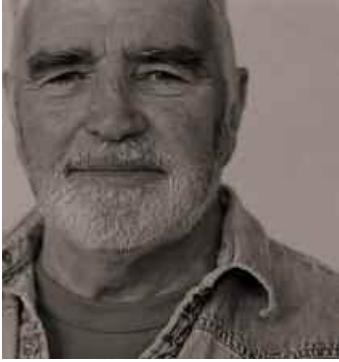


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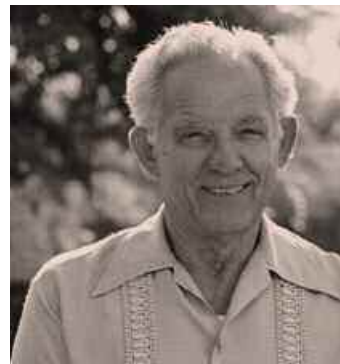
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Treating Type 2 Diabetes:

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 21 million people in the U.S. with type 2 diabetes control their blood sugar when diet and lifestyle change are not enough. Our evaluation of these medicines found the following:

- *Newer drugs are no better.* One older type of medicine, the sulfonylureas, and an older drug named metformin work just as well as four newer classes. 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' side effect "profiles" may be the most important factor in your choice.
- *Newer drugs are more expensive.* The newer diabetes medicines cost many times more than the older ones.
- *Taking more than one diabetes drug can improve blood sugar control.* Many people with diabetes do not get enough help from one drug. 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 (\$10 to \$60). 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 drugs cause problems, Actos (pioglitazone) may be an option you and your doctor will want to consider. Actos and Avandia (rosiglitazone) have been heavily promoted to doctors and consumers, however, and have been over-prescribed.

This report was released and last updated in July 2007.

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 www.CRBestBuyDrugs.org.

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 in recent years. That includes thousands of children and young adults.

Type 2 diabetes used to be referred to as “adult onset” diabetes. No longer. In recent years, the incidence among young people has exploded. Much of that surge has been linked to the dramatic increase in the last 20 years in the number of young people who are overweight or obese and who are physically inactive.

The statistics are sobering. An estimated 21 million people in the U.S. have diabetes, about 7 percent of the population. 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. About 1.5 million people are newly diagnosed every year.

But despite widespread attention to the diabetes “epidemic,” about one in three people who have diabetes – some 7 million people – have not been diagnosed and do not know they have it. Timely diagnosis is no assurance either: a third of the people who have been diagnosed with diabetes fail to receive the medical care and medicines that research shows 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. It is as potent a predictor and risk factor for heart disease and heart attack as cigarette smoking, high blood pressure, and uncontrolled high cholesterol. When people with diabetes go untreated for years, the damage it causes 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 (neuropathy), kidney damage; damage to the eye and blindness; liver disease, impotence, poor wound healing, and susceptibility to infections that can fester and require amputations of toes, a foot, 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 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 they 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 but also because they are less likely to get good care).

At the same time, it is important to note that 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

Confusion about diabetes is still widespread. What is it and what is 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. Insulin is produced in the pancreas and plays a key role in regulating the level of glucose in your blood. Glucose is the body's main fuel, and is essentially the end product of eating any carbohydrates (pasta, bread, rice, grains, fruits, and vegetables). Your digestive system breaks down all carbohydrates into glucose. Glucose then enters the blood stream. It also gets stored in the liver as glycogen, a precursor of glucose.

Insulin 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 regular and normal.

In type 1 diabetes – 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. It is an “autoimmune” disease, which means that the part of the pancreas that produces insulin has been destroyed by errant immune cells. People with type 1 diabetes must inject insulin every day. About 1.5 to 2 million people in the U.S. have type 1 diabetes.

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: blood glucose, unable to enter the body's cells, rises. That rise leads to symptoms. And when the blood sugar reaches a certain high level it appears in the urine and causes an increase in the daily volume of urine.

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 especially to problems in the eyes and kidneys, the heart, 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 ideas about the causes of type 2 diabetes, and the insulin resistance that characterizes it. Studies show the disease has a strong genetic (hereditary) component. It runs in families. Another cause – or association – is also quite clear. That is overweight and obesity – due in some cases to a genetic propensity to overweight and obesity but in most cases 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 also means that 45 percent of people with diabetes are not overweight.

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 them – 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 well 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 have 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 you have either never had a blood sugar check or the last one was done a year or more ago, you should get your blood sugar checked 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 indicate that such broader 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, risks, your weight, and family history. Some doctors are inclined to check the blood sugars 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 not eating for 8 or more hours). If you have blood sugar levels of 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,” and 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 (fasting) 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. Namely, the most recent studies indicate that nearly 18 percent of the population – 54 million people – have what is called pre-diabetes, 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 (a) are at very high risk of developing diabetes and (b) at elevated risk of heart disease and stroke even if their glucose level never rises above 125 mg/dl.

In the most recent analysis of this – published in June 2007 – people 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 without diabetes. The study was of 10,428 people in Australia.

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

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 under a program that you'll stick to.

Lifestyle modifications have become a mainstay of treatment for people with full-blown diabetes, too. Studies consistently show that lifestyle changes alone – and particularly losing weight – can prevent the complications of diabetes. For some people, they 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, with diet and lifestyle changes and with medicines.

Oral diabetes medicines – pills you take by mouth – are thus just one treatment among several that doctors use to help people with diabetes and keep them healthy. That said, they are a critical element of treatment.

Today, nine classes of drugs are available to treat type 2 diabetes. That includes insulin and two other types of drugs that must be injected. That leaves six categories of pills. In this report we evaluate and compare all six groups, and the drugs in them. We do not evaluate the injectable drugs, including the newest one, Byetta (exenatide). We also don't compare treatment with insulin or the other injectable drugs with pills. And we do not

analyze another new diabetes drug – Exubera, a form of insulin that can be inhaled.

Note that even though most people prefer to avoid injections, insulin and other such drugs often become necessary if diet, exercise, and pills fail to keep their 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 to keep things simple but unfortunately we can't avoid using the drug category names and the names of the individual drugs.

The first table below presents the groups of diabetes drugs, including those now available in combination form. The second table presents the individual drugs, with their generic and brand names. In both, we indicate either whether the class has a generic available or whether an individual drug is available in generic form. Generics are much less expensive and become available after a drug has been on the market for some 10 or more years.

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 was approved by the Food



Type of Drug	Individual Drugs (Brand and generic names)	Available as a Generic?
Sulfonylureas	<i>Brands:</i> Amaryl, Diabeta, Glynase, Prestab, Glucotrol, Glucotrol XL, Micronase <i>Generics:</i> Glimepiride, Glipizide, Glyburide	Yes
Biguanides	<i>Brands:</i> Glucophage, Glucophage XR <i>Generics:</i> 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	<i>Brands:</i> Glucovance, Metaglip <i>Generics:</i> 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?
<i>Thiazolidinediones</i>		
Pioglitazone	Actos	No
Rosiglitazone	Avandia	No
<i>Meglitinides</i>		
Repaglinide	Prandin	No
Nateglinide	Starlix	No
<i>Alpha-glucosidase Inhibitors</i>		
Acarbose	Precose	No
Miglitol	Glyset	No
<i>Biguanides</i>		
Metformin	Glucophage, Glucophage XR*	Yes
<i>Sulfonylureas</i>		
Glyburide/ glibenclamide	Diabeta, Glynase, Micronase, Prestab	Yes
Glipizide	Glucotrol, Glucotrol XL*	Yes
Glimepiride	Amaryl	Yes
<i>Dipeptidyl peptidase 4 inhibitors</i>		
Sitagliptin	Januvia	No

*XR=extended release, XL=long-acting

and Drug Administration in October 2006. It is the first in a new class of diabetes drugs.

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 over the past 18 months 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, including several to evaluate Januvia which was not addressed in the Johns Hopkins analysis.

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 selected our *Best Buy* diabetes drugs; Consumers Union is solely responsible for those.

This report was released and last updated in July 2007.

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) may help prevent the complications, organ-damaging effects, and premature death 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.

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 a drug will need another type of drug (or insulin) within six years.

The plain fact is that most people with type 2 diabetes will eventually need to take medicine to keep their blood sugar controlled. 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 the two – drugs and lifestyle changes. But many studies also show conclusively that many people with diabetes can lower their blood sugar levels almost as much with modest lifestyle changes *alone* as with medicines, especially in the early stages of the disease.

Thus, given that (a) all the diabetes drugs have the potential to cause adverse effects and (b) lifestyle changes have benefits to your health beyond controlling blood sugar, most doctors will recommend you try diet and lifestyle 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



Table 1. Goals for People with Diabetes

Measures	Recommended Goal
<i>Blood Sugar</i>	
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)	Below 7% (Below 6.5% is better)
<i>Cholesterol</i>	
Total cholesterol	Below 200mg/dl
LDL ("bad" cholesterol)	Below 100 mg/dl (below 75 is better)
HDL ("good" cholesterol)	Above 40mg/dl for men and 50 mg/dl for women
<i>Triglycerides</i>	Below 150 mg/dl
<i>Blood pressure</i>	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.
 Definitions: LDL= low-density lipoprotein cholesterol; HDL= high-density lipoprotein cholesterol; mg = milligrams; dl=deciliter of blood; mmHg = millimeters mercury.

prescribe a diabetes drug when you are diagnosed, along with diet and lifestyle changes and classes in diabetes self-management.

Indeed, so many people with diabetes have other conditions and heart disease risk factors that doctors often treat them as “multi-disease” patients whose care and drugs must be managed particularly closely. Because heart disease risks 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 above 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 is better) and to eliminate or significantly reduce your symptoms.

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 7 percent. Below that is good. Above it is not good. (Technically anything above 6 percent is considered abnormal. So some doctors would rather see your HbA1c be 6.5 percent or lower.)

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 effects on HbA1c for a year or less.

Another medium-term and long-term goal of treatment is to make sure you are free of the well-known diabetes complications as time goes on. This takes constant monitoring. Indeed, the intensity of care needed by most people with diabetes is such that experts advise all to be cared for in formal diabetes programs.

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

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 a rare 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)
- Leucopenia (low white blood cell counts)
- Macular edema (eye problems)
- Liver disease/liver failure

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 or nutritionist, 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 people with the disease as a formal program. People without insurance or those with inadequate coverage should find such a doctor since they have limited access to formal diabetes programs.

Safety and Side Effects

All the diabetes medicines can have adverse 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 clearly outweigh the risks.

Even so, adverse 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. 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 often leads doctors to prescribe one diabetes drug over another. The symptoms of hypoglycemia are listed in the box to the left. Unfortunately, some people do not have minor symptoms to warn them that their blood sugar is getting dangerously low. That is 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 people with diabetes are trying to lose weight, this side effect can be particularly 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 Buys* 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 people, or the long-term effects of the drugs, over many years. Most followed people for just a year or less.

Even so, the studies help clarify the benefits and adverse effects of the 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 a 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.

Tables 2, 3 and 4 on pages 16 to 20 summarize the comparative evidence on the diabetes drugs. The tables reflect an evaluation of the results from more than 200 studies. Table 2 presents summary evidence of the various classes of 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 class of diabetes. The tables contain material that is duplicative. On balance, though, they give you three ways of assessing the important differences among the 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 section 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 diabetes drug based on the available evidence. This medicine lowers HbA1c the same amount or more than other drugs, does not cause weight gain, decreases low-density lipoprotein (LDL) 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, metformin can not be taken by everyone.
- *Taking two diabetes drugs has a positive additive effect on reducing HbA1c.* This is a major plus for 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 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.)

As mentioned earlier, the diabetes drugs have distinctly different “safety profiles.” It’s this that may drive 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). 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, for example.

The risk of hypoglycemia is about the same for the sulfonylureas and repaglinide, 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 in a 100 people without a history of heart disease will develop the condition. 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 mounting evidence on this link, in May 2007 the FDA requested that the manufacturers of Actos and Avandia put a high-profile “black box” warning about the risk of heart failure on the labels for the two drugs. 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.

In addition, Avandia has also recently been associated with a possibly higher risk of heart attack. In a study that received widespread media attention in the spring of 2007, 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 a 100 for people who had diabetes but no heart disease).

Notably, however, other studies comparing Avandia with other diabetes drugs or placebo have not found such a risk, and the type of study used to make the connection has limitations. The upshot is that more research is needed and no definitive conclusions can yet be reached about heart attack risks posed by Avandia.

If your doctor prescribes Avandia, we join other groups (including the American Diabetes Association, American Heart Association, and American College of Cardiology) in urging you to talk to him or her about the risks and benefits and the appropriateness of this choice. If in addition to diabetes, you have multiple risk factors for heart disease, we would advise against Avandia until further studies clarify whether it poses any heightened risk of heart attack.

Avandia also has been recently associated with an increased risk of fractures of the wrist and arm in women. This unexpected finding is being further investigated and needs confirmation.

As good as it looks in other ways, metformin has been associated with rare occurrences of lactic acidosis – the build up of lactic acid in the blood, which can lead to severe consequences. This rare risk appears to exist mostly for diabetics who also have moderate 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 particularly with acarbose than the other drugs.

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 in combination with glipizide or glimepiride
- *Glipizide and Glipizide Sustained Release* – alone or in combination with metformin
- *Glimepiride* – alone or in combination 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 alone.

Based on the systematic evaluation of diabetes drugs that forms the basis for this report, we concur with that advice: metformin first, unless your health status prevents it. If metformin fails to bring your blood

glucose into normal range, you may need a second drug. Most commonly that should be one of two other *Best Buys* we have chosen above. 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. Despite the elevated risk of hypoglycemia, we recommend trying glipizine 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 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 would be metformin plus Actos.

Avandia may still be a viable option for some people. But as indicated above, its present disadvantages compel a clear rationale for its choice, either as a solo treatment or in combination with another drug. If your doctor prescribes Avandia as the first drug

you take after diagnosis, you should question that decision. There are some clinical circumstances in which this would be a wise choice, but only for a small percentage of people.

Unfortunately, Actos and Avandia have been heavily promoted to doctors and consumers in the U.S. As a result, both drugs have been over-prescribed to people who should instead be taking metformin and/or a sulfonylurea. Both drugs 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 and Hispanic or American Indian patients than in others.

Januvia is a promising new addition to the diabetes medicine cabinet. But it has not yet been well studied. It is not as effective at lowering blood glucose and HbA1c as other diabetes drugs, but it has not been linked to date with weight gain or hypoglycemia either – a plus. Until it has been better studied and prescribed more broadly over a longer period, we would not advise it as a first-line drug. It is also expensive.

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	Sulfonylureas vs. Meglitinide¹	Metformin vs. Thiazolidinediones
<i>Hemoglobin A1c</i>	No difference	No difference	No difference	No difference
<i>Weight</i>	Metformin better	No difference	No difference	Metformin better
<i>Blood Pressure</i>	No difference	No difference	Not enough evidence	No difference
<i>LDL (bad) cholesterol</i>	Metformin better	Sulfonylureas better	No difference	Metformin better
<i>HDL (good) cholesterol</i>	No difference	Thiazolidinediones better	No difference	Thiazolidinediones better
<i>Triglycerides</i>	Metformin better	No difference ²	No difference	One thiazolidinedione better ³
<i>Risk of Hypoglycemia</i>	Metformin better	Thiazolidinediones better	No difference	No difference
<i>Risk of GI problems</i>	Sulfonylureas better	Not enough evidence	Not enough evidence	Thiazolidinediones better
<i>Risk of Congestive Heart Failure</i>	No difference	Sulfonylureas better	Not enough evidence	Metformin better
<i>Risk of Anemia</i>	Not enough evidence	Sulfonylureas better	Not enough evidence	Metformin better
<i>Risk of Edema (fluid build-up)</i>	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>

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 only.
2. Pioglitazone (Actos) decreased triglycerides while rosiglitazone (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 rosiglitazone (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 Hypoglycemia (% of people) ¹	Average change in weight (lbs)
<i>Sulfonylureas</i>							
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
<i>Biguanides</i>							
Metformin	▼ 0.9-1.4	◆	▲ 5-7	◆	▼ 15-25	0-7%	◆
<i>Thiazolidinediones</i>							
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
<i>Meglitinides</i>							
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
<i>Alpha-glucosidase inhibitors</i>							
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
<i>Dipeptidyl peptidase 4 inhibitor</i>							
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 Hypoglycemia (% of people) ¹	Average change in weight (lbs)
<i>Selected Combinations</i>							
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

Source: Bolen S., et al, Comparative Effectiveness and Safety of Oral Diabetes Medications for Adults with Type 2 Diabetes.

<http://www.effectivehealthcare.ahrq.gov>

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.

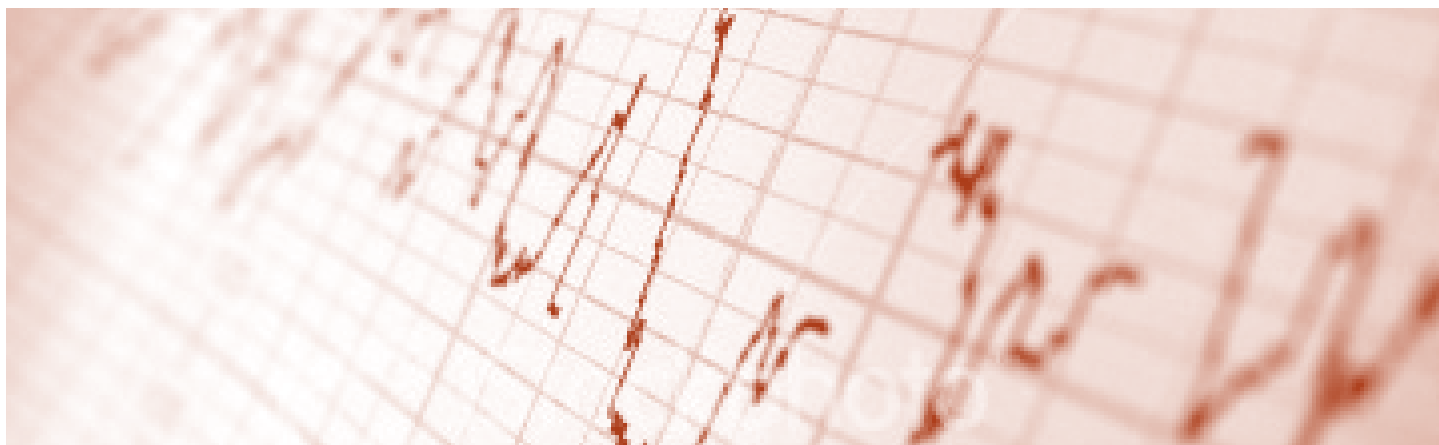


Table 4. Advantages and Disadvantages of the Diabetes Drugs

Advantages:	Disadvantages:
The sulfonylureas (glyburide, glimepiride, glipizide)	
<ul style="list-style-type: none"> - Fast onset of action - No effect on blood pressure - No effect on LDL cholesterol - Convenient dosing - Low cost 	<ul style="list-style-type: none"> - Weight gain (5 to 10 pounds on average) - Heightened risk of hypoglycemia - Glyburide has slightly higher risk of hypoglycemia compared with glimepiride and glipizide
Metformin	
<ul style="list-style-type: none"> - Low risk of hypoglycemia - Not linked to weight gain - Good effect on LDL cholesterol - Good effect on triglycerides - No ill effect on blood pressure - Low cost 	<ul style="list-style-type: none"> - Higher risk of GI side effects (nausea and diarrhea) - Can not be taken by people with diabetes who have moderate kidney disease or heart failure because of risk of lactic acid build-up - Less convenient dosing
The alpha-glucosidase inhibitors (acarbose, miglitol)	
<ul style="list-style-type: none"> - Slightly lower risk of hypoglycemia compared to sulfonylureas - Not associated with weight gain - Decreases triglycerides - No adverse effects on cholesterol 	<ul style="list-style-type: none"> - Less effective than most other diabetes pills in lowering HbA1c - Higher risk of GI side effects than other diabetes pills except metformin - Inconvenient dosing - High cost
The thiazolidinediones (Actos, Avandia)	
<ul style="list-style-type: none"> - Low risk of hypoglycemia - Slight increase in "good" (HDL) cholesterol - Actos linked to decreased triglycerides - Convenient dosing 	<ul style="list-style-type: none"> - Higher risk of heart failure - Weight gain (5 to 10 pounds) - Link to higher risk of edema (fluid build-up) - Link to higher risk of anemia - Increase in "bad" (LDL) cholesterol - Avandia linked to increased triglycerides and possibly (not yet confirmed) higher risk of heart attack - Slower onset of action - Rare risk of liver problems; required monitoring - High cost

Table 4. Advantages and Disadvantages of the Diabetes Drugs

Advantages:	Disadvantages:
The meglitinides (nateglinide, repaglinide)	
<ul style="list-style-type: none"> - No bad effect on cholesterol - Rapid onset of action 	<ul style="list-style-type: none"> - Repaglinide associated with risk of hypoglycemia and weight gain similar to the sulfonylureas - Nateglinide has less effect on HbA1c - Inconvenient dosing - High cost
Januvia (sitagliptin)*	
<ul style="list-style-type: none"> - Apparent low risk of hypoglycemia - Few known side effects (but new drug) - No weight gain - Convenient dosing 	<ul style="list-style-type: none"> - Reduces HbA1c less than several other diabetes drugs - May only be valuable as a second drug; use as the first drug only if unable to take other diabetes drugs, until further research is conducted - Less data on potential side effects compared to older drugs - 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: (1) Bolen S., et al, Comparative Effectiveness and Safety of Oral Diabetes Medications for Adults with Type 2 Diabetes. <http://www.effectivehealthcare.ahrq.gov>; (2) "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 5 mg tablet	Generic	One	5 mg	\$12
Glyburide 5 mg tablet	Micronase	One	5 mg	\$41
Glyburide 5 mg tablet	Diabeta	One	5 mg	\$31
Glyburide 5 mg tablet + 2.5 mg tablet	Generic	One	7.5 mg	\$23
Glyburide 5 mg tablet + 2.5 mg tablet	Micronase	One	7.5 mg	\$69
Glyburide 5 mg tablet + 2.5 mg tablet	Diabeta	One	7.5 mg	-
Glyburide 5 mg tablet	Generic	Two	10 mg	\$39
Glyburide 5 mg tablet	Micronase	Two	10 mg	\$81
Glyburide 5 mg tablet	Diabeta	Two	10 mg	\$62
Glyburide micronized 3 mg tablet	Glynase	One	3 mg	\$42
Glyburide micronized 3 mg tablet	Generic	One	3 mg	\$12
Glyburide micronized 6 mg tablet	Glynase	One	6 mg	\$66
Glyburide micronized 6 mg tablet	Generic	One	6 mg	\$19
Glyburide micronized 6 mg tablet + 1.5 mg tablet	Glynase	One	7.5 mg	\$89
Glyburide micronized 6 mg tablet + 1.5 mg tablet	Generic	One	7.5 mg	\$29
Glipizide 5 mg tablet	Glucotrol	One	5 mg	\$22
 Glipizide 5 mg tablet	Generic	One	5 mg	\$9
Glipizide 10 mg tablet	Glucotrol	One	10 mg	\$34
 Glipizide 10 mg tablet	Generic	One	10 mg	\$11

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
	Glipizide 10 mg tablet	Glucotrol	Two	20 mg	\$68
CR BEST BUY	Glipizide 10 mg tablet	Generic	Two	20 mg	\$22
	Glipizide 5 mg tablet, sustained release	Glucotrol	One	5 mg	\$22
CR BEST BUY	Glipizide 5 mg tablet, sustained release	Generic	One	5 mg	\$14 to \$17
	Glipizide 5 mg + 2.5 mg tablets, sustained release	Glucotrol	One	7.5 mg	\$43
CR BEST BUY	Glipizide 5 mg + 2.5 mg tablets, sustained release	Generic	One	7.5 mg	\$28
	Glipizide 10 mg tablet, sustained release	Glucotrol	One	10 mg	\$39
CR BEST BUY	Glipizide 10 mg tablet, sustained release	Generic	One	10 mg	\$23 to \$29
	Glipizide 10 mg + 5 tablets, Sustained Release	Glucotrol	One	15 mg	\$61
CR BEST BUY	Glipizide 10 mg + 5 tablets, sustained release	Generic	One	15 mg	\$43
	Glipizide 10 mg tablets, sustained release	Glucotrol	Two	20 mg	\$78
CR BEST BUY	Glipizide 10 mg tablets, sustained release	Generic	Two	20 mg	\$46 to \$58
	Glimepiride 1 mg tablet	Amaryl	One	1 mg	\$20
CR BEST BUY	Glimepiride 1 mg tablet	Generic	One	1 mg	\$12
	Glimepiride 2 mg tablet	Amaryl	One	2 mg	\$29

Table 5: Cost of Diabetes Drugs (continued)

	Generic Name and Dose	Brand Name (or Generic)	Number of Pills (Per day)¹	Total Daily Dose¹	Average Monthly Cost²
CR BEST BUY	Glimepiride 2 mg tablet	Generic	One	2 mg	\$18
	Glimepiride 4 mg tablet	Amaryl	One	4 mg	\$51
CR BEST BUY	Glimepiride 4 mg tablet	Generic	One	4 mg	\$27
	Metformin 500 mg tablet	Glucophage	Three	1500 mg	\$102
CR BEST BUY	Metformin 500 mg tablet	Generic	Three	1500 mg	\$38
	Metformin 1000 mg tablet	Glucophage	Two	2000 mg	\$134
CR BEST BUY	Metformin 1000 mg tablet	Generic	Two	2000 mg	\$45
	Metformin 1000 and 500 mg tablets	Glucophage	Three	2550 mg	\$168
CR BEST BUY	Metformin 1000 and 500 mg tablets	Generic	Three	2500 mg	\$58
	Metformin 850 mg tablet	Glucophage	Three	2550 mg	\$167
CR BEST BUY	Metformin 850 mg tablet	Generic	Three	2550 mg	\$60
	Sitagliptin 100 mg tablet	Januvia	One	100 mg	\$208
	Sitagliptin 50 mg tablet	Januvia	One	50 mg	\$201
	Pioglitazone 15 mg tablet	Actos	One	15 mg	\$142
	Pioglitazone 30 mg tablet	Actos	One	30 mg	\$221
	Pioglitazone 45 mg tablet	Actos	One	45 mg	\$241
	Rosiglitazone 2 mg tablet	Avandia	Two	4 mg	\$180

Table 5: Cost of Diabetes Drugs (continued)

Generic Name and Dose	Brand Name (or Generic)	Number of Pills (Per day)¹	Total Daily Dose¹	Average Monthly Cost²
Rosiglitazone 4 mg tablet	Avandia	One	4 mg	\$131
Rosiglitazone 4 mg tablet	Avandia	Two	8 mg	\$262
Rosiglitazone 8 mg tablet	Avandia	One	8 mg	\$233
Repaglinide 1 mg tablet	Prandin	Three	3 mg	\$162
Repaglinide 1 mg and 0.5 mg tablet	Prandin	Three	4.5 mg	\$321
Repaglinide 2 mg tablet	Prandin	Three	6 mg	\$156
Nateglinide 60 mg tablet	Starlix	Three	180 mg	\$157
Nateglinide 120 mg tablet	Starlix	Three	460 mg	\$162
Acarbose 50 mg tablet	Precose	Three	150 mg	\$106
Acarbose 50 mg plus 25 mg tablets	Precose	Three	225 mg	\$210
Acarbose 100 mg tablet	Precose	Three	300 mg	\$124
Miglitol 50 mg tablet	Glyset	Three	150 mg	\$99
Miglitol 50 mg plus 25 mg tablets	Glyset	Three	225 mg	\$195
Miglitol 100 mg tablet	Glyset	Three	300 mg	\$113
Metformin+glipizide 250 mg/2.5 mg	Metaglip	Two	250/2.5-500/5 mg	\$71
Metformin+glipizide 250 mg/2.5 mg	Generic	Two	500/5 mg	\$57
Metformin+glipizide 500 mg/2.5 mg	Metaglip	Two	1000/5 mg	\$78
Metformin+glipizide 500 mg/2.5 mg	Generic	Two	1000/5 mg	\$63

Table 5: Cost of Diabetes Drugs (continued)

Generic Name and Dose	Brand Name (or Generic)	Number of Pills (Per day)¹	Total Daily Dose¹	Average Monthly Cost²
Metformin+glipizide 500 mg/5 mg	Metaglip	Two	1000/10 mg	\$79
Metformin+glipizide 500 mg/5 mg	Generic	Two	1000/10 mg	\$62
Metformin+glyburide 250 mg/1.25 mg	Glucovance	Two	500/2.5 mg	\$72
Metformin+glyburide 250 mg/1.25 mg	Generic	Two	500/2.5 mg	\$44
Metformin+glyburide 500 mg/2.5 mg	Glucovance	Two	1000/5 mg	\$86
Metformin+glyburide 500 mg/2.5 mg	Generic	Two	1000/5 mg	\$47
Metformin+glyburide 500 mg/5 mg ⁶	Glucovance	Three	1500/15 mg	\$129
Metformin+glyburide 500 mg/5 mg ⁶	Generic	Three	1500/15 mg	\$71
Pioglitazone+ metformin 15mg/ 850 tablet	Actoplus Met	One	850/15 mg	\$105
Pioglitazone+ metformin 15mg/ 500 tablet	Actoplus Met	Two	1000/30 mg	\$206
Pioglitazone+ metformin 15mg/ 850 tablet	Actoplus Met	Two	1500/45 mg	\$210
Rosiglitazone+ glimepiride 4mg/ 1 mg tablet	Avandaryl	One	4/1 mg	\$144
Rosiglitazone+ glimepiride 4mg/ 2 mg tablet	Avandaryl	One	4/2 mg	\$150
Rosiglitazone+ glimepiride 4mg/ 4 mg tablet	Avandaryl	One	4/4 mg	\$148
Rosiglitazone+ glimepiride 4mg/ 8 mg tablet	Avandaryl	One	4/4 mg	\$148

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
Rosiglitazone+ metformin 1 mg/ 500 mg	Avandamet	Two	2/1000 mg	\$83
Rosiglitazone + metformin 1 mg/ 500 mg	Avandamet	Two	4/1000 mg	\$152
Rosiglitazone + metformin 2 mg/ 500 mg	Avandamet	Two	4/2000 mg	\$161
Rosiglitazone + metformin 4 mg/ 1000 mg	Avandamet	Two	8/2000 mg	\$262
Sitagliptin + metformin 50/500	Janumet	Two	100/1000	\$106
Sitagliptin + metformin 50/1000	Janumet	Two	100/1000	\$104

1. As commonly or usually recommended.

2. Prices reflect nationwide retail average for May 2007, rounded to the nearest dollar. Information derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Health, Pharmaceutical Audit Suite.



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 about 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 for 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 were also used in writing this report. Those 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 three 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 site 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 May 2007.

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 www.CRBestBuyDrugs.org.



About Us

Consumers Union, publisher of *Consumer Reports*[®] magazine, is an independent and nonprofit organization whose mission since 1936 has been to provide consumers with unbiased information on goods and services and to create a fair marketplace. Its website is www.consumer.org. The magazine's website is www.consumerreports.org.

Consumer Reports Best Buy Drugs[®] is a public education project administered by Consumers Union. Two outside sources of generous funding made the project possible. They are a major grant from the Engelberg Foundation, a private philanthropy, and a supporting grant from the National Library of Medicine, part of the National Institutes of Health. A more detailed explanation of the project is available at www.CRBestBuyDrugs.org.

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