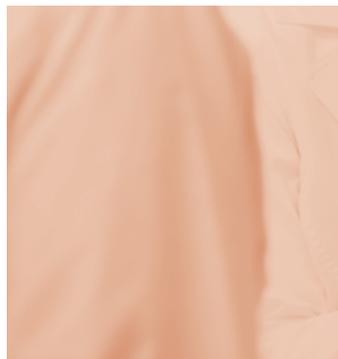


BEST BUY DRUGS™

The Oral Diabetes Drugs

Treating Type 2 Diabetes

Comparing Effectiveness, Safety, and Price



Our Recommendations

Six classes of oral medicines (and 12 individual drugs) are now available to help the 25.8 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, such as Januvia and Onglyza, 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 often 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 Health Best Buy Drugs* if your doctor and you have decided that you need medicine to control your diabetes:

- *Metformin and Metformin Sustained Release* – 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 \$4 to \$43 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.

This report was updated in June 2011.

Welcome

This report compares the effectiveness, safety, and cost of medicines used to treat type 2 diabetes. It is part of a *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 25.8 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 *with nearly 11 million people 65 or older afflicted with diabetes*. And about 1.9 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 7 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 high cholesterol. In 2004, the latest year for which data is available, heart disease was a factor listed on 68 percent of diabetes-related death certificates among people 65 or older.

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; 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 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.

Overall, diabetes is the seventh leading cause of death in the United States. It is also a leading cause of disability. At greatest risk of premature disability and death are women (of all ethnic backgrounds), African Americans, Hispanics, 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 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 blood 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, 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
- Blurred vision
- Frequent urination
- Numbness or tingling in your hands or feet
- Increased thirst and hunger
- 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 65 and older
- People who have a condition called metabolic syndrome
- People who are overweight or obese
- Anyone with a parent or a sibling who has diabetes
- People who are Black Americans, Hispanic 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, 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 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 test 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 200 mg/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 fasting blood sugar levels that are above 110 mg/dl (the upper limit of normal) but less than the 126 mg/dl required for a diagnosis of diabetes. The most recent estimate from the Centers for Disease Control and Prevention indicates that 35 percent of adults 20 and older – 79 million people – have blood glucose levels in this range and thus have what is called pre-diabetes. (It’s also sometimes called borderline diabetes or impaired fasting glucose.)

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, and you can also find more detailed information about lifestyle changes in our free diabetes patient power toolkit at <http://www.consumerreports.org/health/conditions-and-treatments/type-2-diabetes/patient-power-toolkit/index.htm>.

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 in all six groups. We do not evaluate the injectable drugs, including the newest ones, exenatide (Byetta) and liraglutide (Victoza). 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 on page 9 presents the groups of diabetes drugs, including those now available in combination form. The table on page 10 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, metformin, and certain alpha-glucosidase inhibitors and meglitinides are older medicines now available in generic form, while the thiazolidinediones and dipeptidyl peptidase 4 inhibitors are newer. Certain generic diabetes medications cost as little as \$4 for a month's supply through generic drug programs run by major chain stores, such as Kroger, Sam's Club, Target, and

Type of Drug	Individual Drugs (Brand and generic names)	Available as a Generic?
Sulfonylureas	<i>Brands:</i> Amaryl, Diabeta, Glynase Glucotrol, Glucotrol XL <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	<i>Brands:</i> Precose, Glyset <i>Generics:</i> Acarbose	Yes
Meglitinides	<i>Brands:</i> Prandin, Starlix <i>Generics:</i> Nateglinide	Yes
Dipeptidyl peptidase 4 inhibitors	Januvia, Onglyza	No
Combinations of sulfonylureas plus metformin	<i>Brands:</i> Glucovance <i>Generics:</i> known by generic names of the two drugs	Yes
Other Combinations	Actosplus Met, Avandaryl, Avandamet, Duetact, Janumet, Kombiglyze XR	No

Walmart. For an even better bargain, you may be able to obtain a three-month supply for \$10 through these programs. We note in the price chart starting on page 22 which generic medications are available through these programs. Some stores, such as CVS and Walgreens, require a membership fee to participate and might charge higher prices. There might be other restrictions too, so check the details carefully to make sure your drug and dose are covered.

Our evaluation of diabetes drugs is based largely on a thorough, independent review of the scientific research on diabetes drugs. One-hundred and sixty-six studies were closely examined out of thousands screened. The review was conducted in 2010 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, and an analysis of selected classes of diabetes drugs conducted by the Drug Effectiveness Review Project (DERP) based at Oregon Health

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	Yes
<i>Alpha-glucosidase Inhibitors</i>		
Acarbose	Precose	Yes
Miglitol	Glyset	No
<i>Biguanides</i>		
Metformin	Glucophage, Glucophage XR*	Yes
<i>Sulfonylureas</i>		
Glyburide/ glibenclamide	Diabeta, Glynase	Yes
Glipizide	Glucotrol, Glucotrol XL*	Yes
Glimepiride	Amaryl	Yes
<i>Dipeptidyl peptidase 4 inhibitors</i>		
Sitagliptin	Januvia	No
Saxagliptin	Onglyza	No

*XR=extended release, XL=long-acting

& Science University. The full DERP report is available at www.ohsu.edu/xd/research/centers-institutes/evidence-based-policy-center/derp/index.cfm/.

Neither the Johns Hopkins University Evidence-based Practice Center, the Agency for Healthcare Research and Quality, nor DERP 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; *Consumer Reports Health Best Buy Drugs* is solely responsible for those.

This report was updated in June 2011.

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, and (c) decrease the symptoms of high blood sugar.

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.
- The dipeptidyl peptidase 4 inhibitors (Januvia and Onglyza) promote 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, more than 50 percent of people with diabetes who start taking one type of medicine will need another type (or insulin) within three 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, making 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 12 presents these.

The aim of treatment with lifestyle changes and medications is to get your HbA1c lower (and keep it lower) and to reduce your symptoms. 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. Over time, high blood sugar levels cause more glucose to bind with hemoglobin, so a high HbA1c percentage indicates that blood sugar levels are high on average.

Many experts believe that an HbA1c level below 7 percent is associated with a lower risk of diabetes complications, such as kidney disease and eye disease that can lead to blindness. However, there is no definite proof that maintaining HbA1c below 7 percent helps prevent heart disease and premature death because 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

Table 1. Goals for People with Diabetes

Measures	Recommended Goal
<i>Blood Sugar</i>	
Fasting blood glucose	Below 110 mg/dl (Below 100 is better)
Post-meal (2-hour) blood glucose	Below 180 mg/dl (Below 140 is better)
Hemoglobin A1c (HbA1c)	Below 7.0%
<i>Cholesterol</i>	
Total cholesterol	Below 200 mg/dl
LDL ("bad") cholesterol	Below 100 mg/dl
HDL ("good") cholesterol	Above 40 mg/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; recent studies.

Definitions: LDL= low-density lipoprotein cholesterol; HDL= high-density lipoprotein cholesterol; mg = milligrams; dl=deciliter of blood; mmHg = millimeters mercury.

is better for most diabetes patients. In the largest, most well-regarded study of this issue, 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 heart attacks or deaths from heart disease* compared with patients whose HbA1c was maintained at 7.5 percent.

Also, two other 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.

Managing diabetes is complex because it requires careful, sometimes daily attention to diet, monitoring blood sugars, and sometimes frequent adjustment of medication doses. It is also very important to get regular foot and eye exams and, if necessary, treatment for high blood pressure and cholesterol – all of which are proven methods to reduce complications of diabetes.

A formal program or a conscientious primary care doctor can help you manage diabetes appropriately.

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.

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. It's important to discuss any side effects you experience with your doctor.

Side Effects of Oral 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

Since many people with diabetes 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.

Most notably, some diabetes drugs can cause low blood sugar, or hypoglycemia. This is a dangerous 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.

Another worrisome side effect of some of the diabetes drugs is weight gain, or difficulty losing weight.

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 17, 18, and 20, respectively, summarize the comparative evidence on the diabetes drugs. The tables reflect the results from 166 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, four of the newer

medicines — acarbose, miglitol, nateglinide, and sitagliptin — 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 22).

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 seniors or in people who skip meals.

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.

One of the newer classes of drugs poses an elevated risk of heart failure. Evidence overwhelmingly indicates that the thiazolidinediones – Avandia (more about it below) 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 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; Actos a Last Resort

In addition to heart failure, Avandia also increases the risk of heart attack and stroke. For that reason,

the FDA has restricted use of the medication (and combination products that contain it) only for people who have persistent high blood sugar levels even after taking another medication and who can't take an alternative such as Actos. As of November 18, 2011, Avandia and combination products, Avandamet and Avandaryl, will no longer be available at pharmacies. Instead, both you and your doctor will have to register with a special program to have them delivered by mail-order.

If you are already taking Avandia, Avandamet or Avandaryl, and they are working to control your blood sugar, you can continue to take them, but we strongly recommend you discuss with your doctor whether they are appropriate for you.

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.

Actos increases the risk of bladder cancer in people who take it for a year or longer. The risk applies to all drugs containing pioglitazone, including Actoplus Met, Actoplus Met XR, and Duetact. France banned Actos and combination pills due to the cancer risk.

Our medical advisors say that people with diabetes should use Actos only as a last resort, which means only if all other options have failed. People who have previously had or currently have bladder cancer should not use Actos or the combination pills that contain it at all.

If you're on Actos, ask your doctor if it's really necessary and if you should switch to another drug, such as metformin either alone or in combination with glipizide or glimepiride. Also, be alert for signs of bladder cancer, which include blood or red color in your urine, urgent need to urinate or pain while urinating, and pain in your back or lower abdomen. Contact your doctor if you experience any of those symptoms.

Actos has been heavily promoted to doctors and consumers in the U.S. As a result, it may be over-

prescribed 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.

Our picks and recommendations

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

- *Metformin and Metformin Sustained Release* – 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.

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 medicine. Despite the elevated risk of hypoglycemia, we recommend trying glipizide or glimepiride. If glipizide or glimepiride 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.

Januvia and Onglyza – the newest oral diabetes drugs

Januvia and Onglyza are the first two drugs in a new class of diabetes medications called dipeptidyl peptidase 4 inhibitors. No studies on these drugs have followed patients for more than two years, so their effectiveness and safety profiles are not clearly established yet. Neither Januvia nor Onglyza has been shown to lower HbA1c as well as metformin or glipizide, so we do not recommend them as first-line drugs. Another drawback is that both are 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 newer drugs available by injection only.

Table 2. Summary of Comparative Effectiveness of Oral Diabetes Drugs

Outcome	Sulfonylureas vs. Metformin	Sulfonylureas vs. Thiazolidinediones	Sulfonylureas vs. Meglitinide ¹	Sulfonylureas vs. DPP-inhibitors	Metformin vs. Thiazolidinediones	Metformin vs. DPP-inhibitors
Hemoglobin A1c	No difference	No difference	No difference	Sulfonylureas better	No difference	Metformin better
Weight	Metformin better	Sulfonylureas better	No difference	Not enough evidence	Metformin better	Metformin better
Blood Pressure	No difference	No difference	Not enough evidence	Not enough evidence	No difference	Not enough evidence
LDL (bad) cholesterol	Metformin better	Sulfonylureas better	No difference	Not enough evidence	Metformin better	Metformin better
HDL (good) cholesterol	No difference	Thiazolidinediones better	No difference	Not enough evidence	Thiazolidinediones better ⁴	Not enough evidence
Triglycerides	Metformin better	No difference ²	No difference	Not enough evidence	One thiazolidinedione better ³	Not enough evidence
Risk of Hypoglycemia	Metformin better	Thiazolidinediones better	No difference	DPP-inhibitors better	No difference	Not enough evidence
Risk of GI problems	Sulfonylureas better	Not enough evidence	Not enough evidence	Not enough evidence	Thiazolidinediones better	DPP-inhibitors better
Risk of Congestive Heart Failure	No difference	Sulfonylureas better	Not enough evidence	Not enough evidence	Metformin better	Not enough evidence
Risk of Anemia	Not enough evidence	Sulfonylureas better	Not enough evidence	Not enough evidence	Metformin better	Not enough evidence
Risk of Edema (fluid build-up)	Not enough evidence	Sulfonylureas better	Not enough evidence	Not enough evidence	Metformin better	Not enough evidence
Risk of Bone Fractures	Not enough evidence	Not enough evidence	Not enough evidence	Not enough evidence	Metformin better	Not enough evidence

Source: 1. 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>.

2. Bennett WL, et al, *Oral Diabetes Medications for Adults With Type 2 Diabetes: An Update*. Comparative Effectiveness Review No. 27. March 2011 (Prepared by Johns Hopkins University Evidence-based Practice Center under Contract No. 290-02-0018.) AHRQ Publication No. 11-EHC038-EF. Rockville, MD: Agency for Healthcare Research and Quality. March 2011. Available at: 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 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.
4. Pioglitazone was better than metformin.

Table 3. Effects of Oral 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)	▼ 0.9	◆	▲ 8-12	▲ 5	▼ 35-45	0-3%	▲ 5-10
Rosiglitazone (Avandia)	▼ 0.9	◆	▲ 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 IV inhibitor</i>							
Sitagliptin (Januvia)	▼ 0.6-0.8	IE	◆	◆	◆	Low	◆
Saxagliptin (Onglyza)	▼ 0.4-0.9	IE	IE	IE	IE	IE	IE

Table 3. Effects of Oral 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 + sulfonyleurea (Glucovance)	▼ 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
Sulfonyleurea + 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. Results are based on data from two studies.

Table 4. Advantages and Disadvantages of the Oral Diabetes Drugs

Advantages:	Disadvantages:
The sulfonylureas (glyburide, glimepiride, glipizide)	
<ul style="list-style-type: none"> ■ Fast onset of action ■ No affect on blood pressure ■ No affect on LDL cholesterol ■ Convenient dosing ■ Low cost ■ Lower risk of GI side effects than metformin 	<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 effect on blood pressure ■ Low cost 	<ul style="list-style-type: none"> ■ Higher risk of GI side effects (nausea and diarrhea) ■ Cannot be taken by people with diabetes who have moderate or severe 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 effect 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) ■ Linked to higher risk of edema (fluid build-up) ■ Linked to higher risk of anemia ■ Increase in "bad" (LDL) cholesterol ■ Avandia linked to increased triglycerides and higher risk of heart attack ■ Actos linked to increased risk of bladder cancer ■ Slower onset of action ■ Rare risk of liver problems; requires monitoring ■ Linked to increased risk of upper and lower limb fractures ■ High cost

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

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 sulfonylureas ■ Nateglinide has less effect on HbA1c ■ Inconvenient dosing ■ High cost
The DPP-inhibitors (Januvia, Onglyza)	
<ul style="list-style-type: none"> ■ When added to metformin, lower risk of hypoglycemia compared with a sulfonylurea ■ Few known side effects (but they are new drugs) ■ Lower risk of GI side effects than metformin ■ Convenient dosing 	<ul style="list-style-type: none"> ■ Reduce HbA1c less than several other diabetes drugs ■ May only be valuable as second drugs added to another medication ■ Less data on potential side effects compared to older drugs ■ High cost

1. Bennett WL, et al, Oral Diabetes Medications for Adults With Type 2 Diabetes: An Update. Comparative Effectiveness Review No. 27. March 2011 (Prepared by Johns Hopkins University Evidence-based Practice Center under Contract No. 290-02-0018.) AHRQ Publication No. 11-EHC038-EF. Rockville, MD: Agency for Healthcare Research and Quality. March 2011. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.
2. Bennett WL, et al, Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. Ann Int Med. (May 3 2011); Web published in advance of print publication, March 14, 2011.

Table 5: Cost of Oral Diabetes Drugs

Note: If the price box contains a , that indicates the dose of that drug is available for a low monthly cost through programs offered by large chain stores. For example, Kroger, Sam's Club, Target, and Walmart offer a month's supply of selected generic drugs for \$4 or a three-month supply for \$10. Other chain stores, such as Costco, CVS, Kmart, and Walgreens, offer similar programs. Some programs have restrictions or membership fees, so check the details carefully for restrictions and to make sure your drug is covered.

Generic Name and Dose	Brand Name (or Generic)	Number of Pills (Per day) ¹	Total Daily Dose ¹	Average Monthly Cost ²
Acarbose 25 mg	Generic	Three	75 mg	\$78
Acarbose 50 mg	Generic	Three	150 mg	\$82
Acarbose 100 mg	Generic	Three	300 mg	\$99
Acarbose 100 mg	Precose	Three	300 mg	\$122
Glyburide 1.25 mg	Generic	One	1.25 mg	\$10 
Glyburide 2.5 mg	Diabeta	One	2.5 mg	\$29
Glyburide 2.5 mg	Generic	One	2.5 mg	\$6 
Glyburide 5 mg	Generic	One	5 mg	\$6 
Glyburide 5 mg	Diabeta	One	5 mg	\$47
Glyburide micronized 6 mg	Glynase	One	6 mg	\$71
Glyburide micronized 6 mg	Generic	One	6 mg	\$8 
Glipizide 5 mg	Glucotrol	One	5 mg	\$27
 Glipizide 5 mg	Generic	One	5 mg	\$5 
Glipizide 10 mg	Glucotrol	One-Two	10 mg-20 mg	\$41-\$82
 Glipizide 10 mg	Generic	One-Two	10 mg-20 mg	\$4-\$8 
Glipizide 5 mg, sustained release	Glucotrol XL	One	5 mg	\$29
 Glipizide 5 mg, sustained release	Generic	One	5 mg	\$9 
Glipizide 10 mg sustained release	Glucotrol XL	One-Two	10 mg-20 mg	\$52-\$104
 Glipizide 10 mg, sustained release	Generic	One-Two	10 mg-20 mg	\$13-\$26
Glimepiride 1 mg	Amaryl	One	1 mg	\$27
 Glimepiride 1 mg	Generic	One	1 mg	\$6 
Glimepiride 2 mg	Amaryl	One	2 mg	\$39
 Glimepiride 2 mg	Generic	One	2 mg	\$6 
Glimepiride 4 mg	Amaryl	One	4 mg	\$68
 Glimepiride 4 mg	Generic	One	4 mg	\$8 
Metformin 500 mg	Glucophage	Two	1000 mg	\$76
 Metformin 500 mg	Generic	Two	1000 mg	\$14 
Metformin 850 mg	Glucophage	Two	1700 mg	\$129
 Metformin 850 mg	Generic	Two	1700 mg	\$26 

Table 5: Cost of Oral 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 1000 mg	Glucophage	Two	2000 mg	\$151
CR BEST BUY Metformin 1000 mg	Generic	Two	2000 mg	\$24 \$
Metformin sustained release 500 mg	Glucophage XR	One	500 mg	\$40
CR BEST BUY Metformin sustained release 500 mg	Generic	One	500 mg	\$7 \$
Metformin sustained release 750 mg	Glucophage XR	One	750 mg	\$56
CR BEST BUY Metformin sustained release 750 mg	Generic	One	750 mg	\$23
Saxagliptin 2.5 mg	Onglyza	One	2.5 mg	\$252
Saxagliptin 5 mg	Onglyza	One	5 mg	\$247
Sitagliptin 100 mg	Januvia	One	100 mg	\$248
Sitagliptin 50 mg	Januvia	One	50 mg	\$250
Pioglitazone 15 mg	Actos	One	15 mg	\$197
Pioglitazone 30 mg	Actos	One	30 mg	\$291
Pioglitazone 45 mg	Actos	One	45 mg	\$305
Rosiglitazone 2 mg	Avandia	Two	4 mg	\$202
Rosiglitazone 4 mg	Avandia	One	4 mg	\$146
Rosiglitazone 8 mg	Avandia	One	8 mg	\$264
Repaglinide 0.5 mg	Prandin	Three	1.5 mg	\$285
Repaglinide 1 mg	Prandin	Three	3 mg	\$282
Repaglinide 2 mg	Prandin	Three	6 mg	\$285
Nateglinide 60 mg	Generic	Three	180 mg	\$138
Nateglinide 60 mg	Starlix	Three	180 mg	\$211
Nateglinide 120 mg	Generic	Three	360 mg	\$140
Nateglinide 120 mg	Starlix	Three	360 mg	\$224
Miglitol 25 mg	Glyset	Three	75 mg	\$127
Miglitol 50 mg	Glyset	Three	150 mg	\$138
Miglitol 100 mg	Glyset	Three	300 mg	\$155
Metformin+glipizide 250 mg/2.5 mg	Generic	One	250 mg/2.5 mg	\$24
Metformin+glipizide 500 mg/2.5 mg	Generic	One	500 mg/2.5 mg	\$27
Metformin+glipizide 500 mg/5 mg	Generic	One	500 mg/5 mg	\$27
Metformin+glyburide 250 mg/1.25 mg	Generic	Two	500 mg/2.5 mg	\$38 \$
Metformin+glyburide 500 mg/2.5 mg	Glucovance	Two	1000 mg/5 mg	\$99
Metformin+glyburide 500 mg/2.5 mg	Generic	Two	1000 mg/5 mg	\$43 \$
Metformin+glyburide 500 mg/5 mg	Glucovance	Two	1000 mg/10 mg	\$95

Table 5: Cost of Oral 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 500 mg/5 mg	Generic	Two	1000 mg/10 mg	\$39 
Pioglitazone+metformin 15 mg/850 mg	Actoplus Met	One	15 mg/850 mg	\$143
Pioglitazone+metformin 15 mg/500 mg	Actoplus Met	One	15 mg/500 mg	\$154
Pioglitazone+metformin sustained release 15 mg/1000 mg	Actoplus Met XR	One	15 mg/1000 mg	\$161
Pioglitazone+metformin sustained release 30 mg/1000 mg	Actoplus Met XR	One	30 mg/1000 mg	\$314
Pioglitazone+glimepiride 30 mg/2 mg	Duetact	One	30 mg/2 mg	\$306
Pioglitazone+glimepiride 30 mg/4 mg	Duetact	One	30 mg/4 mg	\$291
Repaglinide+metformin 1 mg/500 mg	Prandimet	Three	3 mg/1500 mg	\$248
Repaglinide+metformin 2 mg/500 mg	Prandimet	Three	6 mg/1500 mg	\$253
Rosiglitazone+glimepiride 4 mg/1 mg	Avandaryl	One	4 mg/1 mg	\$168
Rosiglitazone+glimepiride 4 mg/2 mg	Avandaryl	One	4 mg/2 mg	\$165
Rosiglitazone+glimepiride 4 mg/4 mg	Avandaryl	One	4 mg/4 mg	\$165
Rosiglitazone+glimepiride 8 mg/2 mg	Avandaryl	One	8 mg/2 mg	\$273
Rosiglitazone+glimepiride 8 mg/4 mg	Avandaryl	One	8 mg/4 mg	\$267
Rosiglitazone+metformin 1 mg/500 mg	Avandamet	Two	2 mg/1000 mg	\$103
Rosiglitazone+metformin 2 mg/500 mg	Avandamet	Two	4 mg/1000 mg	\$175
Rosiglitazone+metformin 2 mg/1000 mg	Avandamet	Two	4 mg/2000 mg	\$190
Rosiglitazone+metformin 4 mg/500 mg	Avandamet	Two	8 mg/1000 mg	\$287
Rosiglitazone+metformin 4 mg/1000 mg	Avandamet	Two	8 mg/2000 mg	\$278
Saxagliptin+metformin 2.5 mg/1000 mg	Kombiglyze XR	One	2.5 mg/1000 mg	\$129
Saxagliptin+metformin 5 mg/500 mg	Kombiglyze XR	One	5 mg/500 mg	\$258
Saxagliptin+metformin 5 mg/1000 mg	Kombiglyze XR	One	5 mg/1000 mg	\$258
Sitagliptin+metformin 50 mg/500 mg	Janumet	Two	100 mg/1000 mg	\$253
Sitagliptin+metformin 50 mg/1000 mg	Janumet	Two	100 mg/2000 mg	\$251

* For space reasons, not all doses are listed.

1. As usually recommended.

2. Prices reflect nationwide retail average for April 2011, rounded to the nearest dollar. Information derived by *Consumer Reports Health Best Buy Drugs* from data provided by Wolters Kluwer Pharma Solutions, which 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 60 percent 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 Oral 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. Consumer Reports, publishers of *Consumer Reports Health 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), an initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.
- Three reviews of oral diabetes drugs by the Cochrane Collaboration
- An American Medical Association monograph on the oral diabetes drugs
- 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 April 2011.

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 oral diabetes medicines
- Cost roughly the same or less than other oral diabetes medicines

The *Consumer Reports Health 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 Health Best Buy Drugs™ is a public education project administered by Consumers Union. These materials are made possible by 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.

We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Health Best Buy Drugs* website is accurate and describes generally accepted clinical practices. If we find, or are alerted to, an error, we will correct this as quickly as possible. However, *Consumer Reports* and its authors, editors, publishers, licensors and any suppliers cannot be responsible for medical errors or omissions, or any consequences from the use of the information on this site.

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References

1. Bennett W.L., et al, Oral Diabetes Medications for Adults With Type 2 Diabetes: An Update. Comparative Effectiveness Review No. 27. March 2011 (Prepared by Johns Hopkins University Evidence-based Practice Center under Contract No. 290-02-0018.) AHRQ Publication No. 11-EHC038-EF. Rockville, MD: Agency for Healthcare Research and Quality. March 2011. Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm.
2. Bennett W.L., et al, Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. *Ann Int Med.* (May 3 2011); Web published in advance of print publication, March 14, 2011.
3. "Standards of Medical Care in Diabetes—2007," American Diabetes Association Position Statement. *Diabetes Care* 2007 30: S4-S41.
4. Cutler, E.D. and Prescott, P., *Diabetes: Treatment Options Report* (April 2006) Reports prepared for the California HealthCare Foundation. www.chcf.org
5. *Overview: Treatment of Type 2 Diabetes*, American Medical Association Therapeutic Insights (May 2011).
6. American Diabetes Association: Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2007 30: S42-47.
7. *All About Diabetes*, American Diabetes Association. Accessed July 2, 2007. <http://www.diabetes.org/about-diabetes.jsp>.
8. *Guidelines for Clinical Practice for the Management of Diabetes Mellitus*, American Association of Clinical Endocrinologists, American College of Endocrinology, The American Association of Clinical Endocrinologists Medical (May/June 2007). Available at www.aace.com/pub/pdf/guidelines/D_MGuidelines2007.pdf.
9. Diabetes Overview, National Diabetes Information Clearinghouse. Accessed June 22, 2007. www.diabetes.niddk.nih.gov/dm/pubs/overview/index.htm.
10. Drugs for Diabetes – Treatment Guidelines, The Medical Letter (August 2005) Vol. 3, Issue 36.
11. *National Diabetes Fact Sheet – U.S. 2005*, Centers for Disease Control and Prevention. Accessed May 9, 2011. www.cdc.gov/diabetes.
12. Nathan, D. "Finding new treatments for diabetes – how many, how fast, how good," *N Engl J Med.* (February 1, 2007): Vol. 356, No 5, pages 437-440.
13. Gregg, E.W. et al, "Mortality trends in men and women with diabetes, 1971-2000," *Annals of Internal Med.* (June 18, 2007) Published online; print version dated August 7, 2007; Vol. 147, No. 3.
14. Burnet, D.L. et al, "Preventing diabetes in the clinical setting," *J. Gen Int. Med.* (2006) Vol. 21, pages 84-93.
15. Franco, O.H. et al, "Associations of diabetes mellitus with total life expectancy and life expectancy with and without cardiovascular disease," *Arch. Internal Med.* (June 11, 2007) Vol. 167, pages 1145-1151.
16. Barr, E.L. et al, "Risk of cardiovascular and all-cause mortality in individuals with diabetes mellitus, impaired fasting glucose and impaired glucose tolerance," The Australian Diabetes, Obesity, and Lifestyle Study. *Circulation* (July 10, 2007). Vol. 116.
17. Hampton, T., "Diabetes drugs tied to fractures in women," *JAMA* (April 18, 2007): Vol. 297, No. 15, page 1645.
18. Mitka, M., "Report quantifies diabetes complications," *JAMA* (June 6, 2007): Vol. 297, No 21, pages 2337-2338.
19. Dabelea, D. et al, "Incidence of diabetes in youth in the United States," *JAMA* (June 27, 2007): Vol. 297, No 24, pages 2716-2724.
20. Amori, R.E. et al, "Efficacy and safety of incretin therapy in type 2 diabetes – systematic review and meta-analysis," *JAMA* (July 11, 2007): Vol. 298, No. 2, pages 194-206
21. "Sitagliptin/Metformin (Janumet) for Type 2 Diabetes," *The Medical Letter on Drugs and Therapeutics* (June 4, 2007): Vol. 49, Issue 1262, page 1.
22. "Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes," The UK Prospective Diabetes Study Group. *Lancet* (1998): Vol. 352 (9131), pages 837-853.
23. "A randomized trial of efficacy of early addition of metformin in sulfonylurea-treated type 2 diabetes." The UK Prospective Diabetes Study Group. *Diabetes Care* (1998): Vol 21 (1), pages 87-92.
24. "Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)," *Circulation* (2002): Vol. 106(25), pages 3143-3421.
25. "Global guidelines for type 2 diabetes: recommendations for standard, comprehensive, and minimal care. *Diabetes Med* (2006); Vol. 23(6), pages 579-593.
26. Chobanian, A.V. et al, "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 Report." *JAMA* (2003): Vol. 289(19), pages 2560-2572.
27. Holman R.R., et al, "A randomized double-blind trial of acarbose in type 2 diabetes shows improved glycemic control over 3 years," (The UK Prospective Diabetes Study). *Diabetes Care* (1999): Vol. 22(6), pages 960-964.
28. Richter B, Bandeira-Echtler E, Bergerhoff K, Clar C, Ebrahim SH. Pioglitazone for type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD006060. DOI: 10.1002/14651858.CD006060.pub2
29. Salpeter S., et al, "Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus," *Cochrane Database Sys. Rev.* (2006)(1).
30. Van de Laar F.A., et al, "Alpha-glucosidase inhibitors for people with impaired glucose tolerance or impaired fasting blood glucose." *Cochrane Database Syst. Rev.* (2006)(4).
31. Nesto R.W., et al. "Thiazolidinedione use, fluid retention, and congestive heart failure: A consensus statement from the American Heart Association and American Diabetes Association." *Circulation* (December 9, 2003): Vol.108, pages 2941-2948.
32. Nissen S.E., et al, "Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes," *N Engl J Med.* (2007): Vol. 356, pages 2457-2471.
33. Kahn S.E., et al, "ADOPT Study Group: Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy." *N Engl J Med.* (2006): Vol. 355, pages 2427-2443.
34. Home P.D., et al, "Rosiglitazone evaluated for cardiovascular outcomes – an interim analysis," *N Engl J Med.* (2007): Vol. 357(1), pages 28-38.
35. Goldstein B.J. et al, "Effect of initial combination therapy with sitagliptin, a dipeptidyl peptidase-4 inhibitor, and metformin on glycemic control in patients with type 2 diabetes. *Diabetes Care.* (May 7, 2007) (E-pub ahead of print).
36. Dormandy J.A., et al. "Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study – a randomised controlled trial." *Lancet* (2005): Vol. 366 (9493), pages 1279-89.
37. Papa G., et al, "Safety of type 2 diabetes treatment with repaglinide compared with glibenclamide in elderly people: a randomized, open-label, two-period, cross-over trial." *Diabetes Care* (2006): Vol. 29, pages 1918-1920.
38. Damsbo, P. et al, "A double-blind randomized comparison of meal-related glycemic control by repaglinide and glyburide in well-controlled type 2 diabetic patients," *Diabetes Care* (1999): Vol.22, pages 789-94.
39. Vijan, S. et al, "Estimated benefits of glycemic control in microvascular complications in type 2 diabetes," *Ann Intern Med.* (1997): Vol. 127, pages 788-795.
40. Stettler C. et al, "Glycemic control and macrovascular disease in types 1 and 2 diabetes mellitus: meta-analysis of randomized trials," *Am Heart J.* (2006): Vol. 152, pages 27-38 .
41. Meier, C. et al, "Use of thiazolidinediones and fracture risk," *Arch Intern Med.* (2008): Vol. 168 (8), pages 820-825.
42. Selvin, E. et al, "Cardiovascular outcomes in trials of oral diabetes medications: a systematic review," *Arch Intern Med.* (2008): Vol. 168 (19), pages 2070-80.
43. Nathan D.M., et al, "Medical Management of Hyperglycemia in Type 2 Diabetes: a Consensus Algorithm for the Initiation and Adjustment of Therapy," *Diabetes Care.* (2009): Vol. 32(1), pages 193-203.
44. 52-week add-on to Metformin Comparison of Saxagliptin and Sulphonylurea, With a 52-week Extension Period. Study NCT00575588, accessed 9 May 2011 <http://clinicaltrials.gov/ct2/show/results/NCT00575588?term=saxagliptin&rank=12§=X3870615#event>