d) help keep people with diabetes functioning normally; and (e) help prevent the complications and organ-damaging effects that diabetes can cause.

The complexity of the way the different diabetes drugs work defies simple explanation. But it's useful to know the basics.

- The sulfonylureas and meglitinides increase the secretion of insulin by the pancreas.
- Metformin inhibits glucose production by the liver and decreases insulin resistance.
- The alpha-glucosidase inhibitors delay absorption of glucose by the intestine.
- The thiazolidinediones decrease insulin resistance.
- Januvia promotes the release of insulin from the pancreas after eating a meal.

Since the drugs work in different ways, they are sometimes used in combination to enhance the effectiveness of treatment. Indeed, 25 to 50 percent of people with diabetes who start taking one type of medicine will need another type (or insulin) within six years to keep their blood sugar under control. But all will also need to alter their diets and lifestyles as well – losing weight if needed, dietary changes (such as cutting back on carbohydrates), quitting smoking, and becoming more physically active.

Evidence strongly supports the additive effect of lifestyle changes plus medicines. But several studies also show *conclusively* that many people with diabetes can lower their blood sugar levels almost as much with lifestyle changes alone as with medicines, especially in the early stages of their disease.

Thus, given that (a) all the diabetes drugs have the potential to cause side effects and (b) lifestyle changes have benefits to your health beyond controlling blood sugar, most doctors will recommend you try diet and lifestyle modifications *first* – before you try a drug. Many people with diabetes, however, also have high blood pressure and/or elevated cholesterol, or have been diagnosed with coronary artery or vascular disease. If you are in this category, your doctor may prescribe a diabetes drug when you are diagnosed, along with diet and lifestyle changes and classes in diabetes self-management.

Indeed, so many diabetics have other conditions and heart disease risk factors that doctors commonly treat them as "multi-disease" patients whose care and various medications must be managed particularly closely. Because heart disease risk factors, including diabetes, take a cumulative toll, medical groups and physician organizations have set aggressive goals for people with diabetes who have multiple conditions. Table 1 on page 11 presents these.

Treatment with lifestyle changes and drugs has short-term, medium-term, and long-term goals. In the short-term, it aims to get your fasting blood glucose below 110mg/dl (below 100mg/dl may be better) and to eliminate or significantly reduce your symptoms.

| Table 1. Goals for People with Diabetes | |
|---|---|
| Measures | Recommended Goal |
| *Blood Sugar* | |
| Fasting blood glucose | Below 110mg/dl (Below 100 is better) |
| Post-meal (2-hour) blood glucose | Below 180mg/dl (Below 140 or so is better) |
| HemoglobinA1c (HbA1c) | 6.5% – 7.0% |
| *Cholesterol* | |
| Total cholesterol | Below 200mg/dl |
| LDL ("bad") cholesterol | Below 100 mg/dl |
| HDL ("good") cholesterol | Above 40mg/dl for men and 50 mg/dl for women |
| *Triglycerides* | Below 150 mg/dl |
| *Blood pressure* | Below 130/80 mmHg |

Sources: American Diabetes Association; American Association of Clinical Endocrinologists; International Diabetes Federation; National Cholesterol Education Program; Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; recent studies.
Definitions: LDL= low-density lipoprotein cholesterol; HDL= high-density lipoprotein cholesterol; mg = milligrams; dl=deciliter of blood; mmHg = millimeters mercury.

In the medium and long-term, it aims to get your HbA1c measure down below a certain level, and keep it there.

As mentioned already, the HbA1c test is the one your doctor will use to track treatment success (or failure). It measures glucose levels chemically bound to hemoglobin, a protein carried by red blood cells. The current recommended goal for HbA1c is expressed as a percentage. If you have diabetes, the magic number is around 7 percent. Below that may be better for some patients.

Many studies show that an HbA1c level below 7 percent is associated with a lower risk of diabetes complications and premature death. However, importantly for this report, most studies of the oral diabetes drugs have only looked at the affects on HbA1c for a year or less.

Although shooting for an even lower HbA1c level – below 6.5 percent – that's closer to the range found in healthy people who don't have diabetes has been promoted in the past, it's now unclear whether that is better for most diabetes patients. One recent study, for example, found that people with diabetes who achieved an average HbA1c level of 6.4 percent over 3.5 years had an increased risk of death and *no reduction in cardiovascular problems* compared with patients whose HbA1c was maintained at 7.5 percent. However, the participants in this study were at high risk of cardiovascular problems or already had cardiovascular disease when they enrolled, so these results may not apply to all people with diabetes.

Also, two other recent studies did not find an increased risk of death in patients who maintained their HbA1c below 6.5 percent. But these studies were consistent with the one described just above in that they also failed to show a reduction in cardiovascular events (like a heart attack) or deaths.

Given these results and the evolving science, the American Diabetes Association and other diabetes experts now recommend keeping HbA1c around or below 7 percent for most patients, but not below 6.5 percent. Also, a higher HbA1c goal may be appropriate for certain patients, including those with a history of repeated episodes of low blood sugar, coronary heart disease, stroke or limited life expectancies.

Another medium-term and long-term goal of treatment is to make sure you are free of diabetes complications as time goes on. This takes constant monitor-

## Side Effects of Diabetes Drugs

*Most of the side effects listed here ease over time or stop when the medication is discontinued. However, a few can be permanent in certain people*

*Common*

- Hypoglycemia or low blood sugar (usually minor if caught in time but can be serious or fatal if not treated; symptoms include profuse sweating, tremor, shakiness, dizziness, hunger. When serious, includes mental confusion, coma, and risk of stroke or death)
- Weight gain
- Gastrointestinal side effects (abdominal pain, nausea, vomiting, diarrhea, gassiness, and bloating)
- Edema (fluid in legs and ankles)
- Increase in "bad" cholesterol (LDL)

*Uncommon*

- Congestive heart failure
- Anemia (low red blood cell counts)
- Allergic reactions

*Very Rare*

- Thrombocytopenia (low blood platelet counts)
- Lactic acidosis (build up of acid in the blood)
- Leukopenia (low white blood cell counts)
- Macular edema (eye problems)
- Liver disease/liver failure

ing. Indeed, the intensity of care needed by most people with diabetes is such that experts advise all patients to be cared for in formal diabetes programs if possible.

Part of the purpose of such programs is to track the drugs you are taking and at what dose. Your doctors and caregivers will recommend changes if your blood sugar is not controlled. In fact, many doctors will encourage you to adjust the doses of your medicines based on the blood sugar readings you take yourself.

If you have good health insurance, diabetes self-management programs are usually accessible. Such programs (which can be expensive) usually include a dietician, exercise experts, and doctors that specialize in diabetes care (endocrinologists). The team may also include a cardiologist, neurologist, ophthalmologist, kidney expert, and a foot specialist. You will also get training in self-glucose monitoring and other self-care.

A conscientious primary care doctor whose practice has support staff with diabetes training can do just as good a job at managing patients with the condition as formal programs. People without insurance or with inadequate coverage who have limited access to formal diabetes programs should try to find such a doctor.

### Safety and Side Effects

All the diabetes medicines can have side effects. Those vary from drug class to drug class and medicine to medicine. Generally, the risks posed by diabetes drugs are not an impediment to using them if you truly need one. That is, for most people, the benefits of the drugs far outweigh the risks.

Even so, side effects can keep people from taking their diabetes pills. On average, 10 to 20 percent of people with diabetes stop taking their pills due to side effects. And significant side effects occur in about 1 of every 100 people taking diabetes pills.

Most notably, some diabetes drugs can cause low blood sugar, or hypoglycemia. This is a vexing side effect and one that leads some doctors to prescribe one diabetes drug over another. The symptoms of hypoglycemia are listed in the box on this page. Unfortunately, some people do not have minor symptoms to warn them that their blood sugar is getting dangerously low. That's one reason your doctor will emphasize to you that you must check your blood sugar regularly.

The other big, worrisome side effect of some of the diabetes drugs is weight gain, or difficulty losing weight. Since many diabetics are trying to lose weight, this side effect can also be very frustrating.

The box on this page gives a general run down of the side effects linked to diabetes drugs. The potential side effects of each drug are discussed at more length in the next section, which also compares the drugs across a range of criteria (including their cost) and presents our *Best Buy* choices.

# Choosing an Oral Diabetes Medicine — Our *Best Buy* Picks

The good news is that the diabetes drugs have been compared to each other in many good studies, and some of the drugs have been used for years and helped millions of people. The bad news is that most of the careful studies have not tracked the effects of the drugs (pro and con) over many years. Most followed people for just a year or less.

Even so, the studies help clarify the benefits and adverse effects of most diabetes drugs, and signal typical and expected effects among a group of people with diabetes. But very importantly, such studies do not reveal how a specific person with diabetes will respond to any particular drug. Only your doctor and you can decide precisely which drug or drug combination is best for you given your health status, weight, other medical needs, and the severity of your diabetes. And only you and your doctor can track how well a particular drug or combination of drugs is helping you, or not helping you.

Tables 2, 3 and 4 on pages 16, 17 and 18 summarize the comparative evidence on the diabetes drugs. The tables reflect the results from more than 200 studies. Table 2 presents summary evidence of the various classes of diabetes drugs. Table 3 is more specific, with detailed information on the individual drugs. As such, Table 3 takes a bit more time to figure out. But it contains information unique to this report and which may be valuable for your treatment decision.

Table 4 presents a run-down of the pros and cons of each drug class. The tables contain some material that is duplicative. On balance, though, they give you three ways to assess the important differences among diabetes drugs.

Our evaluation leads to the following overall conclusions:

- *The newer drugs are no better.* The thiazolidinediones, meglitinides, alpha-glucosidase inhibitors, and dipeptidyl peptidase 4 inhibitors (all more recently developed) are no more effective than the sulfonylureas and metformin (which have been around for decades). In fact, three of the newer medicines – acarbose, miglitol, and nateglinide – decrease HbA1c less than the other drugs.

- *The newer drugs are no safer.* As discussed in the previous sections and presented in Tables 2, 3 and 4, all diabetes pills have the potential to cause adverse effects – both minor and serious.

- *Metformin emerges as a superior drug based on the available evidence.* This medicine lowers HbA1c the same amount or more than other diabetes drugs, does not cause weight gain, decreases low-density lipoprotein (LDL) cholesterol and triglycerides, and appears to have the safest profile when comparing serious side effects in people who do not have kidney, liver, or heart disease. As further discussed below, however, certain patients should not take metformin.

- *Taking two diabetes drugs can have a positive additive affect on reducing HbA1c.* This is a major plus for the many people with diabetes whose blood glucose is not well controlled by a single drug. The downside is that taking two drugs poses a higher risk of side effects. If lower doses of each drug are used in combination, the added risk of side effects often can be reduced.

- *The newer drugs are more expensive.* The newer oral diabetes medicines cost many times more than the older ones. (See Table 5 beginning on page 21)

As mentioned earlier, the diabetes drugs have distinctly different “safety profiles.” This factor may be the primary driver of your and your doctor’s decision – for initial and on-going treatment.

For example, the evidence clearly shows that the sulfonylureas pose a higher risk of hypoglycemia than metformin or the thiazolidinediones (Avandia and Actos). Specifically, between 9 and 22 percent of people taking one of the sulfonylurea drugs can expect to have an episode of potentially dangerous low blood sugar, compared to zero to 7 percent taking metformin.

The risk of hypoglycemia is about the same for the sulfonylureas and repaglinide (Prandin), but two recent studies suggest that repaglinide may cause less hypoglycemia in the elderly or in people who skip meals.

One of the newer classes of drugs poses an elevated risk of heart failure. Evidence overwhelmingly indicates that the thiazolidinediones (Avandia and Actos) pose a 1.5 to 2 times increased risk of congestive heart failure compared to other diabetes medicines. Between 1 and 3 people in 100 without a history of heart disease will develop the condition if they take one of these drugs. In contrast, metformin and the sulfonylureas do not raise the risk of heart failure in any significant way compared to the general risk of this condition among people with diabetes, which is higher than normal.

Because of the clear evidence of this heart failure risk, both Actos and Avandia carry a high-profile "black box" warning about it on their labels (guidance to doctors and patients on how to use them). If you are taking one of these medicines and have swelling of any part of your body, sudden weight gain, or breathing problems, you should contact your doctor immediately.

## Don't Take Avandia

In addition, Avandia's label now warns that the drug is associated with a possibly higher risk of heart attack. That warning is based on several studies done in the last few years. In one, Avandia was associated with a 43 percent greater risk of heart attack compared to other diabetes pills (though the "absolute" risk was still a relatively low 1 to 3 in 100 for people who had diabetes but not heart disease).

While more research is needed to verify the magnitude of the risk posed by Avandia – and whether it should remain available – we join other groups (including the American Diabetes Association, American Heart Association, and the American College of Cardiology) in urging you to talk to your doctor about the appropriateness of this choice. If your doctor prescribes Avandia as the first diabetes drug you take after diagnosis, you should question that decision.

Both Actos and Avandia have also been linked to a slightly increased risk of fractures of the upper and lower limbs, such as the wrist or ankle, in women. The risk was small – about 2 percent higher in people taking Avandia or Actos compared with those taking other diabetes drugs, according to preliminary studies.

As good as it looks in other ways, metformin has been associated with rare occurrences of lactic acidosis – a build up of lactic acid in the blood that can be fatal. This rare risk appears to exist mostly for people with diabetes who also have kidney disease and/or heart failure. As a result, such patients should not be prescribed metformin.

Minor but annoying side effects may also play a role in your choice of a diabetes medicine. For example, gastrointestinal side effects – including bloating, gas, nausea, and diarrhea – are more frequent with metformin and also acarbose.

## Our picks and recommendations

Taking effectiveness, safety, side effects, dosing, and cost into consideration, we have chosen the following as *Consumer Reports Best Buy Drugs* if your doctor has decided that you need medicine to control your diabetes:

- *Metformin* – alone or with glipizide or glimepiride
- *Glipizide* and *Glipizide Sustained Release* – alone or with metformin
- *Glimepiride* – alone or with metformin

All these medicines are available as low-cost generics, either alone or in combination. (See Table 5.) In recent years, a strong medical consensus has emerged in the U.S., Europe, and Australia that most newly diagnosed people with diabetes who need a medicine should first be prescribed metformin.

Based on the systematic evaluation of diabetes drugs that forms the basis of this report, we concur with that advice. Unless your health status prevents it, try metformin first. If metformin fails to bring your blood glucose into normal range, you may need a second drug. Most commonly that should be one of the two other *Best Buys* we have chosen. Should either of those trigger hypoglycemia, Actos may be an option you and your doctor will want to consider.

If you are unable to take metformin or do not tolerate it well, you face a choice of one of the sulfonylureas or a newer medicine as your first line medi-

cine. Despite the elevated risk of hypoglycemia, we recommend trying glipizide or glimepiride. If either of those triggers hypoglycemia, talk with your doctor about Actos. If glipizide, glimepiride, or Actos alone fail to bring your blood glucose into control and keep your HbA1c at or below 7 percent, your doctor will likely recommend a second drug.

If upon initial diagnosis your glucose and HbA1c are quite high, you may be prescribed a combination of two drugs at the beginning of treatment – usually metformin plus a sulfonylurea. Another option is Actos plus metformin.

Actos has been heavily promoted to doctors and consumers in the U.S. As a result, it may be overprescribed to people who would do just as well to take metformin and/or a sulfonylurea. Both Actos and Avandia (until recently) have been marketed specifically to minorities as well, but there is no good evidence that any diabetes medicine is more effective or safer in African-Americans, Hispanics, or American Indian patients than in other ethnic groups.

### Januvia – the newest diabetes drug

Januvia, too, has been widely advertised and promoted. It's the first in a new class of diabetes drugs, and could turn out to be a promising addition. But it has only been on the market for a few years and thus its effectiveness and safety profile is not yet clearly established.

For example, Januvia has not been shown to be any more effective than metformin or other drugs at lowering blood glucose and HbA1c. Also, although Januvia alone does not trigger hypoglycemia, the drug can lead to the condition when given in combination with one of the sulfonylurea drugs (a lower dose of the sulfonylureas may help reduce the risk). Until Januvia has been better studied and prescribed more broadly over a longer period, we would not recommend it as a first-line drug. Another drawback to Januvia is that it is significantly more expensive than generic versions of other diabetes drugs.

Finally, as a reminder, if your diabetes is not controlled by pills, you may have to take insulin or one of the other drugs available by injection only.

## Table 2. Summary of Comparative Effectiveness of Diabetes Drugs

| Outcome | Sulfonylureas vs. Metformin | Sulfonylureas vs Thiazolidinediones | Sufonylureas vs. Meglitinide[1] | Metformin vs. Thiazolidinediones |
|---|---|---|---|---|
| *Hemoglobin A1c* | No difference | No difference | No difference | No difference |
| *Weight* | Metformin better | No difference | No difference | Metformin better |
| *Blood Pressure* | No difference | No difference | Not enough evidence | No difference |
| *LDL (bad) cholesterol* | Metformin better | Sulfonylureas better | No difference | Metformin better |
| *HDL (good) cholesterol* | No difference | Thiazolidinediones better | No difference | Thiazolidinediones better |
| *Triglycerides* | Metformin better | No difference[2] | No difference | One thiazolidinedione better[3] |
| *Risk of Hypoglycemia* | Metformin better | Thiazolidinediones better | No difference | No difference |
| *Risk of GI problems* | Sulfonylureas better | Not enough evidence | Not enough evidence | Thiazolidinediones better |
| *Risk of Congestive Heart Failure* | No difference | Sulfonylureas better | Not enough evidence | Metformin better |
| *Risk of Anemia* | Not enough evidence | Sulfonylureas better | Not enough evidence | Metformin better |
| *Risk of Edema (fluid build-up)* | Not enough evidence | Sulfonylureas better | Not enough evidence | Metformin better |

Source: Bolen S., et al, *Comparative Effectiveness and Safety of Oral Diabetes Medications for Adults with Type 2 Diabetes.* http://www.effectivehealthcare.ahrq.gov/reports/final.cfm.

*Definitions:* "No difference" means that adequate or good studies have been done and when considered as a whole have found no difference between these two categories of drugs. "Not enough evidence" means not enough studies have been done, or the studies that have been done are not good enough to warrant a judgment about any differences between these two classes of drugs.

1. For repaglinide (Prandin) only.
2. Pioglitazone (Actos) decreased triglycerides while rosiglitizone (Avandia) increased triglycerides; thus, Actos showed similar effects to the sulfonylureas while Avandia was worse than the sulfonylureas. But no direct comparisons were available to draw firm conclusions.
3. Pioglitazone (Actos) was better than metformin while rosiglitizone (Avandia) was worse.

## Table 3. Effects of Diabetes Drugs on Specific Measures

*A down arrow (▼) means a decrease or decline; an up arrow (▲) means increase; and a diamond (◆) means no meaningful effect or change. IE = Insufficient Evidence. Brand names are not given for drugs available as generics.*

| | Average point reduction HbA1c (percent) | Average point change in blood pressure (mmHg) | Average absolute change in LDL cholesterol (mg/dL) | Average absolute change in HDL cholesterol (mg/dL) | Average absolute change in Triglycerides (mg/dL) | Risk of Hypo-glycemia (% of people)[1] | Average change in weight (lbs) |
|---|---|---|---|---|---|---|---|
| *Sulfonylureas* | | | | | | | |
| Glyburide | ▼ 1.3-1.8 | ◆ | ◆ | ◆ | ▼ 10-20 | 10-22% | ▲ 5-10 |
| Glipizide | ▼ 1.3-1.8 | ◆ | ◆ | ◆ | ▼ 10-20 | 10-15% | ▲ 5-10 |
| Glimepiride | ▼ 1.3-1.8 | ◆ | ◆ | ◆ | ▼ 10-20 | 9-14% | ▲ 5-10 |
| *Biguanides* | | | | | | | |
| Metformin | ▼ 0.9-1.4 | ◆ | ▲ 5-7 | ◆ | ▼ 15-25 | 0-7% | ◆ |
| *Thiazolidinediones* | | | | | | | |
| Pioglitazone (Actos) | ▼ 0.8-1.2 | ◆ | ▲ 8-12 | ▲ 5 | ▼ 35-45 | 0-3% | ▲ 5-10 |
| Rosiglitazone (Avandia) | ▼ 0.9-1.4 | ◆ | ▲ 12-15 | ▲ 3 | ▲ 10-20 | 4-11% | ▲ 5-10 |
| *Meglitinides* | | | | | | | |
| Repaglinide (Prandin) | ▼ 0.8-2.0 | IE[2] | ◆ | ◆ | ▼ 10-15 | 11-32% | ▲ 5-10 |
| Nateglinide (Starlix) | ▼ 0.3-0.8 | IE | IE | IE | IE | 13%[3] | IE |
| *Alpha-glucosidase inhibitors* | | | | | | | |
| Acarbose[4] (Precose) | ▼ 0.6-0.9 | IE | ◆ | ◆ | ▼ 10-15 | 0-5% | ◆ |
| Miglitol[4] (Glyset) | ▼ 0.4-0.9 | IE | IE | IE | IE | IE | IE |
| *Dipeptidyl peptidase IV inhibitor* | | | | | | | |
| Sitagliptin[5] (Januvia) | ▼ 0.6-0.8 | IE | ◆ | ◆ | ◆ | Low | ◆ |

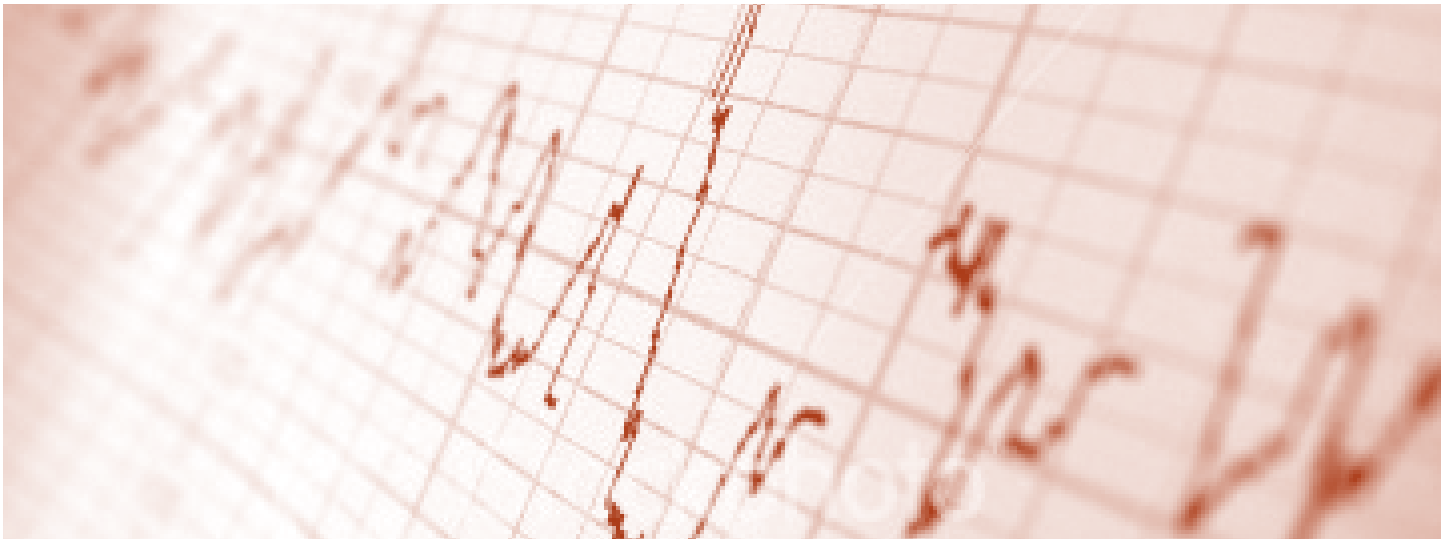
## Table 3. Effects of Diabetes Drugs on Specific Measures (continued)

*A down arrow (▼) means a decrease or decline; an up arrow (▲) means increase; and a diamond (◆) means no meaningful effect or change. IE = Insufficient Evidence. Brand names are not given for drugs available as generics.*

| | Average point reduction HbA1c (percent) | Average point change in blood pressure (mmHg) | Average absolute change in LDL cholesterol (mg/dL) | Average absolute change in HDL cholesterol (mg/dL) | Average absolute change in Triglycerides (mg/dL) | Risk of Hypo-glycemia (% of people)[1] | Average change in weight (lbs) |
|---|---|---|---|---|---|---|---|
| *Selected Combinations* | | | | | | | |
| Metformin + sulfonylurea (Glucovance, Metaglip) | ▼ 1.7-2.3 | IE | ▼ 5-7 | ◆ | ▼ 20-40 | 14-28% | ▲ 5-10 |
| Metformin + rosiglitazone (Avandamet) | ▼ 1.3-2.0 | IE | ▲ 12-15 | ▲ 3 | ◆ | 0-7% | ▲ 5-10 |
| Sulfonylurea + rosiglitazone (Avandaryl) | ▼ 1.7-2.3 | IE | ▲ 10-12 | ▲ 3 | ◆ | 18-30% | ▲ 5-10 |

Definitions/Key: ◆ No meaningful change; ▼ Significant decrease; ▲Significant increase; IE=insufficient data; lbs=pounds; mg/dl=milligrams per deciliter of blood; mmHg=millimeters mercury; HbA1c=hemoglobin A1c; LDL=low-density lipoprotein cholesterol; HDL= high-density lipoprotein cholesterol.

1. Results mostly come from short-duration studies lasting 3 months to 1 year. There are only a few studies longer than one year which show slightly higher rates of hypoglycemia but similar comparative results.
2. IE = insufficient evidence for this drug on this measure to reach any meaningful conclusions.
3. Results based on one short-term study (<1 year).
4. Results are based on data from a systematic review plus a large randomized study.
5. Preliminary data based on product label and a monograph by the Veteran's Administration's national pharmacy service.



## Table 4. Advantages and Disadvantages of the Diabetes Drugs

| Advantages: | Disadvantages: |
|---|---|
| **The sulfonylureas (glyburide, glimepiride, glipizide)** | |
| - Fast onset of action<br>- No affect on blood pressure<br>- No affect on LDL cholesterol<br>- Convenient dosing<br>- Low cost | - Weight gain (5 to 10 pounds on average)<br>- Heightened risk of hypoglycemia<br>- Glyburide has slightly higher risk of hypoglycemia compared with glimepiride and glipizide |
| **Metformin** | |
| - Low risk of hypoglycemia<br>- Not linked to weight gain<br>- Good affect on LDL cholesterol<br>- Good affect on triglycerides<br>- No affect on blood pressure<br>- Low cost | - Higher risk of GI side effects (nausea and diarrhea)<br>- Cannot be taken by people with diabetes who have moderate kidney disease or heart failure because of risk of lactic acid build-up<br>- Less convenient dosing |
| **The alpha-glucosidase inhibitors (acarbose, miglitol)** | |
| - Slightly lower risk of hypoglycemia compared to sulfonylureas<br>- Not associated with weight gain<br>- Decreases triglycerides<br>- No affect on cholesterol | - Less effective than most other diabetes pills in lowering HbA1c. Higher risk of GI side effects than other diabetes pills except metformin<br>- Inconvenient dosing<br>- High cost |
| **The thiazolidinediones (Actos, Avandia)** | |
| - Low risk of hypoglycemia<br>- Slight increase in “good” (HDL) cholesterol<br>- Actos linked to decreased triglycerides<br>- Convenient dosing | - Higher risk of heart failure<br>- Weight gain (5 to 10 pounds)<br>- Linked to higher risk of edema (fluid-up)<br>- Linked to higher risk of anemia<br>- Increase in “bad” (LDL) cholesterol<br>- Avandia linked to increased triglycerides and higher risk of heart attack<br>- Slower onset of action<br>- Rare risk of liver problems; requires monitoring<br>- Linked to increased risk of upper and lower limb fractures<br>- High cost |

## Table 4. Advantages and Disadvantages of the Diabetes Drugs (continued)

| Advantages: | Disadvantages: |
|---|---|
| **The meglitinides (nateglinide, repaglinide)** | |
| - No bad effect on cholesterol<br>- Rapid onset of action | - Repaglinide associated with risk of hypoglycemia and weight gain similar to sulfonylureas<br>- Nateglinide has less effect on HbA1c<br>- Inconvenient dosing<br>- High cost |
| **Januvia (sitagliptin)*** | |
| - Apparent low risk of hypoglycemia<br>- Few known side effects (but it is a new drug)<br>- No weight gain (but it may increase weight and cause hypoglycemia when used in combination with glimepiride or glimepiride combined with metformin)<br>- Convenient dosing | - Reduces HbA1c less than several other diabetes drugs<br>- May only be valuable as a second drug; use as a first drug only if unable to take other diabetes drugs, until further research is conducted<br>- Less data on potential side effects compared to older drugs<br>- High cost |

* This is a new drug approved in October 2006. There is less research and experience with it than with other diabetes medicines. In addition, no studies have followed patients taking it for longer than one year.

Sources: Source: Bolen S., et al, Comparative Effectiveness and Safety of Oral Diabetes Medications for Adults with Type 2 Diabetes. http://www.effective-healthcare.ahrq.gov/reports/final.cfm; "Oral hypoglycemics in the treatment of type 2 diabetes"; Therapeutic Insights – American Medical Association (June 2007); Januvia labeling and available material

## Table 5: Cost of Diabetes Drugs

| Generic Name and Dose | Brand Name (or Generic) | Number of Pills (Per day)[1] | Total Daily Dose[1] | Average Monthly Cost[2] |
|---|---|---|---|---|
| Glyburide 5mg | Generic | One | 5mg | $6 |
| Glyburide 5mg | Micronase | One | 5mg | $47 |
| Glyburide 5mg | Diabeta | One | 5mg | $38 |
| Glyburide 5mg | Generic | Two | 10mg | $12 |
| Glyburide 5mg | Micronase | Two | 10mg | $94 |
| Glyburide 5mg | Diabeta | Two | 10mg | $76 |
| Glyburide micronized 6mg | Glynase | One | 6mg | $68 |
| Glyburide micronized 6mg | Generic | One | 6mg | $7 |
| Glipizide 10mg | Glucotrol | One-Two | 10mg-20mg | $42-$84 |
| CR BEST BUY Glipizide 10mg | Generic | One-Two | 10mg-20mg | $4-$8 |
| Glipizide 5mg, sustained release | Glucotrol XL | One | 5mg | $25 |
| CR BEST BUY Glipizide 5mg, sustained release | Generic | One | 5mg | $13 |
| Glipizide 10mg sustained release | Glucotrol XL | One-Two | 10mg-20mg | $45-$90 |
| CR BEST BUY Glipizide 10mg, sustained release | Generic | One-Two | 10mg-20mg | $23-$46 |
| Glimepiride 1mg | Amaryl | One | 1mg | $22 |
| CR BEST BUY Glimepiride 1mg | Generic | One | 1mg | $6 |
| Glimepiride 1mg | Amaryl | One | 2mg | $35 |
| CR BEST BUY Glimepiride 2mg | Generic | One | 2mg | $7 |
| Metformin 500mg | Glucophage | Three | 1500mg | $117 |
| CR BEST BUY Metformin 500mg | Generic | Three | 1500mg | $18 |
| Metformin 1000mg | Glucophage | Two | 2000mg | $154 |
| CR BEST BUY Metformin 1000mg | Generic | Two | 2000mg | $18 |

## Table 5: Cost of Diabetes Drugs (continued)

| Generic Name and Dose | Brand Name (or Generic) | Number of Pills (Per day)[1] | Total Daily Dose[1] | Average Monthly Cost[2] |
|---|---|---|---|---|
| Sitagliptin 100mg | Januvia | One | 100mg | $225 |
| Sitagliptin 50mg | Januvia | One | 50mg | $232 |
| Pioglitazone 15mg | Actos | One | 15mg | $164 |
| Pioglitazone 30mg | Actos | One | 30mg | $241 |
| Rosiglitazone 2mg | Avandia | Two | 4mg | $190 |
| Rosiglitazone 4mg | Avandia | One-Two | 4mg-8mg | $137-$274 |
| Repaglinide 1mg | Prandin | Three | 3mg | $195 |
| Repaglinide 2mg | Prandin | Three | 6mg | $186 |
| Nateglinide 60mg | Starlix | Three | 180mg | $174 |
| Nateglinide 120mg | Starlix | Three | 360mg | $174 |
| Acarbose 50mg | Precose | Three | 150mg | $114 |
| Acarbose 100mg | Precose | Three | 300mg | $129 |
| Miglitol 50mg | Glyset | Three | 150mg | $111 |
| Miglitol 100mg | Glyset | Three | 300mg | $132 |
| Metformin+glipizide 250mg/2.5mg | Metaglip | Two | 250mg/2.5mg-500mg/5mg | $74 |
| Metformin+glipizide 250mg/2.5mg | Generic | Two | 500mg/5mg | $50 |
| Metformin+glipizide 500mg/2.5mg | Metaglip | Two | 1000mg/5mg | $86 |
| Metformin+glipizide 500mg/2.5mg | Generic | Two | 1000mg/5mg | $56 |
| Metformin+glyburide 250mg/1.25mg | Glucovance | Two | 500mg/2.5mg | $88 |
| Metformin+glyburide 250mg/1.25mg | Generic | Two | 500mg/2.5mg | $44 |

## Table 5: Cost of Diabetes Drugs (continued)

| Generic Name and Dose | Brand Name (or Generic) | Number of Pills (Per day)[1] | Total Daily Dose[1] | Average Monthly Cost[2] |
|---|---|---|---|---|
| Metformin+glyburide 500mg/2.5mg | Glucovance | Two | 1000mg/5mg | $94 |
| Metformin+glyburide 500mg/2.5mg | Generic | Two | 1000mg/5mg | $50 |
| Pioglitazone+ metformin 15mg/850mg | Actoplus Met | One | 850mg/15mg | $123 |
| Pioglitazone+ metformin 15mg/500mg | Actoplus Met | Two | 1000mg/30mg | $250 |
| Rosiglitazone+ glimepiride 4mg/1mg | Avandaryl | One | 4mg/1mg | $157 |
| Rosiglitazone+ glimepiride 4mg/2mg | Avandaryl | One | 4mg/2mg | $154 |
| Rosiglitazone+ metformin 2mg/500mg | Avandamet | Two | 4mg/1000mg | $162 |
| Rosiglitazone+ metformin 2mg/1000mg | Avandamet | Two | 4mg/2000mg | $168 |
| Sitagliptin + metformin mg/500mg | Janumet | Two | 100mg/1000mg | $232 |
| Sitagliptin + metformin 50mg/1000mg | Janumet | Two | 100mg/2000mg | $228 |

* For space reasons, not all doses are listed.

1. As commonly or usually recommended.
2. Prices reflect nationwide retail average for September 2008, rounded to the nearest dollar. Information derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Health, Pharmaceutical Audit Suite. Wolters Kluwer Health is not involved in our analysis or recommendations.

## Talking With Your Doctor

It's important for you to know that the information we present in this report is not meant to substitute for a doctor's judgment. But we hope it will help your doctor and you arrive at a decision about which diabetes drug and at what dose is best for you.

Bear in mind that many people are reluctant to discuss the cost of medicines with their doctors and that studies show doctors do not routinely take price into account when prescribing medicines. Unless you bring it up, your doctors may assume that cost is not a factor for you.

Many people (including many physicians) also believe that newer drugs are always or almost always better. While that's a natural assumption to make, the fact is that it's not true. Studies consistently show that many older medicines are as good as, and in some cases better than, newer medicines. Think of them as "tried and true," particularly when it comes to their safety record. Newer drugs have not yet met the test of time, and unexpected problems can and do crop up once they hit the market.

Of course, some newer prescription drugs are indeed more effective and safer. Talk with your doctor about the pluses and minuses of newer versus older medicines, including generic drugs.

Prescription medicines go "generic" when a company's patents on a drug lapse, usually after about 12 to 15 years. At that point, other companies can make and sell the drug.

Generics are almost always much less expensive than newer brand name medicines, but they are not lesser quality drugs. Indeed, most generics remain useful medicines even many years after first being marketed. That is why today more than half of all prescriptions in the U.S. are for generics.

Another important issue to talk with your doctor about is keeping a record of the drugs you are taking. There are several reasons for this:

- First, if you see several doctors, they may not always tell each other which drugs have been prescribed for you.
- Second, it is very common for doctors today to prescribe several medicines for you before finding one that works well or best, mostly because people vary in their response to prescription drugs.
- Third, more and more people today take several prescription medications, nonprescription drugs and supplements all at the same time. Many of these interact in ways that can be very dangerous.
- And fourth, the names of prescription drugs—both generic and brand—are often hard to pronounce and remember.

For all these reasons, it's important to keep a list of the drugs you are taking, both prescription and nonprescription and including dietary supplements.

Always be sure, too, that you understand the dose of the medicine being prescribed for you and how many pills you are expected to take each day. Your doctor should tell you this information. When you fill a prescription at the pharmacy, or if you get it by mail, you may want to check to see that the dose and the number of pills per day on the pill bottle match the amounts that your doctor told you.

# How We Conducted Our Review of the Diabetes Drugs

Our evaluation is based in large part on an independent review of the scientific evidence on the effectiveness, safety, and adverse effects of the oral diabetes medicines conducted by the Johns Hopkins University-evidence based Practice Center under contract number 290-02-0018 with the Agency for Healthcare Research and Quality. This analysis reviewed hundreds of studies, including those conducted by the drugs' manufacturers. A synopsis of the results of this analysis, written by the researchers at Johns Hopkins, forms the basis of portions of this report.

However, no statement in this report should be construed as the official position of the Johns Hopkins Evidence-based Practice Center, the Agency for Healthcare Research and Quality, or the U.S. Department of Health and Human Services. In particular, none of those entities played any role in our selection of the *Best Buy* diabetes drugs. Consumers Union and *Consumer Reports Best Buy Drugs* is solely responsible for those, and for all other specific advice and recommendations in this report.

Additional sources used in writing this report include:

- An analysis of selected classes of diabetes drugs conducted by the Drug Effectiveness Review Project (DERP), a 15-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.
- The results of two recent reviews of oral diabetes drugs by the Cochrane Collaboration
- An American Medical Association monograph on the oral diabetes drugs
- *Diabetes: Treatment Options Report*, an April 2006 publication released by the California HealthCare Foundation and prepared by the University of California, Davis Center for Health Services Research in Primary Care
- A Veteran's Administration monograph on diabetes drugs
- Recent guidelines issued by the American Diabetes Association and American College of Cardiology
- Selected recent articles in peer-reviewed journals (See References)

The prescription drug costs we cite were obtained from a healthcare information company that tracks the sales of prescription drugs in the U.S. Prices for a drug can vary quite widely, even within a single city or town. All the prices in this report are national averages based on sales of prescription drugs in retail outlets. They reflect the cash price paid for a month's supply of each drug in September 2008.

Consumers Union and *Consumer Reports* selected the *Best Buy Drugs* using the following criteria. The drug had to:

- Be as effective or more effective than other oral diabetes medicines
- Have a safety record equal to or better than other diabetes medicines
- Cost roughly the same or less than other diabetes medicines

The *Consumers Reports Best Buy Drugs* methodology is described in more detail in the methods section at ConsumerReportsHealth.org/BestBuyDrugs.

## About Us

Consumers Union, publisher of *Consumer Reports*™ magazine, is an independent and non-profit organization whose mission since 1936 has been to provide consumers with unbiased information on goods and services and to create a fair marketplace. Consumers Union's main Web site is ConsumerUnion.org. The magazine's Web site is ConsumerReports.org. Our new health Web site is ConsumerReportsHealth.org.

*Consumer Reports Best Buy Drugs*™ is a public education project administered by Consumers Union. It is partially grant funded. Principle current outside funding comes from the state Attorney General Consumer and Prescriber Education Grant Program, which is funded by the multi-state settlement of consumer fraud claims regarding the marketing of the prescription drug Neurontin.

The Engelberg Foundation provided a major grant to fund the creation of the project from 2004 to 2007. Additional initial funding came from the National Library of Medicine, part of the National Institutes of Health.

A more detailed explanation of the project is available at ConsumerReportsHealth.org.

## Sharing this Report

This report should not be viewed as a substitute for a consultation with a medical or health professional. The information is meant to enhance communication with your doctor, not replace it. Use of our drug reports is also at your own risk. Consumers Union can not be liable for any loss, injury, or other damages related to your use of this report.

You should not make any changes in your medicines without first consulting a physician.

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