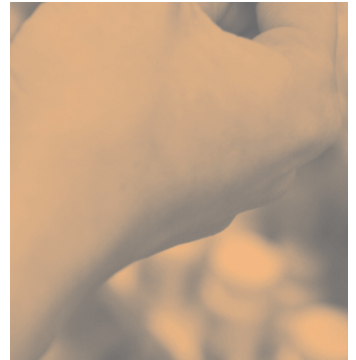
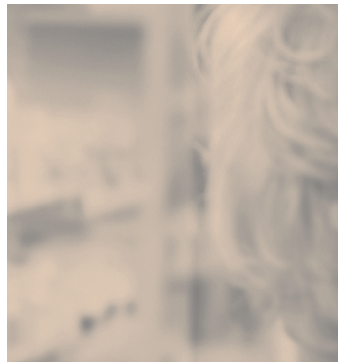
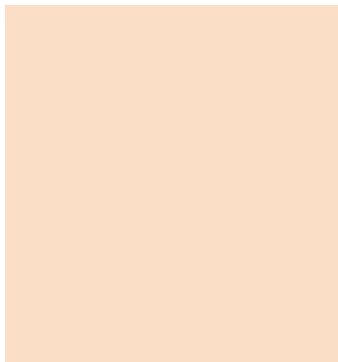


BEST BUY DRUGS[™]

Using Antipsychotics to Treat:

Depression

Comparing Effectiveness, Safety, and Price



Our Recommendations

Although antipsychotics were developed to treat schizophrenia, newer ones are sometimes used to treat depression that has not been relieved by antidepressants or other treatments.

Depression is a common health problem in the U.S., with some 14.8 million adults suffering from the condition in any given year. Psychotherapy and antidepressant medication, if necessary, can often help relieve depression. But the majority of people with the condition—60 to 70 percent—don't get adequate treatment, and antidepressants are ineffective for up to 40 percent of those who try them.

Nine newer antipsychotics, called atypical antipsychotics, are used as "augmentation therapy," or add-ons to treat depression that hasn't responded to antidepressants or other treatments. This is known as "treatment resistant" depression. They are aripiprazole (Abilify), asenapine (Saphris), clozapine (Clozaril and generics), iloperidone (Fanapt), olanzapine (Zyprexa), paliperidone (Invega), quetiapine (Seroquel, Seroquel XR), risperidone (Risperdal and generics), and ziprasidone (Geodon). Three—Abilify, Seroquel XR, and Zyprexa—and a combination pill—Symbyax—that contains olanzapine (Zyprexa) plus the antidepressant fluoxetine (Prozac)—are approved by the Food and Drug Administration for this use, but other antipsychotics are used "off-label" for this purpose.

However, the available evidence indicates that antipsychotics aren't very effective as augmentation therapy for treating "resistant" depression and aren't the best choice for this use for most people. Other options, such as increasing the dose of your antidepressant or switching to a different one, are at least as effective and are safer. Antipsychotics can also cause serious side effects, such as involuntary movements of the tongue, lips, face, trunk, arms, or legs (tardive dyskinesia), significant weight gain, and an increased risk of type 2 diabetes, heart disease, and stroke. In addition, they are very expensive, with some costing more than \$1,000 a month.

For those reasons, the atypical antipsychotics aren't good first choices as add-ons to antidepressants, especially if you are overweight or have heart disease or diabetes. Our medical consultants recommend they be used cautiously and only after first trying the strategies listed below. In this report, we do not choose any as *Best Buy* selections. Instead, we evaluate how well the medications actually work at relieving resistant depression and the risk of side effects.

If your depression hasn't responded to an antidepressant after four to eight weeks, you should first rule out that you don't have other medical or mental-health conditions that could make your depression more difficult to treat, such as bipolar disorder or post-traumatic stress disorder. Other strategies your doctor might try include increasing the dose of your antidepressant, switching to a different one, or combining two of them.

If you've tried all those strategies, then your next option is to talk with your doctor about the treatment options that make sense for your situation. In addition to antipsychotics, other medications used include lithium, thyroid hormone, low doses of stimulants, anticonvulsants, and other classes of antidepressants, such as tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs). Nonmedication options include electroconvulsive therapy, transcranial magnetic stimulation, and vagus nerve stimulation. We don't evaluate any of the other medications or other treatment options in this report or how they compare with antipsychotics. If you decide to try an antipsychotic, our medical advisers suggest that you consult a psychiatrist to help manage the side effects.

This report was published in October 2011.

Welcome

This report evaluates the use of newer antipsychotic drugs for people with major depressive disorder (MDD) who continue to experience symptoms despite taking antidepressant medication.

Depression has become one of the most common health problems in the United States. In any given year, nearly 7 percent of the U.S. adult population 18 years old and over—about 14.8 million people—will have a depressive illness that warrants treatment. For reasons that remain unclear, women appear to develop depression about twice the rate as men. Evidence indicates that today only about 30 to 40 percent of the people with major depression get adequate treatment, meaning that the majority aren't getting the therapies that could bring them relief.

The most commonly prescribed antidepressants are the group referred to as “second-generation antidepressants,” so named because they're the most recently developed class of drugs used to treat depression. They include: bupropion (Budeprion, Wellbutrin); citalopram (Celexa); desvenlafaxine (Pristiq); duloxetine (Cymbalta); escitalopram (Lexapro); fluoxetine (Prozac, Sarafem); fluvoxamine (Luvox); mirtazapine (Remeron); nefazodone (available only as a generic); paroxetine (Paxil, Pexeva); sertraline (Zoloft); and venlafaxine (Effexor). For more on those medications and advice on choosing one that's appropriate for you, see our free Best Buy Drugs report at ConsumerReportsHealth.org/BestBuyDrugs.

About 30 to 45 percent of the people with depression who take second-generation antidepressants won't see their symptoms resolve. If you have had minimal or no improvement in your depression symptoms despite full treatment with two or more antidepressant medications, you might have a form of depression referred to as “treatment resistant” or “treatment refractory.” People who are treated for depression but haven't fully improved are also sometimes described as having an “incomplete,” “inadequate,” or “poor” response to antidepressant treatment.

There is no single, agreed-upon way to diagnose “treatment-resistant depression,” but before deciding that you require a different treatment, your doctor will probably consider:

- If you've been taking a full dose of medication according to the ranges approved by the Food and Drug Administration (FDA) for depression.
- If you've been taking your full dose of medication exactly as prescribed for at least four to eight weeks.
- Your score on a standardized depression rating scale.
- How many previous antidepressant medications you've taken without relief.

If you aren’t getting better on your current antidepressant medication, your doctor might reevaluate you to make sure you don’t have other medical or mental-health conditions that could make your depression more difficult to treat, such as bipolar disorder or post-traumatic stress disorder.

If you only have depression, your doctor will probably increase the dose of the antidepressant you’re taking or switch you to another one. Some people try as many as three or even four antidepressants before they find one that works. Also, some studies have found that antidepressants often work best in combination with talk therapy, and many experts agree.

If those measures don’t provide relief, another option is to add a different type of medication to your current antidepressant therapy, which is referred to as “augmentation,” “adjunctive,” or “add-on” therapy.

Certain newer antipsychotic drugs may be used in such cases. Antipsychotic drugs are so named because they were first developed to reduce psychotic symptoms such as hallucinations, delusions, disorganized thinking, and agitation in people with schizophrenia. But in more recent years, some antipsychotics have also been approved by the FDA as an additional treatment for depression, primarily for adults who are already taking antidepressants. Others are used “off label,” which means they’re prescribed even though they haven’t been approved by the FDA for this purpose. Off-label prescribing is legal and common. Doctors can prescribe any medication to treat a condition, but it’s illegal for a drug company to promote a drug for a use that has not been approved by the FDA.

In this report, we focus on evaluating the nine newer antipsychotic drugs—often referred to as “atypical” antipsychotics—as add-on medication for treating depression. They’re listed in Table 1, below, along with a combination pill that contains an antipsychotic and an antidepressant.

Table 1. Antipsychotics Evaluated in this Report			
Generic Name	Brand Name(s)	Available as a Generic?	FDA approved for resistant depression?
Aripiprazole	Abilify	No	Yes
Asenapine	Saphris	No	No
Clozapine	Clozaril	Yes	No
Iloperidone	Fanapt	No	No
Olanzapine	Zyprexa, Zyprexa Zydis	No	Yes*
Paliperidone	Invega	No	No
Quetiapine	Seroquel	No	Yes
Risperidone	Risperdal, Risperdal M-Tab	Yes	No
Ziprasidone	Geodon	No	No
Combination Pill			
Olanzapine and fluoxetine	Symbyax (Zyprexa and Prozac)	No	Yes

* Zyprexa approval is based on Symbyax data, and it is approved only for use with fluoxetine.

Who needs an antipsychotic for treating depression?

It's not entirely clear how the newer antipsychotic drugs and second-generation antidepressants work together to help people with depression who haven't gotten better with other treatments. Both are thought to work by affecting levels of chemicals in the brain called neurotransmitters. The most important neurotransmitters that appear to be affected by second-generation antidepressants are serotonin, norepinephrine, and dopamine. The antidepressant effects of newer antipsychotic drugs are thought to come from their effects on norepinephrine.

Everyone feels “down” or unhappy once in a while, especially if you're dealing with a lot of stress or a major negative event, such as the loss of a job, the breakup of a relationship, or the death of a loved one. Symptoms will usually ease on their own within a few weeks or months, aided, if necessary, by family support and professional counseling but without the use of an antidepressant.

However, for the millions of Americans with major depressive disorder, depression can kick in for no apparent reason and overwhelm their lives for weeks, months, or even years with feelings of unhappiness, hopelessness, pessimism, low self-esteem, worthlessness, guilt, suicidal thoughts, reduced interest and pleasure in activities, decreased energy, sleeping problems, difficulty concentrating, changes in appetite, irritability, anxiety, and unexplained physical pain.

Professional counseling or psychotherapy can often help. But in some cases, medication might be necessary. As previously noted, second-generation antidepressants are the most commonly-used medication for treating depression. Studies have found that a majority of people who take one—55 to 70 percent—will have a “positive response” to treatment, meaning they will have at least a 50 percent improvement in their depression symptoms. But symptoms for the other 30 to 45 percent of people taking a second-generation antidepressant medication don't lessen or resolve.

There are many reasons antidepressant medications might not help. Table 2, on page 6, lists some issues you and your doctor should discuss that might help

you understand why your depression hasn't resolved and identify some treatment options to consider.

In some cases, though, there is no clear reason why your antidepressant medication is not working. Some people with depression will notice a partial improvement or none at all, even after trying multiple antidepressant medications. If this is the case for you, your doctor will probably try other strategies, including adding a second antidepressant medication or another type of prescription medication.

Three antipsychotic drugs—aripiprazole (Abilify), olanzapine (Zyprexa), and quetiapine (Seroquel XR)—are approved by the FDA specifically as add-on treatments for people with depression and who are already taking an antidepressant. Also, the combination pill Symbyax—which combines Zyprexa and the antidepressant fluoxetine (Prozac)—is FDA-approved for treatment-resistant depression. Abilify and Seroquel XR have been heavily marketed for use in depression. You have probably seen at least one commercial or ad promoting their use.

Adding an antipsychotic can sometimes help relieve depression that hasn't responded to other treatments, but the symptoms do not fully resolve for most people. And there's no conclusive evidence that adding an antipsychotic is more effective than switching to a different antidepressant or other treatment options (more about those below), all of which are better-studied and safer than antipsychotics. Our medical consultants believe that for almost all patients there are better choices than adding an antipsychotic.

A few recent meta-analyses—the combined results of many different studies—including the comparative effectiveness review by researchers with the Drug Effectiveness Review Project at Oregon's Health & Science University, which this report is based on, found that 10 to 20 percent more people who added one of the newer antipsychotic drugs instead of placebo to their current antidepressant medication had their symptoms go away completely. Four of the newer antipsychotic drugs—aripiprazole (Abilify), olanzapine (Zyprexa), quetiapine (Seroquel XR), and risperidone (Risperdal and generics)—are more effec-

Table 2. Reasons your antidepressant might not be working

1. You have other mental-health conditions

In many cases, depression occurs along with other common anxiety disorders, personality disorders, eating disorders and/or substance abuse or dependence. They could be making your depression more difficult to treat, and you might require a different type of medication. You should discuss this with your doctor.

2. You have other medical conditions

Certain medical conditions, such as thyroid disease, can either cause or worsen depression. If the root cause of your depression is a medical condition, your body might not be able to respond to antidepressants until the underlying medical condition is properly treated. Ask your doctor about whether you should schedule a physical exam and have some simple blood tests done to check for other possible causes of your depression.

3. You are not taking the right dose of antidepressant medication

Doctors often will—and should—start your antidepressant medication at the lowest possible dose and gradually increase it if your depression symptoms aren't resolving after several weeks and you're able to tolerate side effects. Ask your doctor whether you need to switch to a higher dose of your antidepressant medication. Make sure that you tell him or her if you haven't been taking your antidepressant medication exactly as prescribed. If you had to skip or lower a dose for any reason, it would reduce the effectiveness of the medication for relieving your depression symptoms.

4. You haven't been taking your antidepressant long enough

Although most people will experience some unpleasant side effects right away, many have to take an antidepressant medication at a stable dose for at least four to eight weeks before they start feeling better. It can be hard to wait that long to see improvement in your depression. But your doctor will probably recommend that you continue to take your antidepressant medication exactly as prescribed for at least four weeks before determining that it isn't effective for you and considering other options.

tive than a placebo when added to ongoing second-generation antidepressant medications.

But there are a few issues that you and your doctor should consider before you begin using one of these antipsychotic drugs for depression.

One reason doctors limit the use of the newer antipsychotic drugs when treating schizophrenia—one of the primary conditions those medications were developed to treat—is that the side effects can be troublesome. (See Table 3 on page 7.) Those include the inability to sit still (akathisia) and other uncontrollable movements (extrapyramidal symptoms), blurred vision, constipation, dry mouth, dizziness, and drowsiness. In addition, the drugs are linked to several serious side effects with long-term consequences, such as permanent, involuntary movements of the tongue, lips, face, trunk, arms, or legs (tardive dyskinesia). Other serious side effects include significant weight gain (greater than 7 percent of body weight), and changes in metabolism that can cause blood sugar abnormalities and other problems that can lead to type 2 diabetes and a higher risk of heart disease and stroke.

In addition to Table 3, the side effects associated with each antipsychotic are discussed in more detail on pages 10-11. Before taking any medication, always read the label or package insert. It contains important information about side effects, precautions, warnings, and drug interactions you should be aware of.

It's not yet clear whether the risks of serious side effects with newer antipsychotic drugs are similar when they're used for treating depression than when used to treat other conditions, like schizophrenia. That's because there are few long-term studies that have looked at newer antipsychotics as add-on treatments for depression. Most studies only followed people for four to 12 weeks.

Overall, antipsychotics won't completely resolve depressive symptoms for most people. But they might help certain people. To take one example, 29 percent of the people who took aripiprazole saw a remission of their depression, which is nearly twice the percentage of those who took antidepressants alone. Unfortunately, there's no way to know

Table 3. Harms of adding atypical antipsychotics to antidepressants

Antipsychotic	More people stopped treatment due to side effects*	More people gained 7 percent of weight or more*
Aripiprazole (Abilify)	Yes	Yes
Asenapine (Saphris)	No data	No data
Clozapine (Clozaril)	No data	No data
Iloperidone (Fanapt)	No data	No data
Olanzapine (Zyprexa)	No data	No data
Combination olanzapine plus fluoxetine (Symbyax)	Yes	Yes
Paliperidone (Invega)	No data	No data
Quetiapine (Seroquel)	Yes	No
Quetiapine (Seroquel XR)	Yes	No
Risperidone (Risperdal)	No	No
Ziprasidone (Geodon)	Yes	No data

* Compared with those taking an antidepressant and a placebo.

beforehand who will benefit from antipsychotics and who won't.

Also, as Table 4 on page 8 shows, there's no data for five of the drugs—asenapine (Saphris), clozapine (Clozaril), iloperidone (Fanapt), olanzapine (Zyprexa), and paliperidone (Invega)—because they haven't been studied in people with treatment-resistant depression. One of those, clozapine, has safety risks—including seizures and a reduction in the body's ability to produce white blood cells, which could increase the risk of developing infections—that make it a poor choice for resistant depression. And studies have shown that ziprasidone (Geodon) is no better than a placebo.

The newer antipsychotic drugs are also expensive. The ones that have FDA-approval as add-on treatments—Abilify, Seroquel XR, Zyprexa, and the combination pill, Symbyax—are not available as lower-cost generics. As Table 5 on page 9 shows, they can run from several hundred dollars a month to more than \$1,000 depending on dose. Risperidone (Risperdal)—the remaining newer antipsychotic drug that has been found to be more effective than a placebo when used “off-label” as an add-on—is available as a generic, but it will still cost \$69 to \$244 per month depending on dose.

Should you take an antipsychotic to treat depression?

Few studies have evaluated the newer antipsychotic drugs as add-on treatments to antidepressants for people who have had an incomplete response to previous treatments. No head-to-head trials have directly compared one newer antipsychotic drug with another. What we do know is that the available evidence indicates that although add-on antipsychotics can increase the number of people who recover from depression by 10 to 20 percent after 4 to 12 weeks, a majority of people still don't get better.

In addition, as we have previously noted, antipsychotics can cause serious side effects, such as involuntary movements of the tongue, lips, face, trunk, arms, or legs (“tardive dyskinesia”), significant weight gain, and an increased risk of type 2 diabetes, heart disease, and stroke. Many people find the side effects intolerable and stop taking the medication.

For those reasons, atypical antipsychotics aren't good first choices for add-ons to second-generation antidepressants, especially if you're already overweight or have heart disease or diabetes. And our medical advisers recommend that antipsychotics be used cautiously and only after trying the strategies on page 6 first. For these reasons, we have not chosen any as *Best Buy* selections in this report.

Table 4. Effectiveness of adding atypical antipsychotics to antidepressants

Antipsychotic	More patients responded to treatment ^{A*}	More patients had a full remission of depression symptoms*
Aripiprazole (Abilify)	Yes	Yes
Asenapine (Saphris)	No data	No data
Clozapine (Clozaril)	No data	No data
Iloperidone (Fanapt)	No data	No data
Olanzapine (Zyprexa)	No data	No data
Combination olanzapine plus fluoxetine (Symbyax)	No	Yes
Paliperidone (Invega)	No data	No data
Quetiapine (Seroquel)	Yes	No
Quetiapine (Seroquel XR)	Yes with 300 mg No with 150 mg	Yes for both doses
Risperidone (Risperdal)	Yes	Yes
Ziprasidone (Geodon)	No	No

* Compared with those taking an antidepressant and a placebo.

A. Response to treatment was defined as a 50 percent or greater reduction in depression symptoms.

While taking an antidepressant, you should be in close touch with your doctor. If your depression symptoms aren't improving after four to eight weeks, your doctor and you should consider the recommendations on page 6. This includes ruling out that you don't have other medical or mental-health conditions that could make your depression more difficult to treat. Other strategies you and your doctor might try include increasing the dose of your antidepressant, switching to a different one (some people try several before finding one that works for them), or adding a second one.

If you have tried all of those strategies, we recommend you talk with your doctor about the treatment options that make sense for your situation. Other medications used for resistant depression include lithium, thyroid hormone, low doses of stimulants, anticonvulsants, and other classes of antidepressants, such as tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs). Nonmedication options include electroconvulsive therapy, transcranial magnetic stimulation, and vagus nerve stimulation. We haven't evaluated any of the other medications or other treatment options in this report or how they compare with antipsychotics.

If you decide to try an antipsychotic, our medical advisers suggest that you consult a psychiatrist to help manage the side effects. Before you start taking an antipsychotic, we also recommend you have a serious discussion about whether the potential for serious side effects is worth the modest, if any, benefit of the medication.

There are some other important issues you and your doctor should consider first. Overall, the short-term benefits of the newer antipsychotic drugs as an add-on to antidepressants over a placebo aren't all that impressive. Adding an antipsychotic could increase the number of people by 20 percent who have their depressive symptoms reduced by half or more. And the number of people who experience a full remission could be increased by up to 20 percent. This modest potential for a benefit should be weighed against the chances of short- and long-term side effects.

Also, it remains unclear whether augmentation with a newer antipsychotic is more effective than a placebo in preventing a relapse or return of depression when taken longer-term.

Table 5. Cost of antipsychotics for treatment-resistant depression

Generic Name	Brand Name	Average monthly cost ^A
Aripiprazole tablet	Abilify	\$636 - \$939
Asenapine tablet	Saphris	\$758 - \$761
Clozapine tablet	Clozaril	\$219 - \$568
Clozapine tablet	Generic	\$77 - \$356
Iloperidone tablet	Fanapt	\$701 - \$749
Combination capsule with olanzapine plus fluoxetine	Symbyax (Zyprexa plus Prozac)	\$402 - \$742
Olanzapine tablet	Zyprexa	\$423 - \$1,242
Olanzapine dissolvable tablet	Zyprexa Zydis	\$500 - \$1,441
Paliperidone tablet	Invega	\$590 - \$881
Quetiapine tablet	Seroquel	\$272 - \$1,197
Quetiapine tablet	Seroquel XR	\$182 - \$549
Risperidone tablet	Risperdal	\$186 - \$535
Risperidone tablet	Generic	\$68 - \$233
Ziprasidone capsule	Geodon	\$575 - \$669

A. Prices reflect nationwide retail average for July 2011, rounded to the nearest dollar. Information derived by *Consumer Reports Best Buy Drugs* from data provided by Wolters Kluwer Pharma Solutions, which is not involved in our analysis or recommendations.

The main differences among Abilify, Seroquel XR, Zyprexa, and the combination pill, Symbyax, relate to their side effect profiles. Symbyax has the highest risk of weight gain, so it might not be a good choice for people who are already overweight or have heart disease or diabetes.

Zyprexa has only been studied in combination with one antidepressant, fluoxetine, in the form of the fixed-dose combination pill, Symbyax. So the potential benefits of adding Zyprexa to any other antidepressants is unknown. And just like with Symbyax, Zyprexa and fluoxetine taken separately might not be a good choice for people who are already overweight or have heart disease or diabetes.

The main disadvantage of Abilify is that it is the only antipsychotic drug in studies of depression that was found to increase the risk of akathisia—the feeling of restlessness and inability to sit still. But it also had the lowest risk of stopping the drug due to side effects, so this suggests that the akathisia

symptoms might have been mild enough to tolerate, at least on a short-term basis.

A potential advantage of Seroquel XR is that it has to be taken only once a day. But in studies of people who had not responded fully to antidepressants, it had the greatest increase over a placebo in the number of those with intolerable side effects that led them to stop taking the medicine.

Risperidone (Risperdal) is the only antipsychotic drug without FDA approval for treatment-resistant depression with evidence of similar benefits over a placebo when compared with those with FDA-approval for similar use. But it's important to note that risperidone has been studied in fewer than half as many people as Abilify, Seroquel XR, and Symbyax. So our confidence in the evidence for risperidone is lower. But risperidone has the advantage of being available in less expensive generic forms and has the second to lowest risk of discontinuations due to side effects.

The evidence

This report is based on an analysis that focused on 16 studies that were published in the peer-reviewed medical literature between 2001 and 2010. All of them compared one newer antipsychotic drug with a placebo when used to augment ongoing antidepressant medication in adults with treatment-resistant depression. There are no studies yet that directly compare one newer antipsychotic drug with another for this use.

Effectiveness

Four antipsychotics—the three that are FDA approved and another, risperidone (Risperdal and generic) used off-label—can be effective at treating depression when they are taken with an antidepressant, but not by much. In studies, 37 to 58 percent of the people who added one of those four antipsychotic drugs to their antidepressant medication experienced a 50 percent reduction or more in their depressive symptoms. This compares with 22 to 46 percent of the people who took a placebo pill in addition to their antidepressant. Overall, the four newer antipsychotics increase the number of people who see an improvement in depressive symptoms by 12 to 20 percent over a placebo.

Some people reported their depressive symptoms disappeared entirely. Overall, 26 to 36 percent of those who added one of the four newer antipsychotics had a full remission. This was the case for only 14 to 24 percent of people who added a placebo to their antidepressant. This represents a possible 10 to 20 percent increase in the number of people who might have their depressive symptoms go away completely.

But there's still a lack of studies evaluating the ability of newer antipsychotic drugs to improve a person's quality of life and the ability to carry out normal daily activities, such as going to work or school, and interacting with family and friends, which are all important outcomes for people with depression.

Also, it remains unclear whether augmentation with a newer antipsychotic is more effective than a placebo in preventing a relapse or return of depres-

sion symptoms if taken for longer than 12 weeks. So far, there has been only one study of 243 people with treatment-resistant depression that evaluated the longer-term benefits of add-on therapy to the second-generation antidepressant citalopram (Celexa and generics) with the antipsychotic risperidone. It found that almost the same percentage of people relapsed whether they were taking risperidone (53 percent) or a placebo (55 percent).

Side effects

Overall, 4 to 12 percent of the people who added a newer antipsychotic drug to their ongoing second-generation antidepressant had to drop out of studies early because they could not or did not want to tolerate the side effects, which is two to six times the rate of people who dropped out due to side effects while taking a placebo.

The three antipsychotics approved for resistant depression—Abilify, Seroquel XR, and Zyprexa—Symbyax, and risperidone have a different set of strengths and weaknesses when it comes to their side effects. Below we discuss each antipsychotic drug based on information from studies on treatment-resistant depression.

Abilify

This is the only newer antipsychotic drug that has been found in studies repeatedly more likely than a placebo to cause “akathisia”—a feeling of restlessness and an inability to sit still. About 20 percent more people taking aripiprazole than a placebo—or one in five—experienced akathisia across all studies. But aripiprazole also had the lowest risk of people stopping early due to side effects. For every 38 people taking add-on aripiprazole instead of a placebo over six weeks, one additional person quit because of side effects. So although aripiprazole might be more likely to cause akathisia, it's possible that the symptoms will be mild enough to tolerate on a short-term basis.

Risperidone (Risperdal)

Studies found that it has the second lowest risk among antipsychotics of people stopping early due

to side effects. For every 24 people treated with add-on risperidone instead of a placebo, one additional person quit because of side effects. It didn't significantly increase the risk over a placebo for weight gain, akathisia, or other uncontrollable movements (extrapyramidal symptoms). But it has been studied in fewer people than the other antipsychotics, so its side-effects profile might not be fully known.

Seroquel XR

This drug has the highest risk of people stopping early due to side effects. For every 11 people taking add-on quetiapine instead of a placebo, one additional person quit because they couldn't tolerate the side effects.

Symbyax

Olanzapine-the antipsychotic in this combination drug-carries the greatest risk among antipsychotics of significant weight gain (7 percent of bodyweight or greater) for people with treatment-resistant depression. Studies show that compared with people taking a placebo plus fluoxetine, those taking olanzapine plus fluoxetine gained an average of 10

more pounds over 8 to 12 weeks. In comparison, people taking other newer antipsychotic drugs gained an average of 2 to 3 pounds more than those taking a placebo.

Zyprexa

Zyprexa's indication for resistant depression is based on the data from the combination drug Symbyax. So the potential benefits of adding Zyprexa to antidepressants other than fluoxetine remains unknown. Also, taking separate pills of Zyprexa and fluoxetine carry the same risk of weight gain as Symbyax, so it's not a good first choice for people who are already overweight or have heart disease or diabetes.

Age, Race, and Gender Differences

There's no evidence that any newer antipsychotic drug is more or less effective or safe for any particular group of people with treatment-resistant depression based on age, gender, or race/ethnicity. In general, studies of newer antipsychotic drugs in treatment-resistant depression involved mostly women with a mean age that ranged from 35 to 48 years.

Talking With Your Doctor

It's important for you to know that the information we present here is not meant to substitute for a doctor's judgment. But we hope it will help you and your doctor arrive at a decision about which antipsychotic add-on may be best for you—if one is warranted at all—and which will give you the most value for your health-care dollar.

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

Many people (including physicians) think that newer drugs are better. While that's a natural assumption to make, it's not necessarily true. Studies consistently find 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 vs. older medicine, including generic drugs.

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

Generics are much less expensive than newer brand-name medicine, but they're not lesser quality drugs. Indeed, most generics remain useful even many years after first being marketed. That's why more than 60 percent of all prescriptions in the U.S. today are written for generics.

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

- First, if you see several doctors, each might not be aware of medicine the others have prescribed.
- Second, since people differ in their response to medication, it's common for doctors today to prescribe several before finding one that works well or best.
- Third, many people take several prescription medications, nonprescription drugs, and dietary supplements at the same time. They can interact in ways that can either reduce the benefit you get from the drug or be dangerous.
- Fourth, the names of prescription drugs—both generic and brand—are often hard to pronounce and remember.

For all those reasons, it's important to keep a written list of all the drugs and supplements you are taking, and to periodically review it with your doctors.

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

How We Evaluated Antipsychotics

Our evaluation is primarily based on an independent scientific review of the evidence on the effectiveness, safety, and adverse effects of antipsychotics. A team of physicians and researchers at the Oregon Health & Science University Evidence-Based Practice Center conducted the analysis as part of the Drug Effectiveness Review Project, or DERP. DERP is a first-of-its-kind multi-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP's analysis of antipsychotics forms the basis for this report. A consultant to *Consumer Reports Best Buy Drugs* is also a member of the Oregon-based research team, which has no financial interest in any pharmaceutical company or product.

The full DERP review of antipsychotics is available at <http://www.ohsu.edu/drugeffectiveness/reports/final.cfm>. (This is a long and technical document written for physicians.)

Drug costs we cite were obtained from a health-care 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. The prices 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 July 2011.

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

About Us

Consumers Reports, 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. The magazine's website is www.consumerreports.org.

Consumer Reports Best Buy Drugs is a public-education project administered by Consumers Reports. These materials were made possible from a grant from the state Attorney General Consumer and Prescriber Education Grant Program, which is funded by a multistate 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/BestBuyDrugs.

We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Best Buy Drugs* website is accurate and describes generally accepted clinical practices. If we find an error or are alerted to one, we will correct it as quickly as possible. But *Consumer Reports* and its authors, editors, publishers, licensors, and suppliers can't be responsible for medical errors or omissions, or any consequences from the use of the information on this site. Please refer to our user agreement at ConsumerReportsHealth.org/BestBuyDrugs for further information.

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