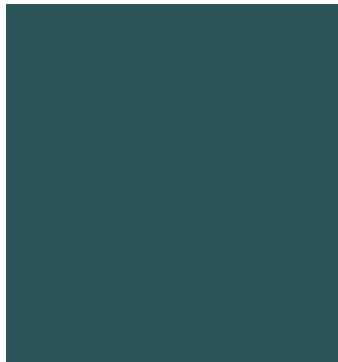
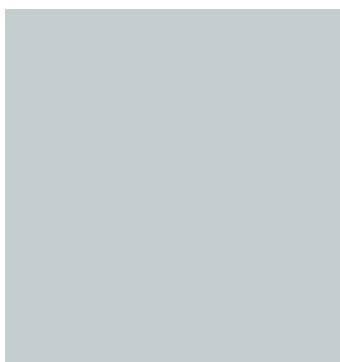


BEST BUY DRUGS[™]

Use of Antipsychotic Medication in Children and Teens to Treat:
**Behavior and Developmental Disorders,
Bipolar Disorder, and Schizophrenia**

Comparing safety and effectiveness



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Our Recommendations

Prescription medications called atypical antipsychotics, which include aripiprazole (Abilify), asenapine (Saphris), clozapine (Clozaril), iloperidone (Fanapt), olanzapine (Zyprexa), paliperidone (Invega), quetiapine (Seroquel), risperidone (Risperdal), and ziprasidone (Geodon), are given to children and teenagers to treat schizophrenia and bipolar disorder. They are also used to try to reduce aggression, irritability, and self-injuring behaviors associated with pervasive developmental disorders, including autism and Asperger syndrome, and disruptive behavior disorders. But prescribing these drugs to young people is controversial because they have not been well-studied, and the long-term safety and effectiveness for children and teens is unknown.

Studies in adults have found that atypical antipsychotics can cause serious side effects, so long-term safety is a particular concern about their use in children. Some of the most worrisome include uncontrollable movements and tremors that resemble Parkinson's disease (known as extrapyramidal symptoms), an increased risk of diabetes, substantial weight gain, and elevated cholesterol and triglyceride levels. Atypical antipsychotic drugs can also increase the risk of premature death, primarily due to strokes, in older adults with dementia. These risks have been studied primarily in adults; the effects in children are not fully known at this time.

Because of the lack of evidence, we are unable to choose a *Best Buy* atypical antipsychotic for children with schizophrenia, bipolar disorder, pervasive developmental disorders, or disruptive behavior disorders. Instead, our medical advisors recommend that parents carefully consider the potential risks and benefits. Children with those disorders should receive comprehensive treatment, which includes cognitive behavioral therapy, parent management training, and specialized educational programs, along with any potential drug therapy.

Deciding whether to use one of these medications should be done in conjunction with your child's doctor. Important considerations include cost, which can be substantial, potential side effects, and whether the medication has been shown to be effective for your child's most prominent condition or symptoms. If your child has a co-existing condition—for example, ADHD or depression—you should make sure they are appropriately treated, because this might improve your child's symptoms.

This report was published in March 2012.

Welcome

This report focuses on the use of prescription medications called atypical antipsychotics by children and teenagers, ages 18 and younger. Atypical antipsychotics are used to treat schizophrenia and bipolar disorder. They are also used to try to reduce aggression, irritability, social withdrawal/lethargy, and other symptoms in children and teens with pervasive developmental disorders, including autism and Asperger syndrome, and disruptive behavior disorders (but it should be noted that atypical antipsychotics do not help the core communication problems of autism and similar disorders.)

Prescribing children and teens antipsychotic medication is controversial because there's little evidence about the safety or effectiveness for use in these age groups. Most of what we know comes from studies of adults. As Table 1 on page 5 shows, most atypical antipsychotics are not approved by the Food and Drug Administration for use by children. But they can legally be used "off-label," which means the drug can be prescribed to treat a condition for which it does not have FDA approval. (More about this on page 6.)

Despite a lack of evidence, these medications are often prescribed to children and teens. This has helped make atypical antipsychotics the fifth highest selling class of drugs in the U.S. in 2010, with \$16.1 billion in sales, according to IMS Health.

Clozapine (Clozaril), which became available in the U.S. in 1989, was the first atypical antipsychotic approved by the FDA. Today, it is usually given only when other drugs fail because it can cause a serious blood disorder in some people. It was followed by several other atypical antipsychotics, including aripiprazole (Abilify), asenapine (Saphris), iloperidone (Fanapt), olanzapine (Zyprexa), paliperidone (Invega), quetiapine (Seroquel), risperidone (Risperdal), and ziprasidone (Geodon). (See Table 1 on page 5.)

Atypical antipsychotics can cause troubling side effects, including muscle rigidity, slow movement and involuntary tremors (known as extrapyramidal symptoms), substantial weight gain, an increased risk of type 2 diabetes, and elevated cholesterol levels. (Side effects are listed in Table 2 on page 11.) Many people who start taking one don't take it for long, even if it reduces their symptoms, because they can't or don't want to tolerate the side effects.

Managing children with developmental or behavioral disorders can be challenging for parents and doctors. Because so little is known about the use of atypical antipsychotics in kids, and because of the complexities associated with those disorders, *Consumer Reports Best Buy Drugs* hasn't recommended specific treatment options or selected a *Best Buy* in this spe-

cial report. Instead, we evaluate the medical research to help you understand the benefits and risks of atypical antipsychotics so you can decide, with your child’s doctor, whether they’re appropriate for your child.

This report 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 CRBestBuyDrugs.org.

Table 1. Atypical Antipsychotic Drugs Evaluated in this Report

Generic name	Brand name(s)	Generic Available	FDA approval for children
Aripiprazole	Abilify	No	Approved for use by adolescents with schizophrenia, adolescents with bipolar disorder mixed or manic episodes, and irritability associated with autism.
Asenapine	Saphris	No	No
Clozapine	Clozaril Fazaclo	Yes	No
Iloperidone	Fanapt	No	No
Olanzapine	Zyprexa Zyprexa Zydis	No*	Approved for use by adolescents with schizophrenia, and adolescents with bipolar disorder mixed or manic episodes.
Paliperidone	Invega	No	No
Quetiapine	Seroquel Seroquel XR	No*	Approved for use in treatment of children with manic episodes in bipolar disorder, and adolescents with schizophrenia.
Risperidone	Risperdal	Yes	Approved for use by adolescents with schizophrenia, adolescents with bipolar disorder mixed or manic episodes, and for irritability associated with autism.
Ziprasidone	Geodon	No	No

* The Food and Drug Administration has given tentative approval for a generic product but none are available at this time.

Abbreviations: ER, extended release; ODT, orally disintegrating tablet; XR, extended release.

How Do Atypical Antipsychotics Work and Who Needs Them?

It's not known exactly how antipsychotics work to help relieve symptoms. But what we do know is that they affect levels of chemicals in the brain called neurotransmitters, which play important roles in behavior and cognition, as well as sleep, mood, attention, memory, and learning. This might be how they reduce psychotic symptoms, such as hallucinations, delusions, disorganized thinking, and agitation in schizophrenia and bipolar disorder. It also might explain how they can reduce aggression, irritability, and self-injuring behaviors associated with pervasive developmental disorders and disruptive behavior disorders. But from the limited available evidence, it's still unclear how well they do this, and whether they remain effective over the long-term.

Conditions Treated with Atypical Antipsychotics

Most of the studies on atypical antipsychotics have focused on treating schizophrenia and bipolar disorder. Some of the drugs have FDA approval to treat those conditions in children and teens as well as adults. But they're also used "off-label," which means they're prescribed by doctors to treat conditions for which it has not been FDA-approved.

Off-label prescribing by doctors is a common and legal practice, although it's illegal for pharmaceutical companies to promote their drugs for off-label use. Off-label uses for atypical antipsychotics in children include the treatment of pervasive development disorders, such as autism and Asperger syndrome, and disruptive behavior disorders. (Aripiprazole and risperidone are approved for those with autism-spectrum disorders, but the other atypical antipsychotics aren't.)

For all four conditions—bipolar disorder, schizophrenia, pervasive development disorders, and disruptive behavior disorders—the evidence supporting the use of atypical antipsychotics by young people is limited to a few, small short-term studies, with no good-quality evidence on longer-term effectiveness and safety.

Overall, studies on the use of atypical antipsychotics by children have involved only about 2,640 of them. About 1,000 children had bipolar disorder, 600 had pervasive developmental disorders, 640

had disruptive behavior disorders, and fewer than 400 had schizophrenia.

The box on page 7 shows which drugs have been studied in children, and for which conditions. Only aripiprazole (Abilify), olanzapine (Zyprexa), quetiapine (Seroquel), and risperidone (Risperdal) have been studied in children with bipolar disorder. In teenagers with new-onset schizophrenia, only olanzapine (Zyprexa), quetiapine (Seroquel), and risperidone (Risperdal) have been studied. Aripiprazole (Abilify), olanzapine (Zyprexa), and risperidone (Risperdal) have been studied in children with pervasive developmental disorders, while only risperidone (Risperdal) has been studied in children with disruptive behavior disorders.

For each of these conditions in children, evidence directly comparing one atypical antipsychotic to another is either extremely limited or nonexistent. The evidence for benefit and harm is mentioned below by condition for each drug.

Schizophrenia

It's unclear how many children suffer from schizophrenia because the disorder isn't usually diagnosed until adulthood, according to the National Institute of Mental Health. Schizophrenia has been diagnosed in children as young as 5 but this is very rare. Men usually experience the first symptoms in their late teens and early to mid-20s; women are usually first diagnosed in their 20s to mid-30s.

People with schizophrenia suffer from disjointed and illogical thinking, but contrary to popular belief, they don't have multiple personalities. They might be withdrawn, fearful, and agitated, and experience hallucinations and delusions. And they might have great difficulty connecting to others emotionally.

Many people with schizophrenia live meaningful lives and function well with proper treatment. Most studies of atypical antipsychotic drugs have focused on adults with schizophrenia. They have been found to help reduce symptoms, improve the

Atypical Antipsychotics Studied in Children and Teens, by Disorder

Generic Name	Brand Name	Disorder			
		Children with bipolar disorder	Teenagers with new-onset schizophrenia	Children with disruptive behavior disorders	Children with pervasive developmental disorders
Aripiprazole	Abilify	√			√
Olanzapine	Zyprexa	√	√		√
Quetiapine	Seroquel	√	√		
Risperidone	Risperdal	√	√	√	√

√ indicates the drug has been studied as a treatment for that disorder in children and/or teens. Asenapine (Saphris), Clozapine (Clozaril), iloperidone (Fanapt), paliperidone, and ziprasidone (Geodon) are not listed because they have not been studied in children.

quality of life, and lessen the chance of a person doing harm to himself or others. But studies on the use of antipsychotics by teenagers whose schizophrenia was recently diagnosed are limited.

Studies of adults show that about half of those with schizophrenia experience a meaningful reduction in their symptoms after taking an antipsychotic. Some symptoms, such as agitation, may get better in just a few days. Others, such as delusions and hallucinations, can take four to six weeks to ease. As a result, nearly every person diagnosed with schizophrenia will receive an antipsychotic drug.

But atypical antipsychotics don't work for everyone. About 20 percent of people with schizophrenia don't get any benefit from them, and another 25 to 30 percent experience only a partial reduction in symptoms.

Two small studies that directly compared the effect of atypical antipsychotics used by teenagers with schizophrenia didn't find significant differences among the drugs tested. Olanzapine (Zyprexa) and quetiapine (Seroquel) had a similar effect on symptoms after six months in a very small study of teenagers who had new diagnoses of schizophrenia. Risperidone (Risperdal) and olanzapine (Zyprexa) led to similar improvements in symptoms over eight weeks.

Bipolar Disorder

Most people with bipolar disorder are usually given a diagnosis in their late teens or early 20s. The National Institute of Mental Health estimates that the condition affects less than 3 percent of teenagers, but the exact prevalence is unknown because the disorder is difficult to diagnose in children. This is partly because the symptoms are less clear in children than in adults, and they can overlap with other childhood conditions, such as ADHD or conduct disorder.

The hallmark symptoms of bipolar disorder are sharp swings between very high moods—or mania—and very low moods—or depression. In most cases, those extremes in mood last for several weeks. There's often an in-between period with a "normal" mood. But some people with bipolar disorder may have periods where symptoms of mania and depression are present simultaneously. These are called "mixed" episodes.

Atypical antipsychotics are generally not used to treat bipolar disorder until people have first tried other medications, including lithium, divalproex, and carbamazepine.

Studies of adults have found that all the antipsychotics can help reduce mania symptoms of bipolar disorder, with 40 to 75 percent of people experiencing

a decrease in symptoms. But there have been fewer studies on the effect of the drugs on adults with bipolar disorder than with schizophrenia, and even fewer among children with bipolar disorder.

Here's what is known so far:

Aripiprazole (Abilify)

In one study, short-term response—meaning a 50 percent or greater reduction in symptoms—was seen in 45 to 64 percent of children and teenagers taking aripiprazole after four weeks of treatment compared with 26 percent who took a placebo. Remission—a nearly complete resolution of symptoms—was achieved in 25 to 72 percent of children taking aripiprazole compared with 5 to 32 percent on a placebo. But at the end of the study, the children taking aripiprazole rated their quality of life lower than those who were treated with a placebo.

Quetiapine (Seroquel)

In one study, 58 to 64 percent of children and teenagers with mania symptoms showed a response after three weeks of treatment with quetiapine compared with 37 percent who took a placebo. Remission was seen in more than half who took quetiapine compared with 30 percent on a placebo.

When quetiapine was used with another drug, divalproex, by teenagers with acute mania episodes, 87 percent showed a response after six weeks compared with 53 percent who took divalproex alone. In another study that compared quetiapine to divalproex in teenagers with bipolar disorder, both drugs resulted in improved quality of life at the end of four weeks. Improvements were seen in their ability to get along with others and manage their behavior, resulting in fewer disturbances in family life. And the parents of those on quetiapine said their children functioned better in school, both socially and academically, and also felt better about themselves.

Quetiapine is no better than a placebo when it comes to depressive periods of bipolar disorder. In a study of 32 teenagers with a depressive episode associated with bipolar disorder, quetiapine did not lead to improvements in symptoms or an improved rate of remission following eight weeks of treatment when compared with a placebo.

Olanzapine and Risperidone

One small study compared risperidone (Risperdal) and olanzapine (Zyprexa) in 31 preschool children with bipolar disorder who were displaying mania symptoms. The drugs showed similar effectiveness in relieving symptoms following eight weeks of treatment. A larger study is needed to confirm those findings.

Studies of teenagers with mania symptoms found that 59 to 63 percent who took risperidone (Risperdal) for three weeks experienced a response compared with 26 percent who took a placebo. In a similar study with olanzapine (Zyprexa), 49 percent of teenagers taking the medication showed a response compared with 22 percent who took a placebo. Both studies also found that risperidone and olanzapine resulted in more patients experiencing remission compared with a placebo.

Pervasive Development Disorders

Pervasive developmental disorders include the autism spectrum disorders (autism and Asperger syndrome) as well as Rett syndrome, childhood disintegrative disorder, and general pervasive developmental disorder (often called “pervasive developmental disorder, not otherwise specified”).

On average, one in 110 children in the U.S. has some form of autistic disorder, according to the Centers for Disease Control and Prevention. Autism, which is more common in boys than in girls, typically becomes apparent before age 3. The cause is unknown. People with autism have trouble with interpersonal and communication skills, and emotional reciprocity, and they generally demonstrate restricted and repetitive behavior, activities, and interests.

There is no cure, but there are treatments that can help. Structured educational or daily living programs focused on skill enhancement and communication strategies are typically used, along with behavior-management techniques and cognitive behavioral therapy. Antipsychotics are prescribed, if necessary, with the aim of reducing disruptive behavior, including hyperactivity, impulsivity, aggressiveness, and self-injuring behavior. Other medication might be used to treat other disorders, such as anxiety or depression.

Few studies have looked at the use of antipsychotics by children with these disorders. The largest study, which involved 101 children with pervasive developmental disorder, found that 69 percent of those who took risperidone (Risperdal) were rated “much improved” after eight weeks of treatment compared with 12 percent who took a placebo. Risperidone (Risperdal) is the only atypical antipsychotic that has been studied in preschool age children with pervasive developmental disorder, but it has not been found to be better than a placebo.

It’s not clear if benefits of risperidone last over the long-term. Limited evidence shows that after four months of treatment, 10 percent of children who show improvement will stop taking the drug either because it is no longer effective or they experience side effects. This led to a relapse—a return of symptoms to their initial level—in 63 percent, whereas only 13 percent of those who continued taking the drug an additional two months relapsed.

In two studies involving 316 children, those who took aripiprazole (Abilify) were less likely to cause harm to themselves or display aggression toward others compared with those who received a placebo. They were also less irritable, had fewer angry outbursts, suffered from fewer mood changes or depressed moods, and were less prone to yell or scream inappropriately.

Very limited evidence is available on the use of olanzapine (Zyprexa) by children with pervasive developmental disorders. Only two studies involving fewer than 25 children are available. The results suggest that olanzapine is superior to a placebo and similar to the older antipsychotic haloperidol (Haldol). But because of the extremely small number of children studied, larger studies are needed to determine whether those findings can be applied more broadly to children with pervasive developmental disorders.

Disruptive Behavior Disorders

Disruptive behavior disorders include oppositional defiant disorder, conduct disorder, and general disruptive behavior disorder (which in the medical literature is often called “disruptive behavior disorder, not otherwise specified”). Oppositional defiant

disorder occurs in approximately 1 to 6 percent of youth, and conduct disorder occurs in roughly 1 to 4 percent.

The symptoms seen in children diagnosed with oppositional defiant disorder include hostility, negativism, and defiance toward authority. It appears before age 8, and is more common in boys. In some cases, the severity of symptoms can increase with age and become more characteristic of conduct disorder. Children who have been diagnosed with disruptive behavior disorders often also exhibit attention deficit/hyperactivity disorder (ADHD).

Children with conduct disorder demonstrate a pattern of aggressiveness toward people and animals, vandalism and/or theft of property, and other serious rule violations, often without a sense of remorse. Conduct disorder is usually diagnosed before age 16, and is more common in boys. Both oppositional defiant disorder and conduct disorder are associated with significant problems functioning at home, in school, and, later, at work. Children with oppositional defiant disorder often experience discipline problems in school, and frequently have legal problems as adults.

Children with similar, but less severe, patterns of behavior, compared with those with oppositional defiant or conduct disorders, might be diagnosed with general disruptive behavior disorder or disruptive behavior disorder, not otherwise specified. Children with this condition demonstrate significantly impaired interpersonal and family relationships, and/or disturbed school functioning.

The primary treatment of disruptive behavior disorders is family-based and includes parent management training. Medication therapy is considered additive and is aimed at specific symptoms. In the decision to start a medication, it is often important to take into account other conditions the child might have. For example, ADHD medications might be useful if the child has both a disruptive behavior disorder and ADHD. In children with conduct disorder, mood stabilizers, such as lithium and valproate, might be helpful. Antipsychotics are prescribed to children with disruptive behavior disorders to reduce aggression associated with these conditions, but only two antipsychotics—risperidone and quetiap-

ine—have been studied for this use. No antipsychotic medications are approved by the FDA for the treatment of disruptive behavior disorders.

In a study of children with fairly severe disruptive behavior disorder symptoms, those who received risperidone showed approximately twice the rate of improvement in conduct problem behaviors over six to 10 weeks of treatment compared with those who took a placebo. About 27 percent of children who continued taking risperidone for six months had a relapse compared with 42 percent of the children who did not receive medication, but the degree of improvement decreased in both groups.

In a study of teenagers with disruptive behavior symptoms requiring hospitalization, risperidone improved their overall assessments, with 21 percent assessed as “markedly or severely disturbed” compared with 84 percent taking a placebo.

Quetiapine (Seroquel) has not been found to be effective in improving aggressive behavior associated with conduct disorder. In the only available study, quetiapine was no better than a placebo at reducing aggression and hyperactivity in teenagers with conduct disorder and moderate-to-severe aggressive behavior. One of nine of the children (11 percent) stopped taking the medication due to akathisia, a side effect that makes people feel as if they can’t sit still. Quetiapine was superior to a placebo on global measures of symptom improvement and quality of life.

Safety of Atypical Antipsychotics

Atypical antipsychotics can cause significant side effects, which limit their overall usefulness. (See Table 2, below.) Many people who start taking one don't take it for long, even if it reduces their symptoms, because they can't or don't want to tolerate the side effects. In addition, people with schizophrenia and bipolar disorder are highly prone to stopping their medicine because of the nature of their disease. They might not understand that they have a psychiatric disorder, fail to accept that they benefit from medication, forget to take it, or quit taking it when the most serious symptoms ease.

One serious side effect of atypical antipsychotics is movement-related (extrapyramidal) —uncontrollable tics and tremors that resemble Parkinson's disease. Extrapyramidal side effects generally go away when the drug is discontinued or the dosage is lowered. But a specific movement disorder called tardive dyskinesia can develop with more prolonged use and might persist even after a patient stops taking the antipsychotic.

Atypical antipsychotic drugs also cause other serious side effects, including an increased risk of type

Table 2. Side Effects Associated with Atypical Antipsychotics

Minor to Moderately Severe Side Effects—These can ease or disappear over time, or be reduced if the dose is lowered. They go away when the drug is stopped. The list below is alphabetical and not in order of importance, severity, or frequency. Most people have more than one of these effects. But experience with, and severity of, side effects varies substantially by person.

■ Abnormal limb and body movements, muscle twitches, tremors and spasms	■ Insomnia
■ Abnormal menstruation	■ Lip smacking and abnormal tongue movements
■ Blurred vision	■ Muscle stiffness or weakness
■ Constipation	■ Rapid heartbeat
■ Dizziness on standing or moving quickly	■ Restlessness
■ Dry mouth	■ Sedation, drowsiness
■ Excessive salivation	■ Sexual dysfunction
■ Feeling more hungry than usual	■ Skin rashes

Potentially Serious Side Effects—These may require discontinuing the drug or switching to a different one. They are often reversible, but can, in some cases, become permanent, and, in the case of agranulocytosis, even life-threatening.

- **Agranulocytosis**†—Failure of the bone marrow to produce disease-fighting white blood cells, which can lead to serious or fatal infections. This risk is associated primarily with clozapine, and regular blood tests are required when taking it.
- **Changes in metabolism** that cause blood sugar abnormalities and other problems, which can lead to type 2 diabetes and a higher risk of heart disease and strokes in adults.
- **Myocarditis**†—An inflammation of the heart muscle that can be fatal. This risk is associated primarily with clozapine.
- **Seizures**†—This risk is associated primarily with clozapine.
- **Significant weight gain**—7 percent or greater increase in pretreatment body weight (total amount depends on child's starting weight). Clozapine and olanzapine both cause greater weight gain than other antipsychotics.
- **Tardive dyskinesia**—Uncontrollable body movements that may include tremors and spasms.

† Associated primarily with clozapine; regular blood tests are required when taking it.

2 diabetes, substantial weight gain, and elevated cholesterol and triglyceride levels. In addition, they have been found to increase the risk of premature death, primarily due to strokes, in older adults with dementia. These risks have been studied primarily in adults; the effects in children are not fully known at this time.

Overall, 80 to 90 percent of adults who take an antipsychotic of any kind will have at least one side effect; most will have more than one. Of those who experience side effects:

- 20 to 30 percent will have a serious or intolerable adverse effect and stop taking the medicine within days, weeks, or a few months.
- 35 to 45 percent will stop taking the medicine within six months.
- 65 to 80 percent will stop taking the medicine within 12 to 18 months.

Safety concerns with atypical antipsychotics in children and teenagers

Due to the limited studies of children and teenagers, the adverse effects of atypical antipsychotics are not fully known. The side-effect profile varies by drug, so when considering one for your child, the risks of each specific drug should be considered against the potential benefit. The following sections are an overview of the side effects found in studies involving children and teens.

Weight Gain

Weight gain is perhaps the most common side effect associated with atypical antipsychotics taken by children and teenagers. Risperidone (Risperdal) given at low doses, for example, leads to an average weight gain of about 4 pounds in children with pervasive development disorders or disruptive behavior disorders compared with those given a placebo. It is not yet clear whether this weight gain stabilizes or continues to increase over the long-term. Current evidence suggests continued weight gain, with estimates of 4 to 12 pounds in one year and up to 18 pounds after two years.

Weight gain is also the most problematic side effect with aripiprazole (Abilify). In one study, 15 percent of children taking it experienced a notable weight gain (at least 7 percent above starting weight) over eight weeks. In another study, 32 percent of children experienced a notable weight gain while on aripiprazole. In both studies, children taking a placebo experienced negligible weight gain. Whether the weight gain associated with aripiprazole continues over the long-term is unclear because no long-term studies of weight gain with continued treatment are available.

Olanzapine (Zyprexa) is also associated with weight gain, with children gaining 7.5 to 9 pounds over six to 10 weeks of treatment. One study found that two-thirds of children gained at least 7 percent more than their starting weight. As in the case with aripiprazole (Abilify), studies of weight gain in children who continue to take olanzapine for a longer term are not available.

Table 3. Weight Gain with Atypical Antipsychotics in Children and Teenagers

Drug	Weight gain in pounds over 6 to 8 weeks		
	<i>Pervasive Developmental Disorder or Disruptive Behavior Disorder</i>	<i>Bipolar Disorder</i>	<i>Schizophrenia</i>
Aripiprazole (Abilify)	3-4	<1	—
Olanzapine (Zyprexa)	7.5 to 9	7.4	—
Quetiapine (Seroquel)	—	3	4-5
Risperidone (Risperdal)	4	2	2

Quetiapine also causes weight gain. For example, in a study in children with a depressed episode of bipolar disorder, those who received quetiapine gained about 3 pounds more than those who received a placebo.

Heart Problems and Diabetes

Some atypical antipsychotic drugs can increase total cholesterol (LDL and triglycerides). In addition, those drugs—with the possible exception of aripiprazole (Abilify)—can increase blood sugar, or other markers of diabetes, in some children, or worsen blood sugar control for those with pre-existing diabetes.

It is not possible to say how much of an increased risk the drugs add, or if one drug is worse than another for children. Based on published studies, olanzapine (Zyprexa) might cause a bigger increase in cholesterol levels in children than in adults.

While heart-rhythm patterns (EKGs) were normal, one study showed a temporary increase in heart rate with risperidone during the first two weeks of treatment. The participants' heart rates returned to normal after two weeks of treatment.

Suicidal behavior

In studies of children taking atypical antipsychotics, there were a few who exhibited suicidal behavior, but it is not possible to tell if this represents an increase or decrease in the risk of suicidal behavior, or no impact at all.

Psychoactive medications, such as certain antidepressants, have been found to increase this risk in adolescents. Because aripiprazole (Abilify) and quetiapine (Seroquel) share some of the same neurotransmitter activity in the brain as these antidepressants, the drugs carry a serious warning that they might increase the risk of suicidal thinking and behavior, even though the evidence is not clear.

In adults with schizophrenia, clozapine (Clozaril, Fazaclon ODT) is the only atypical antipsychotic drug that has been found to reduce the risk of suicide or suicidal behavior. This has not been studied in children.

Other Side Effects

Studies of risperidone (Risperdal) have found low rates of other side effects, but this might be due to

the low doses used, and the short follow up. Abnormal limb and body movements (extrapyramidal symptoms), were infrequent in short-term trials, but they were reported more often than with patients taking a placebo.

Risperidone is known to cause increased levels of the hormone prolactin, which helps in the production of breast milk after pregnancy. In non-pregnant women and men, increased prolactin can result in enlarged breasts and problems with sexual function. Studies of children found that risperidone elevated prolactin levels, but none showed signs or symptoms such as breast enlargement. It's not clear if, over time, prolactin levels stay elevated or return to normal.

Other side effects seen more frequently with aripiprazole (Abilify) than a placebo include sleepiness, drooling, tremors, nausea, or vomiting. Abnormal movements of the arms, legs, or body were also seen more often in children taking aripiprazole. Further study is needed to determine if these side effects resolve, remain constant, or worsen over time with continued treatment.

In a study of the use of quetiapine (Seroquel) in the treatment of teenagers with conduct disorder, 11 percent of those taking the medication stopped due to akathisia, a condition where a person feels quite restless, as though they can't sit still. Otherwise, the drug was well-tolerated.

Other side effects reported by children taking olanzapine included sedation and increased appetite.

Overall, side effects were reported more often with olanzapine (Zyprexa) than with either quetiapine (Seroquel) or risperidone (Risperdal). Rigidity was more frequently present in patients treated with olanzapine compared with quetiapine, and fatigue was more frequent with olanzapine compared with risperidone. But more patients taking risperidone reported a movement-related side effect compared with those taking olanzapine.

Choosing an Atypical Antipsychotic for Children

Because of the small body of evidence about the use of atypical antipsychotics by children and teenagers, it's difficult to determine their short-term effectiveness and safety. And nothing is known about their long-term safety and efficacy because the studies involving younger people have been relatively small and short in duration.

So we are unable choose a *Best Buy* atypical antipsychotic for use by children and teenagers with schizophrenia, bipolar disorder, pervasive developmental disorders, or disruptive behavior disorders. Instead, our medical advisers recommend that parents carefully weigh the risks and benefits. A comprehensive treatment plan for children with these disorders should include cognitive behavioral therapy, parent-management training and specialized educational programs, along with any potential drug therapy.

Deciding whether to use one of these medications at all, and if so, which one, should be done in conjunction with your child's doctor and should be based on several important considerations. For example, what are your child's most significant, distressing, or impairing symptoms? Are these

symptoms that antipsychotic drugs have been found to relieve? Are the benefits adequate or valuable to you and your child?

You should also take into account the cost of the medication, which might be considerable. And review the drug's side effects in light of your child's health history to make sure it's appropriate. These drugs have been inadequately studied in children with respect to side effects, so you'll need to also consider the evidence from studies of adults.

If your child has a co-existing condition—for example, ADHD or depression—you should make sure these are treated. This might improve your child's symptoms. For bipolar disorder, there are other, more well-researched drugs available, such as lithium, divalproex, and carbamazepine, that should be tried first before considering atypical antipsychotics.

If you decide to give your child an antipsychotic, we suggest using the lowest effective dose to minimize the possibility of side effects. And make sure your child is periodically re-evaluated by a doctor to determine whether the medication is still helpful and necessary.

Talking With Your Doctor

The information we present here is not meant to be a substitute for a doctor's judgment. But we hope it will help you and your child's doctor determine whether an antipsychotic is appropriate.

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 doctor 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 medicine. 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 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.
- Finally, 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 container match the amount 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://derp.ohsu.edu/about/final-document-display.cfm>. (This is a long and technical document written for physicians.)

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

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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. It's website is www.CRBestBuyDrugs.org. The magazine's website is ConsumerReports.org.

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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 CRBestBuyDrugs.org.

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, licensers, 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 CRBestBuyDrugs.org for further information.

Consumer Reports Best Buy Drugs should not be viewed as a substitute for a consultation with a medical or health professional. This report and the information on CRBestBuyDrugs.org are provided to enhance the communication with your doctor rather than to replace it.

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