Risperidone (Risperdal) is an antipsychotic in the family of second-generation antipsychotics (SGAs), or atypical antipsychotics. The SGAs came after earlier antipsychotics known as first-generation antipsychotics (FGAs) or conventional or typical antipsychotics, such as chlorpromazine (Thorazine) and haloperidol (Haldol), and they have largely replaced the typical antipsychotics in clinical medicine. The SGAs are considered atypical because they have a wider spectrum of activity with improved efficacy over the FGAs in treating negative symptoms (e.g., flat affect, poverty of speech, lack of motivation and interest, poor grooming and hygiene) of schizophrenia. The SGAs are also less likely to induce side effects associated with movement disorders, such as extrapyramidal symptoms (EPS) and tardive dyskinesia (TD), than the FGAs.

SGAs are not limited to their antipsychotic action; they may also be used in the treatment of bipolar disorder, depression, and anxiety disorders and possibly other neuropsychiatric disorders as well. The efficacy of the SGAs may be mediated primarily by the combination of dopamine and serotonin antagonism, two important neurotransmitters in the brain. Dysfunctions in areas of the brain that involve dopamine and serotonin neurotransmission have been implicated in neuropsychiatric disorders such as schizophrenia and depressive disorders. It is this wider range of action of the SGAs that also accounts for their characterization as atypical.

When first marketed in the United States in 1993, Risperdal was approved only for treatment of schizophrenia in adults. Since then, the U.S. Food and Drug Administration (FDA) approved the use of Risperdal for treatment of schizophrenia in adults and in adolescents ages 13–17 years; short-term treatment of acute mania or mixed episodes in bipolar disorder in adults and in pediatric patients ages 10–17 years; and treatment of irritability associated with autism spectrum disorder, including symptoms of aggression,

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Risperidone</th>
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</thead>
<tbody>
<tr>
<td>Available brands</td>
<td>Risperdal, Risperdal M-Tab, Risperdal Consta</td>
</tr>
<tr>
<td>Available strengths and formulations</td>
<td>0.25-mg, 0.5-mg, 1-mg, 2-mg, 3-mg, and 4-mg tablets</td>
</tr>
<tr>
<td></td>
<td>0.25-mg, 0.5-mg, 1-mg, 2-mg, 3-mg, and 4-mg orally disintegrating tablets (Risperdal-M Tab)</td>
</tr>
<tr>
<td></td>
<td>1-mg/mL oral solution</td>
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<tr>
<td></td>
<td>12.5-mg, 25-mg, 37.5-mg, and 50-mg intramuscular injections (Risperdal Consta)</td>
</tr>
<tr>
<td>Available in generic</td>
<td>Yes, except Risperdal Consta</td>
</tr>
</tbody>
</table>
SECOND-GENERATION ANTIPSYCHOTICS

self-injurious behavior, and uncontrollable temper tantrums. Beyond treatment of acute mania in both adults and children, there are inadequate data to support use of risperidone for long-term management of bipolar disorder to prevent relapse.

The use of a medication for its FDA-approved indications is called its labeled use. In clinical practice, however, practitioners may prescribe medications for unapproved indications (off-label uses) when published clinical studies indicate the efficacy, and the standards of medical practice support the safety, of those treatments. Risperidone may be used off-label to treat other neuropsychiatric disorders, including psychotic depression, Tourette’s disorder (a chronic tic disorder), and obsessive-compulsive disorder.

DOSSING INFORMATION

For treatment of schizophrenia in adults, the initial dosage of risperidone is 2 mg, administered once a day or in two divided doses. The dosage is increased to a target of 4–8 mg/day, with a maximum recommended dosage of 16 mg/day. For treating adolescents (ages 13–17 years) with schizophrenia, the initial dosage of risperidone is 0.5 mg as a single dose at bedtime. The dosage is increased to a recommended target dosage of 3 mg/day, which may be administered in two divided doses or a single dose at bedtime. The maximum recommended dosage for adolescents should not exceed 6 mg/day.

For treating acute mania in adults with bipolar disorder, the initial dosage of risperidone is 2–3 mg/day, and the usual target dosage is 1–6 mg/day. For treating pediatric patients (ages 10–17 years) with bipolar mania, the initial dosage is 0.5 mg administered as a single dose in the morning or evening. The target dosage is 1–2.5 mg/day.

Risperidone is also used to treat irritability in children (ages 5–16 years) with autism spectrum disorder. Dosages are based on the child’s weight. The initial dosage for children 20 kg (44 lb) or less is 0.25 mg/day; for children weighing more than 20 kg, it is 0.5 mg/day. The usual dosage for patients weighing 20 kg or less is 0.5 mg, and for children weighing more than 20 kg, it is 1.0 mg. The effective dosage range is 1–3 mg/day.

Risperidone comes in orally disintegrating tablets (Risperdal M-Tab) that dissolve in the mouth and prevent “cheeking” of the tablet. It also comes in a solution that can be mixed in water or other liquids, but it is not compatible with tea or cola.

Risperdal Consta is a long-acting intramuscular injection that must be administered by a medical practitioner. For patients who do not adhere to their daily medication regimen, Risperdal Consta is an alternative treatment program. Patients receiving injections are usually followed more closely by mental health workers to remind them of their biweekly appointment. The recommended starting dosage is 25 mg every 2 weeks. It takes about 3 weeks for Risperdal Consta to build up adequate blood levels, thus oral Risperdal or another antipsychotic medication must be continued for 3 weeks after the first dose of Risperdal Consta is given in order to prevent worsening of symptoms. Most patients’ symptoms respond to 25 mg given every 2 weeks. If symptoms do not respond to 25 mg, a higher dosage of 37.5 mg or 50 mg every 2 weeks may be needed. The dosage should not exceed the recommended maximum of 50 mg every 2 weeks.

COMMON SIDE EFFECTS

At lower dosages, risperidone is generally well tolerated. Common side effects include sedation, dizziness, headache, nausea, vomiting, constipation, insomnia, and agitation. There is a higher incidence of EPS when the dosage of risperidone exceeds 6 mg/day. EPS are neurological disturbances caused by antipsychotics (or a neurological disorder) in the area of the brain that controls motor coordination. When disruption occurs in a particular area of the brain, it can produce symptoms that mimic Parkinson’s disease (parkinsonism), including muscle stiffness, rigidity, tremor, drooling, and a “masklike” facial expression. However, unlike Parkinson’s disease, which is a progressive neurological disease, parkinsonism from treatment with an antipsychotic is reversible. Some patients experience akathisia, which is a subjective sense of restlessness accompanied by fidgeting and inability to sit or stand still. EPS may be managed by decreasing the antipsychotic dosage or adding an anticholinergic medication (e.g., Cogentin)
to counteract the side effect. A beta-blocker, such as propranolol, is usually more effective for akathisia than anticholinergic agents.

Risperidone may cause weight gain for some patients. However, weight gain associated with risperidone is moderate compared with some other antipsychotics. Control of weight can usually be managed by diet (e.g., avoiding excessive sugar intake) and exercise without stopping risperidone.

Risperidone may cause drowsiness and sedation and impair physical coordination and mental alertness. Patients should avoid potentially hazardous activities, such as driving a car or operating machinery, until they are sure that these side effects will not affect their ability to perform these tasks.

**ADVERSE REACTIONS AND PRECAUTIONS**

Patients taking risperidone may experience dizziness upon standing from a recumbent position, which may lead to syncope, the loss of consciousness resulting from insufficient blood flow to the brain. This is due to the opposing effect of risperidone on blood vessels that normally compensate for postural change, resulting in a momentary drop in blood pressure. Dizziness ensues when insufficient blood is supplied to the brain. This reaction is known as orthostatic hypotension and is occasionally seen with risperidone. Patients generally develop tolerance to orthostatic hypotension, but they should be cautious when rising too quickly, especially when starting therapy or when increasing dosages. Elderly patients and patients taking medications for high blood pressure may be more prone to orthostatic hypotension and are susceptible to syncope (fainting) and falling. Using compression or support stockings may help with blood circulation (i.e., venous return) and offset hypotension. As a precaution, patients should be aware of positional shifts and not rise to their feet suddenly. When lying down, they should get up gradually to a sitting position before standing. If feeling light-headed or dizzy, they should sit and wait for a minute or two before standing up to allow the blood pressure to adjust.

**Tardive dyskinesia** is a potential adverse reaction to antipsychotic medications. It is characterized by late-onset abnormal involuntary movements. This is a potentially irreversible condition that commonly manifests idiosyncratic symptoms such as “pill-rolling” movements of the fingers, darting and writhing movements of the tongue, lip puckering, facial grimacing, and other irregular movements. The risk of TD is very small with risperidone and other SGAs, even with long-term use. The FGAs, on the other hand, are associated with a higher risk of TD, especially in older patients and with duration of exposure to the medication.

**Neuroleptic malignant syndrome (NMS)** is a rare, toxic reaction to antipsychotics. The symptoms are severe muscle stiffness, rigidity, elevated body temperature, increased heart rate and blood pressure, irregular pulse, and profuse sweating. NMS may lead to delirium and coma. It can be fatal if medical intervention is not immediately provided. There are no tests to predict whether an individual is susceptible to developing NMS when exposed to an antipsychotic. Thus NMS must be recognized early because it is a medical emergency that requires immediate discontinuation of the antipsychotic, hospitalization, and intensive medical treatment.

Antipsychotics, including risperidone, can interfere with the patient’s ability to reduce core body temperature when it becomes elevated under conditions of strenuous exercise or exposure to extreme heat. This can result in heatstroke, and fatal heat strokes have been reported in patients taking antipsychotics. Taking concomitant anticholinergic medications (e.g., Cogentin) or being dehydrated under those conditions may increase the risk of heatstroke. Patients taking antipsychotic medications should avoid prolonged exposure to extreme heat and should drink adequate amounts of fluids to stay hydrated on hot days or with strenuous exercise.

Risperidone may elevate prolactin (hyperprolactinemia), a hormone produced in the area of the brain called the pituitary gland. Prolactin levels rise in women following childbirth, stimulating lactation, or milk production. Normally, prolactin secretion is suppressed, but this normal inhibition may be opposed when taking antipsychotic medications (as well as from other causes). Elevated prolactin in males may cause excessive development of the breast (gynecomastia). Elevated prolactin levels may stimulate spontaneous lactation (galactorrhea) in both women and men, induce irregular menstruation or suppress menses (amenorrhea) in women, and cause loss of libido and infertility in women and men. Chronic hyperprolac-
tinemia may also lead to decreased bone density and osteoporosis in adults, especially women. Children and adolescents are particularly susceptible to hyperprolactinemia because this may affect sexual development by impairing synthesis of sex hormones. A serum prolactin level can confirm hyperprolactinemia when clinical symptoms are suspected. Serum prolactin should be monitored periodically for children and adolescents taking an antipsychotic medication. When side effects from elevated prolactin occur, switching to another antipsychotic with less effect on prolactin is the usual clinical approach.

Risperidone and other SGAs are associated with abnormalities in glucose regulation. Risperidone may elevate blood glucose levels (hyperglycemia) and in some cases cause diabetes mellitus. While glucose abnormalities and diabetes are sometimes related to weight gain, these conditions may occur in patients without significant weight gain. Patients who gain excessive weight are more susceptible to risperidone’s negative impact on blood sugar and lipids (fats). The FDA requires warning of hyperglycemia and diabetes mellitus and elevated lipids associated with the SGAs, including risperidone. Patients taking risperidone, especially those with a family history or an established diagnosis of diabetes, should be aware of this adverse reaction and should routinely monitor glucose levels and lipids.

Elderly patients treated with antipsychotics for dementia-related psychosis were found to have an increased risk of death associated with antipsychotic medications. Although this correlation is not clear, most of the deaths in this group were associated with cardiovascular (e.g., heart failure) or infectious (e.g., pneumonia) causes. The FDA has stated that antipsychotic medications are not safe for treating elderly patients with dementia-related psychosis and requires that all manufacturers of antipsychotics issue warnings to this effect.

**RISK DURING PREGNANCY AND BREAST-FEEDING**

Risperidone has not been studied in human pregnancy to determine its safety, and its effect on delivery and labor is largely unknown. Risperidone and its metabolite cross the human placenta. In animal reproductive studies, risperidone was not associated with congenital abnormalities. Animal studies, however, are not always predictive of effects in humans. The safety of risperidone in pregnancy may be gleaned from the small number of cases reported in medical journals. In the women who were treated with risperidone during pregnancy, the babies were born without birth defects or complications from risperidone exposure.

Babies who were exposed to antipsychotic medications, including risperidone, during the third trimester of pregnancy are at risk of developing EPS and/or withdrawal symptoms following delivery. Symptoms include agitation, abnormal muscle tone, feeding difficulty, respiratory distress, somnolence, and tremors. In most cases, these symptoms eventually resolved without complications, although some babies may require supportive care and prolonged hospitalization. Risperidone should not be used during pregnancy unless the potential benefits outweigh the potential risk to the fetus. Women of childbearing age should be cautioned of the potential hazards to the fetus if they become pregnant while taking this drug.

Nursing mothers should not take risperidone because it passes into breast milk and can be ingested by the baby. If stopping the drug is not an alternative, breast-feeding should not be started or should be discontinued.

For more information on pregnancy exposure to atypical antipsychotics, contact the National Pregnancy Registry for Atypical Antipsychotics at 1–866–961–2388 or visit https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/ataypicalantipsychotic/.

**POTENTIAL DRUG INTERACTIONS**

Risperidone is metabolized in the liver to its active metabolite. Certain drugs may significantly inhibit this metabolism, increasing the blood levels of risperidone and the risk of adverse reactions. These include some antidepressants (e.g., fluoxetine, paroxetine, bupropion, duloxetine, sertraline), amiodarone, quinidine, and cimetidine, as well as other medications that can inhibit its metabolism. Conversely, some medications may speed up the metabolism of risperidone, decreasing blood levels and reducing the effectiveness of the drug (e.g., carbamazepine, rifampin, St. John’s wort).
OVERDOSE

In the reported cases of risperidone overdose, there were no known fatalities, even with ingestion of doses up to 360 mg. The frequent symptoms of acute overdose with risperidone include drowsiness, sedation, low blood pressure, EPS, and rapid heartbeat. In very severe cases, because of risperidone’s anticholinergic effects, acute overdose may potentially cause cardiac arrhythmias, delirium, coma, seizures, and death. The outcome depends on the amount ingested and whether risperidone was combined with other medications.

Any suspected overdose should be treated as an emergency. The person should be taken to the emergency department for observation and treatment. The prescription bottle of medication (and any other medication suspected in the overdose) should be brought along as well because the information on the prescription label can be helpful to the treating practitioner in determining the number of pills ingested.

The American Association of Poison Control Centers (www.aapcc.org) can also be contacted via their helpline at 1-800-222-1222, and they can provide the location of the local poison center.

TREATMENT SUMMARY

- Do not discontinue risperidone without consulting your practitioner.
- If you miss a dose, take it as soon as possible that day. If it is close to the next scheduled dose, skip the missed dose and continue on your regular dosing schedule. Do not take double doses.
- Risperidone may be taken with or without food.
- Avoid prolonged exposure to extreme heat, and drink adequate amounts of fluids to stay hydrated on hot days or with strenuous exercise.
- Risperidone may cause sedation and drowsiness, especially during initiation of therapy, and impair your alertness. Use caution when driving or performing tasks that require alertness. Avoid alcohol when taking risperidone because alcohol may intensify these effects.
- Be aware that risperidone can induce dizziness and light-headedness upon standing from a recumbent position, which may lead to orthostatic hypotension. This reaction is more prone to occur when starting the medication and in elderly patients. Rise slowly and allow your body to adjust to the change in position.
- If you experience rapid heart rate or irregular heartbeat, profuse sweating, stiffness or rigidity, spasms of the neck muscles, breathing difficulty, protrusion of the tongue, or tightness of the throat, seek immediate medical attention.
- Talk to your practitioner if you gain weight after starting risperidone. If you experience any signs of hyperglycemia or diabetes, such as excessive thirst or frequent urination, alert your practitioner as soon as possible.
- Store the medication in its originally labeled, light-resistant container, away from heat and moisture. Heat and moisture may precipitate breakdown of your medication, and the medication may lose its therapeutic effects.
- Keep your medication out of the reach of children.

If you have any questions about your medication, consult your medical practitioner or pharmacist.

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